Literature Review for the Revision of the New Zealand Smoking Cessation Guidelines

May 2007

This project was led by the Clinical Trials Research Unit, University of Auckland, in association with the Guidelines Development Team.

Published in June 2008 by the Ministry of Health
PO Box 5013, Wellington, New Zealand

ISBN: 9780-478-31750-3 (online)
HP 4578

This document is available on the Ministry of Health website:
http://www.moh.govt.nz
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Background to this review

Smoking is a major public health problem in New Zealand. About 23% of all New Zealanders are smokers. Smoking is twice as prevalent among Māori than among non-Māori. In addition to being directly linked to more than 4,000 deaths each year in New Zealand, smoking causes significant morbidity and contributes to ethnic inequalities in health.

Abundant evidence shows that stopping smoking is associated with health benefits.

The Ministry of Health allocates half the Tobacco Control budget to smoking cessation treatments. A variety of smoking cessation services exist, including telephone counselling, face-to-face support, and nicotine replacement therapy (NRT) through a subsidised scheme. Furthermore, these services are accessible to a wider number of people now than before the Tobacco Control Policy was implemented. Before the implementation of this policy smokers had a variable degree of access to cessation services provided by private organisations and non-government organisations.

The New Zealand Guidelines for Smoking Cessation, which were first published in 1999, then revised in 2002, have shaped smoking cessation training and treatment. Since 2002 new data on best practice and new pharmacotherapy and other treatments have become available.

Patterns of smoking are changing and evidence of the effectiveness of smoking cessation interventions for specific population groups is needed. It is, therefore, timely to evaluate new evidence and, where appropriate, to update practice and training. This document reviews current best evidence for what smoking cessation practices work, paying particular attention to specific population groups such as people who use mental health services, and considers more recent and ‘alternative’ cessation therapies.
Purpose of this review

The Ministry of Health contracted us to provide a literature review that accurately summarises the most recent best practice information and evidence in smoking cessation from New Zealand and overseas. This review provides the information and guidance on which to base the revision of the New Zealand Smoking Cessation Guidelines (2002 version).

Specifically, this review summarises the:

- evidence on smoking cessation for priority groups such as Māori, Pacific peoples, repeat quitters, people who use mental health services, young people, and pregnant women
- efficacy of alternative therapies for smoking cessation, including hypnotherapy, acupuncture, Allen Carr’s smoking cessation programme, Nicobrevin, and NicoBloc
- evidence on the use of NRT:
  - by people aged under 18
  - during pregnancy and breastfeeding
  - in combination with other treatments
  - to reduce cigarette consumption as a means of eventually quitting
- role of antidepressants and other non-nicotine treatments for smoking cessation.

Treatments were included in the review based on their popularity, the existence of reviewable literature, and their perceived promise. We included all three main treatment approaches commercially available within the United Kingdom (UK) (hypnosis, acupuncture, and Allen Carr’s Easy Way). We also included commercial medications and devices with at least some literature available on their effects (NicoBloc, Nicobrevin, and St John’s wort), pharmacological treatments not commercially disseminated in New Zealand but considered promising by experts in the field (cytisine and glucose), and the behavioural treatment with the largest volume of controlled trials that also has some evidence of efficacy (rapid smoking). Ideally, we would have reviewed a wider range of methods, but time constraints did not allow this.
Methodology of this review

Literature search

Key sources of data

The key sources of data were relevant systematic reviews published by the Cochrane Collaboration and a systematic review undertaken by the United States (US) Department of Health and Human Services, which informed the US treating tobacco use guidelines. These reviews are the latest and most comprehensive international systematic reviews. They cover the same topics as are covered in this review and are conducted to the highest standard.

The reviews assess studies that directly compare the intervention being examined with appropriate controls, rather than look at differences between studies. They use strict and relatively consistent inclusion criteria (eg, randomised controlled trials that report rates of at least six months’ abstinence), describe the included studies, and are regularly updated. In most cases, these reviews reach the same conclusions.

This approach has some disadvantages. The inclusion of the most recent literature depends on when the review was last updated, so it does not allow statements to be made about topics in papers that have not been submitted for systematic review. Meta-analyses indicate the overall effectiveness of a particular intervention, but some of the true effects of interventions may be masked because of the heterogeneity of study populations and the study’s design.

Therefore, we supplemented the major reviews with findings from other systematic reviews and randomised controlled trials. Only those published in English between the last New Zealand guidelines revision (February 2002) and March 2006 were considered. Unpublished data were also included where appropriate. Studies reporting non-randomised trials were included only when limited higher-level evidence was available. ‘Grey literature’ was not systematically searched.

Databases searched and search strategy

We searched seven databases:

- MEDLINE
- the Cochrane Database of Systematic Reviews
- the Cochrane Controlled Trials Register (CENTRAL)
- DARE
- AMED
- Embase
- PsycINFO.
Each search strategy combined intervention-specific terms with smoking-specific terms. For information about the search strategy, see Appendix 1.

**Selection of studies for inclusion**

Figure 1 shows the process for selecting reviews and trials for this review. The titles and abstracts of papers thus identified were downloaded into EndNote (bibliographic referencing software)™ then two reviewers screened them to assess their potential relevance to the review. Studies that did not primarily address smoking cessation or the specific intervention being assessed were excluded. Full papers of the relevant references were then obtained and further assessed. We excluded reviews if they were not conducted systematically. We excluded trials if they did not report the results of a randomised trial unless only non-randomised controlled trials were available on that particular topic. Other relevant publications were considered when no controlled trials were available.

**Figure 1: Process for selecting reviews and trials**

[Diagram of the selection process]

1. **First screen**
   - **Does the paper focus on the intervention as a smoking cessation treatment?**
     - Yes
     - **Is the paper a review?**
       - Yes
         - **Is the review conducted systematically?**
           - Yes
             - Include
           - No
             - Exclude
         - No
         - Exclude
       - No
         - **Is the paper a study?**
           - Yes
             - Exclude
           - No
             - **Is the paper a randomised controlled trial?**
               - Yes
                 - Include
               - No
                 - Exclude
             - **Are there any randomised controlled trials on this topic?**
               - Yes
                 - Consider
               - No
                 - Include

2. **Second screen**
Measurement of cessation outcome

The measurement of the smoking cessation outcome is important in clinical trials and clinical practice. The criteria by which the outcome is measured needs to be understood before the results of smoking cessation literature can be correctly interpreted. The following points should be considered.

Definition of smoking abstinence

Self-reported smoking status

The simplest way to assess abstinence is to ask smokers whether they have smoked (‘self-report’). This method is easy because it can be undertaken by telephone, by questionnaire, or over the internet. However, its accuracy relies on the client’s honesty. Rates of misreported smoking status vary, depending on the population treated (eg, people feeling under social pressure to quit such as pregnant women and teenagers may be more likely to misreport their smoking status than other people) and the intervention provided (eg, people developing a personal relationship with a counsellor may also feel more pressure to misreport their success).\(^5\)

Validated smoking status

To limit misreporting, smoking status should be verified.\(^5,6\) The most commonly used methods for verifying self-reported smoking status are shown in Table 1.
Table 1: Advantages and disadvantages of ‘gold standard’ methods of biochemical verification of self-reported smoking status

<table>
<thead>
<tr>
<th>Carbon monoxide (CO) in expired air</th>
<th>Cotinine (nicotine metabolite) (typically, measured in saliva, urine, or blood)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Advantages</strong></td>
</tr>
<tr>
<td>Simplest method of verification.</td>
<td>Has a longer half-life than carbon monoxide and nicotine, so can provide confirmation of smoking status over a longer period (up to seven days).</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
<tr>
<td>Has a short half-life (2–8 hours depending on the level of activity), so is capable of verifying abstinence only over the previous 24 hours.⁹</td>
<td>Half-life can differ across ethnic groups and in pregnancy the half-life is significantly reduced.¹¹</td>
</tr>
<tr>
<td>Good for verification in heavy smokers, but light smokers may never achieve CO readings greater than 10 parts per million (the typical cut-off point).</td>
<td>Biohazard risk and physical constraints of collection, carriage, and storage of potentially infectious specimens.</td>
</tr>
<tr>
<td>Not specific for tobacco smoke, so other sources of CO (eg, car exhausts) can confound results.</td>
<td>Blood or urine sample collection may be physically unpleasant or culturally unacceptable.</td>
</tr>
<tr>
<td>Expense of machine, consumables, and personal visit.</td>
<td>More expensive than CO monitoring (the cost of analysing a saliva sample for cotinine is approximately $45; and cotinine test strips are circa $14) as well as costs of personal visit.</td>
</tr>
</tbody>
</table>

**Common problem**
Face-to-face contact is needed to carry out validation. This is usually possible in clinical trials that involve contact with individuals, but in population-based studies or population monitoring of smoking activity this is not feasible.

Nicotine content in hair can also provide an accurate long-term indicator of exposure to tobacco smoke. Measurements of nicotine in body fluids assess exposure to smoke in the last day or so, whereas measurements using hair indicate exposure to smoke over weeks. Because hair grows at a regular rate (about 1 cm/month) a chronological picture of exposure can be determined; that is, the hair closest to the head can be used to quantify recent exposure.⁷ Significant differences in the mean content of nicotine in hair between smokers and non-smokers have been reported in the literature. Several small studies have used nicotine content in hair to validate the outcome of smoking cessation interventions, although this is uncommon.⁸

**Point prevalence compared with continuous abstinence**
Point prevalence abstinence is defined as not smoking at the point of follow-up. This is often given for a seven-day period before the follow-up point.
Continuous abstinence is defined as not smoking over the entire follow-up period. This might be from the target quit date or from a point that allows for a short grace period (i.e., not counting the first two weeks after the quit date).

These two abstinence measures are quite different and sometimes a significant result can be detected with one but not the other. The continuous abstinence rate more accurately reflects the effectiveness of the intervention being tested but has been criticized for not allowing for ‘slips’ (e.g., a one-off cigarette or a few puffs), which are common.

Standards for measuring smoking cessation outcome in research have been developed. The Russell Standard stipulates a follow-up six or 12 months from the target quit date or from the end of a predefined ‘grace period’; self-reported smoking abstinence over the whole period, allowing for up to five cigarettes smoked in total; and biochemical verification of abstinence at the end of follow-up. The Russell Standard also states that research studies should use an intention-to-treat analysis, that ‘protocol violators’ should be followed up and included in the analysis, and that follow-up should be undertaken without knowledge of the treatment allocation.

Duration of abstinence

In general, the longer the period of follow-up, the more likely this is to reflect a permanent remission from smoking. Most experts suggest a minimum of six months from the target quit date (i.e., the pre-selected day by which the smoker aims to stop smoking whether the smoker quits on this day or not), although many studies report 12-month outcomes as well. Follow-up periods of less than six months are less robust than longer periods in predicting long-term sustained cessation.

Quality appraisal and level of evidence

Additional systematic reviews and studies not already included in the Cochrane reviews were evaluated by assessing the methods used in relation to the research question(s) being addressed, then assessing their methodological rigour and quality against criteria using the critical appraisal checklists of the UK National Institute for Health and Clinical Excellence.

Each study was then graded using a code ‘++’, ‘+’, or ‘–’, based on the extent to which the potential sources of bias had been minimized (see Table 2).
**Table 2: Description of the codes used to grade each study**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>++</td>
<td>All or most of the criteria have been fulfilled. When criteria have not been fulfilled, the conclusions of the study or review are thought very unlikely to alter.</td>
</tr>
<tr>
<td>+</td>
<td>Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions.</td>
</tr>
<tr>
<td>–</td>
<td>Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.</td>
</tr>
</tbody>
</table>


The level of evidence was classified according to NICE guidelines (see Table 3).

**Table 3: Levels of evidence**

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

* Studies with a level of evidence of ‘–’ should not be used as a basis for making a recommendation (see section 7.4 in the source document for this table).

Statistical evaluation

Undertaking meta-analyses
As our primary source of data comes from Cochrane systematic reviews that undertake meta-analyses, it was not necessary to perform our own statistical assessment. However, when no Cochrane review existed and data from randomised controlled trials were available and appropriate, we undertook our own meta-analyses by extracting data from the included studies and entering them into the RevMan software programme. We calculated a pooled odds ratio using a fixed effects model, except when there was significant heterogeneity, in which case we used a random effects model.

Reporting results
Studies generally report quit rates (eg, 20% of participants had stopped smoking at six months) in the groups described. When a group using the intervention is being compared with a control group, the odds ratio (OR) is often used to show the size of the effect of the intervention.

The odds ratio is the odds of success in the intervention group compared with those in a control group (see Table 4). An odds ratio greater than 1 indicates that the odds of quitting smoking are greater in the intervention group than in the control group. An odds ratio less than 1 indicates that the odds of quitting are less in the intervention group than in the control group. Odds ratios are reported with a 95% confidence interval, a range of feasible values within which the true effect may lie. If the confidence interval around an odds ratio includes 1, then the effect of the intervention is not significantly different from the comparison treatment.

Table 4: Calculating odds ratios

<table>
<thead>
<tr>
<th></th>
<th>Abstinent</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention group</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Control group</td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

Odds of quitting in the intervention group = A/B
Odds of quitting in the control group = C/D
Odds ratio = (odds of quitting in the intervention group)/(odds of quitting in the control group) = (A/B)/(C/D) = (AD)/(BC)

Another way to assess the effect of an intervention is to use the risk difference, which is the difference in outcome (or risk) between two groups (ie, the risk in one group minus the risk in the other). For example, if an intervention helps 20% of smokers remain abstinent for a year compared with the 10% who remain abstinent in the control group, then the risk difference is:

20% − 10% = 10%
The number needed to treat (NNT) indicates how many people need to be treated for every one person who stops smoking. The number needed to treat is the inverse of the risk difference:

\[ \text{NNT} = \frac{1}{\text{risk difference}}. \]

For example, if the risk difference of brief advice from a physician is 2.5% then:

\[ \text{NNT} = \frac{1}{0.025} = 40 \]

This means that for every 40 people who receive brief advice to stop smoking one will stop smoking.

**Synthesis of evidence statements**

To summarise the findings of each treatment the wording along the lines of the following evidence statements are used.\(^{10}\)

- There is robust evidence from randomised controlled trials that ‘intervention X’ improves/does not improve six-month continuous abstinence rates.
- There is evidence from one randomised controlled trial that ‘intervention X’ improves/does not improve six-month continuous abstinence rates.
- There is insufficient evidence concerning whether ‘intervention X’ improves six-month continuous abstinence rates but evidence from short-term studies or studies with no biochemical verification suggests that definitive trials are warranted.
- There is mixed or inconsistent evidence on whether ‘intervention X’ improves six-month continuous abstinence rates.
- There is insufficient evidence on ‘intervention X’ to draw any conclusions.
Brief advice to stop smoking from healthcare professionals

Brief advice from general practitioners

Advice to quit smoking from a doctor has a small, but important, effect. The most recent Cochrane review of advice identified 17 studies that compared a group who received brief or minimal advice with a control group.\textsuperscript{11}

Brief advice was defined as verbal advice to stop smoking from a physician delivered with or without information regarding the harmful effects of smoking.

Pooling 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: 2.0%, 3.0%) and a number needed to treat of 40.

The effect of brief advice appears primarily to be triggering the person to make a quit attempt rather than increasing the chances of success of quit attempts.\textsuperscript{12} Direct comparisons of higher intensity compared with lower intensity advice show little difference in outcome (OR=1.24; 95% CI: 1.02, 1.50). Those studies that included more than one session had greater abstinence rates (OR=2.55; 95% CI: 2.04, 3.19) compared with those where brief advice was delivered in a single session (OR=1.63; 95% CI: 1.39, 1.91). However, studies that directly compared the effect of a single session with that of additional sessions showed only a small benefit (OR=1.61; 95% CI: 1.10, 2.37).

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. One study found no advantage of motivational counselling over standard brief advice.\textsuperscript{13}

An assessment of the stage of change is unnecessary because advice should be provided to all smokers irrespective of whether they want to stop smoking or not.

Despite the proven efficacy of giving brief advice, many general practitioners (GPs) do not advise their patients who smoke to quit smoking. Several studies have tried to assess the barriers to providing this advice that face GPs. The reasons range from not wanting to damage the doctor–patient relationship, having a lack of knowledge about how to provide advice and help to patients, and having a belief that their advice is ineffective.\textsuperscript{14–17}

**Summary:** All physicians should provide brief advice to quit smoking to all their patients who smoke. An assessment of the stage of change is unnecessary because advice should be provided to all 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. Physicians would be better to provide more advice to more smokers.

**Strength of evidence:** 1++
Evidence statement: There is robust evidence from randomised controlled trials that brief advice to stop smoking from a doctor improves six-month abstinence rates.

Brief advice from other healthcare workers

The evidence for the effectiveness of brief advice delivered by healthcare workers other than GPs is less clear.\textsuperscript{18–20} However, there is no reason to expect that advice from dentists, dental hygienists, nurses, pharmacists and other health care professionals would not have some benefit. Given the relatively small amount of time and skill required to deliver brief advice, all healthcare workers should provide it.
Written self-help materials

Most smokers try to stop smoking on their own at some time, and providing materials to further assist these unaided quit attempts is a logical step. 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.21

Self-help materials may have a greater effect on cessation than no intervention has. The Cochrane review22 identified 60 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 enable personalised advice to smokers in a way that traditional written materials do not.23 Seventeen studies examined the efficacy of self-help materials compared with ‘no treatment’ in nearly 20,000 smokers. No study included face-to-face support for smokers.

Pooling the results showed a small but significant benefit of self-help materials (OR=1.33; 95% CI: 1.18, 1.51) with a risk difference of 2% (1–2%). Using self-help materials in addition to brief advice showed no additional benefit. When the results of all studies examining written materials (with or without face-to-face contact) are pooled, the overall effectiveness of written materials is marginal (OR=1.11; 95% CI: 1.00, 1.22), increasing long-term quit rates by only 1% (95% CI: 0%, 1.0%). There is no evidence to support adding self-help materials to NRT.

Tailoring self-help materials does seem to make a difference in outcome. Tailored materials compared with no materials increases long-term quit rates (OR=1.38; 95% CI: 1.15, 1.66). Furthermore, tailored materials appear to be better than non-tailored materials at promoting abstinence, although the effect size is relatively small (OR=1.50; 95% CI: 1.12, 2.02. RD=2.0%; 95% CI: 0%, 3.0%). A more recent study not included in the Cochrane review supports these findings.24

Some internet-based interventions have reported greater differences between intervention and control groups (eg, 23% compared with 18% 12-week continuous abstinence rates),23 but there is lack of long-term (six 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; that is, to assist ‘cold turkey’ quit attempts. Adding self-help materials to other interventions does not appear to increase the effectiveness of those interventions. Tailored self-help materials are likely to be more effective than non-tailored materials. It is important to note that these materials are self-help aids, not teaching aids to be used by smoking cessation providers.

Strength of evidence: 1++
Evidence statement: There is robust evidence from randomised controlled trials that self-help materials make a small improvement in six-month continuous abstinence rates.
Cessation support

This review uses the term 'cessation support' to describe all behavioural and pharmacological treatments for aiding smoking cessation. In some instances, the term ‘counselling’ is used, mainly where this refers to the findings of a particular study or systematic review.

The provision of behavioural or psychosocial interventions to smokers during a quit attempt is an important component of any smoking cessation treatment. Behavioural support refers to all cessation assistance that imparts knowledge about smoking and quitting, provides support, and teaches skills and strategies for changing behaviour. Different methods have been used but there are few data comparing the efficacy of these different approaches, so no recommendations can be made on programme content (see Table 5). However, successful interventions have two common elements: a quit date and multi-session behavioural support.

Table 5: Efficacy of and estimated abstinence rates for various counselling and behavioural therapies (n=62 studies)

<table>
<thead>
<tr>
<th>Type of counselling and behavioural therapy</th>
<th>Estimated odds ratio (95% CI)</th>
<th>Estimated abstinence rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No counselling/behavioural therapy</td>
<td>1.0</td>
<td>11.2</td>
</tr>
<tr>
<td>Relaxation/breathing</td>
<td>1.0 (0.7, 1.3)</td>
<td>10.8 (7.9, 13.8)</td>
</tr>
<tr>
<td>Contingency contracting</td>
<td>1.0 (0.7, 1.4)</td>
<td>11.2 (7.8, 14.6)</td>
</tr>
<tr>
<td>Weight/diet</td>
<td>1.0 (0.8, 1.3)</td>
<td>11.2 (8.5, 14.0)</td>
</tr>
<tr>
<td>Cigarette fading</td>
<td>1.1 (0.8, 1.5)</td>
<td>11.8 (8.4, 15.3)</td>
</tr>
<tr>
<td>Negative affect</td>
<td>1.2 (0.8, 1.9)</td>
<td>13.6 (8.7, 18.5)</td>
</tr>
<tr>
<td>Intra-treatment social support</td>
<td>1.3 (1.1, 1.6)</td>
<td>14.4 (12.3, 16.5)</td>
</tr>
<tr>
<td>Extra-treatment social support</td>
<td>1.5 (1.1, 2.1)</td>
<td>16.2 (11.8, 20.6)</td>
</tr>
<tr>
<td>General problem solving</td>
<td>1.5 (1.3, 1.8)</td>
<td>16.2 (14.0, 18.5)</td>
</tr>
</tbody>
</table>


Treatment choice can vary depending on the practitioners’ and smokers’ beliefs about smoking. For example, proponents of the biopsychosocial model try to combine treatment modalities that address the biological (physical nicotine dependency), the psychological (through cognitive behavioural therapy), and the social (looking at and trying to change the environmental triggers to smoke). Some approaches focus on motivation and use educational principles.

Cessation support often includes getting smokers to recognise dangerous situations that lead to relapse (eg, being around other smokers, getting drunk, having a 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 withdrawal symptoms, the risk of a single puff, and tobacco dependence. Other techniques that enhance social support may also
be implemented. Clinicians also use techniques to maintain morale and motivation throughout the early stages of the quit attempt. Although little evidence supports relapse prevention strategies the offer of ongoing support is usually well received by the smoker. Support of this nature may take place in the form of ongoing telephone contact, letters of support, group meetings, and so on.

One aspect that is often overlooked is a spiritual component. Some religions, such as the Church of Jesus Christ of Latter-Day Saints (the Mormon Church) and the Seventh-Day Adventist Church, have long been providers of smoking cessation programmes. When appropriate, faith, prayer, and the use of traditional medicinal practices can be included in the mix of treatment provided.

There is correlational evidence that more-intensive support (eg, more time spent with smokers) is associated with higher abstinence rates. However, the confidence intervals overlap, so no clear distinction can be made. The few studies that have directly compared high- and low-intensity support have not demonstrated a difference in outcomes. However, the authors of the US guidelines undertook a subgroup analysis by the number of treatment sessions provided. This showed that those interventions that provided more than eight sessions were more effective (OR=2.3; 95% CI: 2.1, 3.0) than those that provided no or one session (which was the reference group), but also more effective than those that provided two or three sessions (OR=1.4; 95% CI: 1.1, 1.7) compared with the reference group. The results for the interventions using more than eight sessions and those delivering treatment in four or more sessions overlapped.

Based on the evidence reviewed, the US guidelines made the following recommendations (USDHHS, *Treating Tobacco Use and Dependence*, Rockville, MD: United States Department of Health and Human Services, Agency for Healthcare Research Quality, 2000 page 57).

- Minimal interventions of up to three minutes (ie, brief advice) increase overall quit rates, so should be offered to every smoker regardless of whether they want to quit and regardless of whether they are referred on to specialist stop smoking services.
- There is a dose-dependent relationship between the intensity of the treatment provided and smoking cessation. Therefore, more-intensive treatments should be recommended wherever possible.
- Services should aim to see smokers at four or more sessions.
Telephone support

Telephone support is an effective method for smoking cessation. Telephone support is a cost-effective approach that has the potential to reach more people than face-to-face interventions. Evidence suggests that some smokers prefer telephone support to face-to-face support.27 There is also evidence that telephone quitlines provide a service for smokers who may not be reached by other smoking cessation services.28 Telephone support 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; proactive telephone support (eg, that offered by a quitline) involves the counsellor initiating 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 (ie, in the first few days and weeks of a quit attempt). Telephone support usually focuses on boosting motivation to make a quit attempt, reinforcing the ‘not-even-one-puff’ message, advising on withdrawal symptoms and medication use, and answering questions.

The Cochrane review of telephone counselling for smoking cessation included 27 randomised controlled trials that measured abstinence rates for at least six months following the commencement of treatment.29 The most common delivery format was three calls over three months. This is similar to that of the New Zealand Quitline. The support was typically scripted and often based on the stage of change or general motivational approaches.

Thirteen studies compared the effectiveness of telephone support in addition to minimal intervention (eg, self-help materials) with minimal intervention only. However, an odds ratio of the pooled results was not undertaken because of the significant heterogeneity among the studies. To correct this, the authors reassessed the data and used all the groups without telephone support or intensive support as controls for each study. This removed the heterogeneity and showed a significant benefit of telephone support (OR=1.56; 95% CI: 1.38, 1.77). These results are reflected in another recently published meta-analysis.30

A randomised controlled trial undertaken in the UK failed to show an effect of proactive telephone support compared with usual care on six-month abstinence rates (9.3% compared with 9.5%, non significant difference).31 One reason cited by the authors for this lack of effect is a non-structured support protocol and client-led support. Compared with other trials of a similar nature clients were not allocated to a single counsellor, so there was no continuity of care. This may be an important factor in the outcome, although no studies look directly at this comparison.

Use of telephone support in specific groups

There is some evidence from one study that an enhanced telephone support service that provides personalised advice (eg, advice tailored to the client’s potential barriers to success) may be better for men than for women.33
One randomised controlled trial specifically investigated the effectiveness of telephone support in young adults (aged 18–25) and demonstrated that telephone support produced higher six-month (two-day self-report point prevalence) abstinence rates than did written self-help materials (9% compared with 2%, p<0.005). However, this study reports only two-day point prevalence and had a high number of participants who were lost to follow-up.

Telephone support has been shown to be superior to standard care in a primary care setting. Those patients who received telephone support (seven calls over two months) compared with those randomised to standard care (self-help materials) were more likely to be abstinent for six months at 12 months after randomisation (self-reported).

Finally, a study trial of women with a recent abnormal cervical smear who were randomly allocated to a tailored telephone support programme (up to four brief motivational calls (ie, less than 15 minutes), over six months) or usual care. Those receiving the calls were more likely to report being abstinent (seven-day point prevalence) at six months than those in the control group (20% compared with 12%, p<0.05), although this difference was lost at 12 months.

**Combined telephone and face-to-face support**

Adding telephone support to face-to-face support to further increase the chances of continued abstinence is a seemingly logical approach. However, no evidence supports this approach.

Despite this lack of evidence, there are situations where proactive telephone support is indicated. When the intensity of face-to-face support is low, for example, a single session for hospital inpatients, additional follow-up telephone support has been shown to have a positive effect (eg, Miller et al 1997). This may be a practical approach to take in other situations when smokers cannot attend more than a single face-to-face support session, although it is worth noting that a single call after hospital discharge is unlikely to be effective, and a series of support calls will be required.

**Adding telephone support to pharmacotherapy**

We identified two recent randomised controlled trials that investigated the benefit of adding telephone support to pharmacotherapy. Only one reported six-month abstinence rates (self-reported continuous abstinence over the past 28 days), and demonstrated that adding telephone support (five sessions) to NRT increased abstinence rates compared with using NRT alone (30% compared with 22%, p=0.01). The other reported only the three-month outcome (self-reported seven-day point prevalence), but showed higher abstinence rates in the group that received telephone support in addition to NRT or bupropion (33%) compared with the group that received medication only (27%) (OR=1.31; 95% CI: 1.01, 1.71).
Telephone follow-ups to treatment

No evidence suggests that telephone support following intensive treatment reduces relapse rates. However, ongoing telephone contact may reduce the number of people who are lost to follow-up when the smoking cessation outcome is measured (usually at six or 12 months) and can identify clients who have relapsed. These clients can then be supported in making another quit attempt.

Reactive telephone support

Reactive telephone support, which includes helplines, has not been so rigorously evaluated as proactive telephone support. This is partly due to methodological difficulties in doing this (e.g., a control group would have to be refused help). However, indirect evidence suggests helplines may be helpful.

Summary: Proactive telephone support for smoking cessation increases long-term abstinence rates. There is no evidence of an advantage of adding telephone support to face-to-face support. However, in some situations telephone support in addition to face-to-face support may be indicated.

Strength of evidence: 1++

Evidence statements:

• There is robust evidence from randomised controlled trials that proactive telephone smoking cessation support improves six-month abstinence rates.
• There is inconsistent evidence on whether adding telephone support to face-to-face support improves six-month abstinence rates.
• There is insufficient evidence on reactive telephone helplines to draw any conclusions.
Face-to-face support

About 1 in 20 people who would not otherwise have stopped smoking will do so for at least six months after receiving face-to-face support. Support can be provided to an individual or in a group-based setting. These formats are discussed below.

Individual support

The Cochrane review considered the efficacy of smoking cessation behavioural support delivered to smokers on an individual or a one-to-one basis. This included the results of randomised controlled trials that investigated the efficacy of support delivered by a trained counsellor to a smoker. The term counselling was broadly defined as time spent in contact with the smoker rather than specific counselling techniques. Also, to avoid confusion with other interventions this review included only unconfounded interventions. Twenty-one studies, involving some 7,000 smokers, were included. Interventions differed by level of intensity, counselling method, study population, and intervention component. Support interventions typically included taking a smoking history, motivating a person to quit, identifying high-risk situations, and teaching problem-solving strategies for dealing with typical and difficult situations. The professional background of the counsellors also varied.

When the results of the 17 studies investigating the effects of minimal support compared with the no treatment (minimal contact) control are pooled there is a clear benefit from behavioural support (OR=1.56; 95% CI: 1.32, 1.84). Most of the studies were conducted with hospitalised smokers, although there is evidence that behavioural support is effective in other settings such as in workplaces and the general community. Absolute quit rates varied and were generally higher when pharmacotherapy was used in addition to counselling. As one would expect, absolute quit rates were lower when pharmacotherapy was delivered to groups that are typically more dependent and harder to treat. Only three studies compared less-intensive with more-intensive support. The pooled results of these studies showed no additional benefit from intensive support. There is also no evidence for a difference in the effectiveness of different counselling approaches.

The conclusion drawn from the meta-analysis is that the evidence is clear and consistent that individual behavioural support increases smoking cessation rates more than minimal support does. These findings are similar to those of the meta-analysis undertaken for the US guidelines. This showed that individual behavioural support was more effective than no intervention (OR=1.7; 95% CI: 1.4, 2.0). The support interventions included in this review generally included multi-session treatment (face to face and/or by telephone).
Summary: Smoking cessation support delivered on a one-to-one basis by smoking cessation counsellors increases the chance of smokers stopping smoking for at least six months. There is no evidence that more-intensive interventions are better than less-intensive interventions. However, all interventions involved sessions of more than 10 minutes and many included additional follow-up sessions, so there may not have been enough difference in intensity to show an effect.

Strength of evidence: 1++

Evidence statement: There is robust evidence from randomised controlled trials that individual counselling improves six-month abstinence rates.

Group-based support

Group-based support has frequently been used in smoking cessation programmes. While some stop smoking services use group-based support as their main treatment method, others find it difficult to recruit smokers to groups. When given a choice between individual or group-based treatment most smokers generally opt for individual treatment. However, this is often because of preconceived ideas of what ‘group therapy’ involves. Generally, group treatment sessions for smoking cessation focus on smoking and smoking cessation and do not cross boundaries into other psychological areas.

Group-based treatments for smoking cessation are described in more detail elsewhere, but in summary two main approaches can be used for group-based treatments. One approach is therapist oriented, which is a didactic approach where the group facilitator provides information on how to achieve and maintain abstinence. The other approach is group oriented and focuses on a group process whereby the members of the group provide support and advice to each other.

One of the main advantages of treating smokers in groups is the cost-effectiveness of such an approach. 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 who have limited time and when there is a high demand from smokers wanting help in stopping. Where therapists treat large numbers of smokers, individual treatment can become repetitive to the therapist and treatment ‘failures’ can knock the therapists confidence. Groups, on the other hand, generate substantial interest and enthusiasm and the focus is always on those clients maintaining abstinence and not those who continue to smoke.

The Cochrane review considered the efficacy of group-based behavioural support for smoking cessation. A total of 55 studies met the inclusion criteria (ie, randomised controlled trials investigating the efficacy of group-based treatments that measured an at least six-month smoking cessation outcome). There were several different types of group programme. Most interventions contained an element of cognitive behavioural therapy, but also included skills training, mood management, and the manipulation of group dynamics (eg,
social support, a didactic format, self-control, nicotine fading, and altering smoking behaviour before the quit date).

The main comparison between group and self-help programmes included data from about 4,000 participants from 13 studies. The meta-analysis showed the superiority of group-based interventions over self-help in achieving at least six months of abstinence (OR=2.64; 95% CI: 1.89, 3.69). Group-based interventions were also more effective than no intervention (OR=2.17; 95% CI: 1.37, 3.45).

There is no evidence that specific components of treatment are better than others. However, more complex interventions seem to provide a small increase in abstinence rates compared with more simple group-based treatments (OR=1.36; 95% CI: 1.03, 1.79).

The review found no difference in the efficacy of group smoking cessation treatments compared with individual smoking cessation treatments (OR=0.86; 95% CI: 0.66, 1.12). Data from the UK National Health Service Stop Smoking Services suggest that group treatment produces higher success rates than individual treatments. However, these data are not from randomised controlled trials, and the results could be explained by differences in counsellors (eg, those counsellors that run group-based treatment may be more experienced) or in the populations treated.

No data regarding cost-effectiveness of group-based treatment was identified from the included studies.

The conclusion drawn from the meta-analysis is that evidence is clear and consistent that group-based smoking cessation treatment increases smoking cessation rates compared with self-help or no treatment. The meta-analysis undertaken for the US guidelines comes to similar conclusions, where the odds ratio for group-based treatment compared with no treatment, was found to be 1.3 (95% CI: 1.1, 1.6). It is difficult to conclude which elements of group-based treatment are important to provide. However, elements such as problem solving and social support are likely to be useful. No evidence shows that relaxation exercises, nicotine/cigarette fading, or mood management are particularly beneficial. There is no evidence that group-based treatments are better or worse than treatments provided on an individual basis.

Summary: Group-based smoking cessation treatment is effective in increasing the chances of smokers stopping for at least six months compared with 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.

Strength of evidence: 1++
Evidence statements:

- There is robust evidence from randomised controlled trials that group-based smoking cessation treatment improves six-month continuous abstinence rates.
- There is insufficient evidence of the comparative efficacy of group compared with individual smoking cessation treatments.
- There is insufficient evidence to draw definitive conclusions about the cost-effectiveness of group-based treatments compared with individual treatments. However, if treatments produce similar outcomes, it is logical to assume that group-based treatments are likely to be more cost-effective.

Provision of smoking cessation support by different healthcare professionals

The US guidelines identified 29 studies that compared the effectiveness of interventions delivered by various types of clinician. There were 39 groups where the intervention was delivered by a clinician who was not a physician (eg, a nurse, dentist, dental hygienist, or pharmacist). Data from these groups were entered into a meta-analysis, which 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 recommended that, “Treatment delivered by a variety of clinician types increases abstinence rates. Therefore, all clinicians should provide smoking cessation interventions”.

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 have halitosis, stained teeth, and problems of altered taste than non-smokers. Tobacco use is of direct relevance to many dental treatments and surgery. The benefits of stopping smoking can contribute to better outcomes.

Many smokers come into contact with their dentist on a regular basis. Dentists and dental hygienists and therapists, as well as reception and administrative staff are in an ideal position to provide advice to stop smoking, and may be able to provide smoking cessation treatment. However, for many dentists, providing brief advice to stop smoking has not become part of their normal routine.

Only a small number of published studies examine the long-term efficacy of interventions provided by dentists, and most of these focus on the cessation of oral tobacco. Interventions range from identifying tobacco users within the practice and providing brief advice to quit to providing more-intensive cessation-based interventions. The Cochrane review pooled the results of six studies that show that interventions provided within the dental setting are effective in aiding the cessation of tobacco use (OR=1.67; 95% CI: 1.09, 2.57). Only one of
these studies tested an intervention aimed at cigarette smokers and this failed to show a significant benefit.\textsuperscript{48}

These results suggest that dentists and allied dental 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.

The review identified three limitations: (1) publication bias could not be discounted; (2) problems with making sure participants and investigators did not know what the treatment allocation was; and (3) significant heterogeneity between studies.

**Summary:** There is insufficient evidence regarding the provision smoking cessation interventions delivered by dentists and associated dental staff. However, there is no reason to believe that evidence-based support from a dentist or allied dental staff would not help smokers to stop.

**Strength of evidence:** 1+

**Evidence statement:** There is insufficient evidence on brief advice to stop smoking from a dentist to draw any conclusions.

**Nurses**

Patients often have greater contact time with nurses than with doctors 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 to provide more-intensive smoking cessation interventions than doctors can provide.

The Cochrane review on nursing interventions for smoking cessation sought to examine the effectiveness of these interventions.\textsuperscript{19} Results are also reported in another systematic review by the same lead authors.\textsuperscript{49} Interventions by nurses were defined as the provision of advice or counselling to help smokers stop. Advice to stop was defined in a similar way to physician interventions, that is, a verbal instruction to stop smoking with or without the provision of information about the adverse health effects of smoking. Interventions were also considered by their degree of intensity. Advice given as part of a single consultation lasting no more than 10 minutes and with no or one follow-up visit was classified as low-intensity support. High-intensity support included interventions where the initial contact lasted more than 10 minutes and included more than one follow-up contact.

A total of 29 randomised controlled trials met the inclusion criteria. Twenty studies investigated the effectiveness of smoking cessation advice from a nurse compared with no intervention. Significant heterogeneity among the studies was apparent, so these data were analysed using a random effects model. This produced an odds ratio of 1.59 (95% CI: 1.22, 1.67) for abstinence at the longest follow-up (at least six months). Subgroup analysis by intensity showed
the superiority of higher-intensity interventions (OR=1.52; 95% CI: 1.30, 1.78) compared with 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 caution, because of the marked heterogeneity among the studies.

The authors concluded that interventions delivered by nurses have the potential to help smokers stop. However, when interventions are of low intensity the effectiveness is reduced.

**Summary:** Smoking cessation interventions delivered by nurses can be effective, especially when the intervention is of a higher intensity. The best interventions are multi-sessional with follow-up support.

**Strength of evidence:** 1+

**Evidence statement:** There is evidence from randomised controlled trials that smoking cessation interventions of higher intensity provided by nurses improve six-month continuous abstinence rates.

**Pharmacists**

Community pharmacists are freely accessible to most communities, and visitors to community pharmacies tend to be both well and ill, providing the opportunity for both preventive advice and treatment to be provided. Community pharmacists usually stock the full range of NRTs and will dispense smoking cessation medications that require prescription. An example of the role pharmacists can play is 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 this role.44

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 a patient’s medication history, so they are required to interact with most inpatients. This means 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.50

A small number of trials aimed 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 identified 14 studies, two of which met the inclusion criteria.20 The majority of studies were excluded because they lacked a control group. The two included studies are described below.
McGuire trained 124 community pharmacists in a three-hour workshop on smoking cessation that included information on smoking statistics, NRT, the Stages of Change Model, and a structured counselling programme. These pharmacists recruited 484 smokers and randomised them to receive either the smoking cessation intervention or usual care (the control group). The results showed higher 12-month self-reported continuous abstinence rates in the intervention group compared with the control group (14.3% compared with 2.7%; OR=5.94; 95% CI: 2.46, 4.34). Sinclair randomised 62 community pharmacies in rural Scotland. Staff in intervention pharmacies received a two-hour training workshop that focused on the stages of change and communications skills for prompting behaviour change. A total of 492 smokers were recruited, and at nine months 12% compared with 7% in the control group claimed a one-month point prevalence abstinence (OR=1.71; 95% CI: 0.92, 3.17).

There is significant heterogeneity in these studies, so the pooled effect was calculated using a random effects model. This showed a non-significant result (OR= 3.06; 95% CI: 0.86, 10.55).

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. 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 would be useful.

**Summary:** Only two well-conducted randomised controlled trials assess the efficacy of pharmacy-led smoking cessation interventions compared with standard care. The confidence interval surrounding the pooled results does not rule out an effect, and it is likely that interventions delivered by pharmacists that follow evidence-based smoking cessation practice will be effective. However, no clear recommendations can be made on the basis on the current evidence.

**Strength of evidence:** 1+

**Evidence statement:** There is mixed evidence on whether interventions provided by community pharmacists and their staff improve 6-month continuous abstinence rates.

**Training healthcare professionals**

A potential way to help more smokers to stop is to train healthcare professionals in smoking cessation. A Cochrane review identified 10 randomised controlled trials that investigated the effect of training healthcare professionals in smoking cessation on long-term (at least six months) abstinence. The majority of studies compared the outcome in groups that had received training with those that had not. The training content varied, but focused on general advice such as setting a quit date, and follow-up sessions. Some included training on pharmacotherapies. Three studies were based on the Stages of Change
Model. The length of the training sessions varied between one hour and one day.

The conclusions drawn were that training healthcare professionals to provide a smoking cessation intervention increased the likelihood of them intervening (1.5–2.5 times more likely than the control group), for example getting them to ask smokers to set a quit day, offering NRT, and so on. Using prompts and reminders increased the frequency of the intervention. However, there was no conclusive evidence that training led to higher quit rates. If there is an increase then it is likely to be small.

**Summary:** Training healthcare professionals in smoking cessation does not translate into higher long-term quit rates but healthcare professionals do provide more advice to quit. The corollary of this is that if healthcare professionals are to receive training this should be concise and incorporate interventions that are known to work, such as brief advice and pharmacotherapy, plus referral to services that can provide multi-session behavioural support and medication. Before investing resources in training however, systems (such as documentation and referral systems and available intensive services) need to be in place that will support any intervention being taught.

**Strength of evidence:** 1+

**Evidence statement:** There is insufficient evidence from randomised controlled trials that training healthcare professionals specifically in smoking cessation practices improves six-month abstinence rates.
Pharmacotherapies

Nicotine replacement therapy

NRT has been used to help smokers stop for more than 20 years. It is safe and effective, and the most widely used and available proven treatment. 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, so the quitting attempt is more likely to succeed.\textsuperscript{54}

Nicotine chewing gum was the first NRT product developed. The nicotine in the gum base is released during chewing and absorbed through the buccal mucosa (the inner lining of the cheeks and lips).

Six NRT products are available and more are being developed.

All NRT products provide less nicotine than the average smoker obtains from smoking, and nicotine plasma concentrations are typically half that achieved from smoking. The time to reach peak plasma concentration is longer than with cigarette smoking.

Efficacy of nicotine replacement therapy

NRT is not a ‘magic bullet’, but, unquestionably, it aids quit attempts and makes a successful outcome more likely. The Cochrane review on NRT for smoking cessation identifies 105 randomised controlled trials that assessed the efficacy of NRT, together involving about 40,000 smokers.\textsuperscript{54} These studies met strict criteria such as at least six months’ follow-up and used a biochemical method to verify self-reported abstinence. Most examined the efficacy of nicotine gum or the nicotine patch. A few studies failed to demonstrate the clear effectiveness of active treatment compared with placebo treatment. Some studies had small sample sizes and insufficient statistical power to detect whether a difference in outcome existed. Nevertheless, the meta-analysis showed that the odds of successfully quitting for at least six months using NRT were significantly greater than for using a placebo (OR=1.77; 95\% CI: 1.66, 1.88). The long-term abstinence rate achieved in the NRT group was 17\% compared with 10\% in the control group. NRT is effective in men and women.\textsuperscript{55} About 1 in 14 people who would not otherwise have stopped smoking will do so for at least six months after completing a course of NRT.

Most of the randomised controlled trials have examined the use of NRT in dependent smokers of more than 10 cigarettes per day. NRT does not appear to be more effective than a placebo in light smokers.\textsuperscript{54} One study of a nicotine lozenge did find it effective in light smokers, who were defined as smoking 15 or fewer cigarettes per day.\textsuperscript{56} Others have not demonstrated a greater effectiveness of NRT over a placebo in light smokers.\textsuperscript{57} However, these findings must be considered with caution when treating smokers who have recently cut down. New Zealand has had a changing smoking pattern and research may not be representative of these patterns.
In a recent systematic review the authors conducted a meta-analysis of NRT trials that reported a one-year follow-up. The pooled results of 70 studies showed that NRT was more effective than control conditions in assisting long-term abstinence (OR=1.71; 95% CI: 1.55, 1.88).\textsuperscript{58} The results remained the same when only those studies (n=52) that reported a sustained one-year abstinence were included.

The odds ratio for each product varies, but overlapping 95% confidence intervals suggest no superiority of any one product over another (see Table 6). In a study comparing the efficacy of four different products (patch, gum, nasal spray, and inhaler) Hajek et al found no difference between them.\textsuperscript{59}

There is a clear advantage in using 4 mg nicotine gum compared with 2 mg gum in highly dependent smokers. A similar dose response has been demonstrated with the nicotine lozenge and nasal spray. Absolute abstinence rates typically remain lower in highly dependent smokers than in less dependent smokers. In the gum studies, highly dependent smokers were defined by measures of smoking behaviour (pattern, level of dependence, and feelings of dependence) whereas Shiffman et al defined a highly dependent smoker as a person who smokes their first cigarette of the day within 30 minutes of waking.\textsuperscript{60}

Table 6: Long-term effectiveness of nicotine products relative to placebo

<table>
<thead>
<tr>
<th>Nicotine product</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gum</td>
<td>1.66</td>
<td>1.51, 1.81</td>
</tr>
<tr>
<td>Patch</td>
<td>1.84</td>
<td>1.65, 2.06</td>
</tr>
<tr>
<td>Nasal spray</td>
<td>2.35</td>
<td>1.63, 3.38</td>
</tr>
<tr>
<td>Inhaler</td>
<td>2.14</td>
<td>1.44, 3.18</td>
</tr>
<tr>
<td>Sublingual tablet or lozenge</td>
<td>2.05</td>
<td>1.62, 2.59</td>
</tr>
<tr>
<td>Overall</td>
<td>1.77</td>
<td>1.66, 1.88</td>
</tr>
</tbody>
</table>

Nicotine patches are available in 24-hour and 16-hour preparations. These come in full strength (21 mg/24 hours and 15 mg/16 hours) and in lower strengths that are marketed for weaning. Both 16 and 24 hour patches provide about 1 mg of nicotine per hour. 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 it found no difference in self-reported abstinence at six months. Full-strength doses of both patches are more effective than the lower-strength preparations in smokers of more than 10 cigarettes per day.\textsuperscript{61} There is some evidence that the 24-hour patch may be more effective in relieving morning urges to smoke,\textsuperscript{62,63} although there is no evidence that this translates into higher abstinence rates. There is no advantage from slowly reducing the patch dose (OR=1.71; 95% CI: 1.52, 1.92) compared with stopping abruptly (OR=2.60; 95% CI: 1.83, 3.71). Two studies directly compared abrupt withdrawal and weaning, and they found no difference between the groups.\textsuperscript{54} Three studies compared length of treatment (12 weeks compared with 28 weeks; three weeks compared with 12 weeks; and three weeks compared with six weeks). They showed no advantage from using the
patch for a longer time.\textsuperscript{54} One study investigating the nicotine pharmacokinetics following the application of patches at different sites showed that the systemic dose was greatest when the patch was applied to the upper arm or back rather than to the stomach.\textsuperscript{54}

There is emerging evidence that genetic differences in the enzyme primarily responsible for metabolising nicotine (P450 (CYP) 2A6) may be important in determining the effectiveness of nicotine patches,\textsuperscript{65} and probably other NRTs. However, this is unlikely to have an impact on clinical treatment at the current time.

There is some evidence for the use of higher dose patches. Cochrane identified six studies comparing higher dose patches (44 and 42 mg/24 hours and 25 mg/16 hours) with standard dose patches. 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).\textsuperscript{54}

Dosing regimens have also been explored. Two studies of 2 mg nicotine gum have compared a fixed dosage with ad libitum use (ie, use as much and as often as desired). Although the fixed dosage showed higher quit rates (OR=1.29), this was not statistically significant (95\% CI: 0.90, 1.85).\textsuperscript{54}

NRT purchased over the counter has similar efficacy NRT obtained in other ways. In a study that compared free patch treatment to paid patch treatment, there was no difference in outcome.\textsuperscript{66–68}

**Combining nicotine replacement therapy products**

Trials examining the effectiveness of combining NRT products compared with the single use of NRT have shown mixed results. Pooling the outcomes of seven studies shows a moderate advantage of using a combination of NRT products compared with using a single product (OR=1.42; 95\% CI: 1.14, 1.76).\textsuperscript{54} Safety concerns with combining products are unfounded. It is unclear whether the slight increase in effectiveness is due to higher nicotine levels or the additional sensory replacement achieved with the second product.

**Combining nicotine replacement therapy and bupropion**

Combining bupropion and a nicotine patch produced significantly greater abstinence rates than treatment with a placebo (OR=4.86; 95\% CI: 2.33, 10.14).\textsuperscript{69} The abstinence rates in this study for a combination of patch and bupropion were significantly greater than with a patch alone (OR=2.65; 95\% CI: 1.58, 4.45) but not compared with bupropion alone (OR=1.28; 95\% CI: 0.82, 1.99).

The first study to compare NRT with bupropion showed smokers using the nicotine patch less likely to be abstinent at 12 months (OR=0.48; 95\% CI: 0.28, 0.82).\textsuperscript{69}
To assess the effect of the level of support in combination with NRT on quitting, the Cochrane review divided studies into low-intensity support (less than 30 minutes spent with the smoker at the initial visit or less than two further assessment visits) or high-intensity support. The odds ratio of quitting using NRT with low-intensity support compared with using a placebo with low-intensity support was shown to be slightly greater than with higher-intensity support (OR=1.81 compared with 1.78). However, this difference is not clinically or statistically significant. Other studies show a slightly different picture with an increasing differential between NRT and placebo with increasing levels of support.\textsuperscript{70}

Smokers recruited from primary care or the community appear to have greater success rates with NRT compared with smokers recruited from secondary care settings.\textsuperscript{54} However, this might be explained by the former group of smokers having higher levels of motivation and lower degrees of dependence than the latter group, which has smoking-related diseases.

**Use of nicotine replacement therapy in pregnancy**

Only a few studies have examined the use of NRT to aid smoking cessation in pregnancy. The evidence is borderline (5% increase in abstinence rates; 95% CI: 0%, 11%).\textsuperscript{71}

In a well-conducted randomised controlled trial of the use of the nicotine patch in treating pregnant smokers, there was no advantage of the active product over the placebo (OR=1.09; 95% CI: 0.54, 2.18).\textsuperscript{72} Participants were asked to use patches for 11 weeks (ie, 77 patches in total). The adherence to treatment was low in this study, with the median patch use being 14 patches (ie, patches used for 14 days). Another small randomised controlled trial (n=40) from Australia failed to shown the benefit of adding NRT to counselling compared with counselling alone.\textsuperscript{73} This study was underpowered to detect any significant difference, and it did not explain any serious adverse effects of patch use in pregnancy.

Animal studies have demonstrated that nicotine has some adverse effects on the foetus. For example, it appears to affect the development of the central nervous system where it is hypothesised to interfere with neurogenesis (the growth and development of nervous tissue).\textsuperscript{74,75} Nicotine may also play a role in sudden infant death syndrome.\textsuperscript{74,75} However, it is unclear how these studies translate to humans and how they apply to NRT.

Few studies have investigated the safety of NRT use in pregnancy, and all have small sample sizes.\textsuperscript{76–78} However, none has demonstrated any significant adverse effects on the women or foetuses. In the study by Wisborg et al,\textsuperscript{72} babies born to women who used a patch had significantly higher birth weights than babies born to women who used a placebo. This suggests nicotine is not the main cause of intra-uterine growth restriction.

Cigarette smoke delivers thousands of chemicals, some of which are known to be toxic to the developing foetus, such as carbon monoxide and cadmium.\textsuperscript{74,75,79}
Carbon monoxide impairs the availability of oxygen to foetal haemoglobin, while nicotine may contribute to foetal ischemia by affecting placental circulation. 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.\(^4,21\) Even if nicotine is associated with adverse effects in pregnancy, there are some differences between NRT and smoking as methods of nicotine exposure.\(^75\) For example, peak venous as well as arterial plasma nicotine concentrations in individuals using nicotine products are lower than those in individuals who are smoking, and the rate of delivery from the currently available nicotine products is slower than that from cigarettes.\(^81\) Of course, NRT delivers nicotine without the many other substances contained in tobacco smoke.

During pregnancy there is an increased metabolic clearance of nicotine and cotinine.\(^79\) It is unknown what impact this has on NRT dosing, but it might be expected that higher doses of NRT are needed.

**Breastfeeding and nicotine replacement therapy**

Nicotine freely passes in and out of breast milk, depending on the concentration of nicotine in maternal blood. Nicotine concentrations in breast milk are, therefore, dependent on the maternal blood nicotine concentration that is in turn affected by cigarette consumption, the frequency of breastfeeding, and the time between smoking and breastfeeding.\(^74,82\) Given that NRT typically provides less nicotine than tobacco smoke, it is likely that breast milk concentrations will be lower when NRT is used. Furthermore, blood nicotine concentrations in the infant are likely to be even lower due to the relatively low oral bioavailability of nicotine.\(^83\) It is unlikely that this low level of nicotine exposure is harmful to the infant.\(^75\) Conversely, second-hand tobacco smoke is known to have adverse effects on young children. A risk–benefit assessment would favour the use of NRT to aid smoking cessation.

**Differences in nicotine replacement therapy licences and contraindications**

The different NRT product licences are inconsistent. For example, some products are contraindicated in pregnant women while others can be used on medical advice or following a risk–benefit assessment.\(^84\)

In April 2002 NICE published *Guidance on the Use of Nicotine Replacement Therapy (NRT) and Bupropion for Smoking Cessation*.\(^85\) The expert panel reviewed the evidence and makes clear that NRT may be considered for use in pregnancy following a risk–benefit assessment. In assessing the risks and benefits of using NRT, NICE recommends that (para 3.2):\(^85\)

‘... when giving such advice to people in these groups who have been unable to quit smoking without using a cessation aid, healthcare professionals should take into account the significant harm associated with continuing to smoke and that it can be expected that NRT will deliver less nicotine (and none of the other
potentially disease-causing agents) that would be obtained from cigarettes'.

More recently, the UK Medicines and Healthcare Products Regulatory Agency and Committee on Safety of Medicines advised that (page 11):

‘... pregnancy and lactation should not be a contraindication to the use of NRT and that the warnings in the product information should be revised and put into the context of the dangers of continuing to smoke. Ideally, a pregnant woman should stop smoking without NRT, but if this is not possible, NRT may be recommended to assist a quit attempt as the risk of using NRT on the fetus is lower than that expected with smoking. There is also no exposure to the other dangerous elements. However, as nicotine does pass to the fetus, the decision to use NRT should be made as early on in pregnancy as possible with the aim of discontinuing after two to three months’ use’.

*Type of nicotine replacement therapy to be used during pregnancy*

It has been recommend that it might be prudent to use shorter-acting or intermittent-use NRT products such as gum, lozenge sublingual tablets, or an inhalator in preference to patches. This is because they typically deliver a lower daily dose of nicotine than patches deliver. However, if a patch is deemed to be the most appropriate product, it should be used only during waking hours (ie, removed at night). This is in agreement with the Medicines and Healthcare Products Regulatory Agency working group, which recommends that (page 12):

‘The product information should advise that slow-release 24-hour patches should not be used in pregnancy and lactation to avoid the administration of nicotine overnight when the fetus would not normally be exposed to smoking-derived nicotine. However, if the woman suffers from nausea and/or vomiting, a 16-hour patch, removed at night, is preferable. For breastfeeding mothers, intermittent NRT products will allow the time between NRT use and feeding to be as long as possible.’

*Use of nicotine replacement therapy by smokers with cardiovascular disease*

The safety of NRT in patients with cardiovascular disease (CVD) is well documented. There is evidence of the effectiveness of NRT in this group of patients. However, there has been some reluctance among healthcare professionals 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.

Guidelines on the use of NRT in smokers with CVD recommend that: (1) NRT can be recommended to smokers with CVD; (2) NRT can be used by smokers who have experienced a serious cardiovascular event or hospitalisation for a cardiovascular complaint in the previous two weeks or who have uncontrolled hypertension, but their consulting physician should be involved in the decision to recommend NRT; (3) dosages should not exceed the 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 should consider using oral products (eg, gum, lozenges, inhaler) rather than patches. There are three theoretical reasons for this: (1) nicotine levels can be reduced more rapidly in the event of problems;\(^{93}\) (2) the nicotine exposure produced by 24-hour patches is different from the exposure from smoking; and (3) concurrent patch use and smoking may lead to nicotine levels higher than those when smoking only.\(^{94}\) 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 compared with a matched sample who did not use patches.\(^{95}\) This suggests patches may also be appropriate for use by this group of patients.

The UK Medicines and Healthcare Products Regulatory Agency and Committee on Safety of Medicines recommended revising NRT product information to include the following (page 10):\(^{82}\)

- in stable cardiovascular disease, NRT presents a lesser hazard than continuing to smoke; dependent smokers hospitalised with a recent myocardial infarct, severe dysrhythmia or recent cerebrovascular accident and/or who are considered to be haemodynamically unstable should be encouraged to stop smoking with non-pharmacological interventions. If this fails, NRT may be considered but as data on safety in this group are limited, initiation should be under medical supervision.

**Use of nicotine replacement therapy by young smokers**

One study randomised 120 young smokers into three groups using nicotine patches or gum or a placebo.\(^{96}\) The six-month biochemically verified continuous abstinence rates did not differ between active and placebo treatment (OR= 8.36; 95% CI: 0.95, 73.3 for patches; OR=2.72; 95% CI: 0.27, 27.3 for gum). This study almost certainly lacked the power to detect a significant difference.

The adverse effects were typical of those seen in adult smokers. In a randomised controlled trial of 100 smokers aged 13–19 adverse events did not differ between those receiving active patches and those receiving the placebo, again demonstrating the safety of NRT in this group.\(^{97}\) No medication-related adverse events led to the withdrawal of participants from these studies.

Pharmacotherapies are not usually recommended for use in people under the age of 18, less because of specific safety concerns than because of a lack of clinical data. No evidence suggests 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 (page 9):\(^{82}\)

- ‘... 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).

Re-using nicotine replacement therapy after unsuccessful quit attempts

NRT can be used again in those who have tried and not succeeded in the past, although quit rates are low.\(^{54}\) This is most likely due to the smoker as opposed to the medicine per se. Other studies suggest that the re-use of NRT, even in a different form, by smokers who have failed on NRT in the past has limited benefit.\(^{98}\)

Pre-treatment with nicotine replacement therapy

There are now studies that examine the technique of pre-treatment (or pre-loading) with NRT before quitting. The rationale for this is that providing nicotine from an alternative source may decrease the person’s 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 before quitting, those using active patches were more likely to be abstinent at follow-up (22% compared with 12%), although this did not reach statistical significance (OR=2.07; 95% CI: 0.96, 4.45).\(^{54}\) There appear to be no safety concerns when NRT is used in this way.\(^{54,99}\)

Long-term use of nicotine replacement therapy

NRT 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.\(^{100}\) Products that deliver nicotine faster seem to have a greater chance of long-term use (eg, the 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%); and nasal spray (13%)).\(^{100}\) Furthermore, the clients who use NRT for longer are typically more highly dependent smokers, so long-term NRT may be necessary to maintain long-term abstinence. There are no safety concerns regarding the long-term use of NRT. Deciding factors in NRT use are more likely to be financial or the client’s worries about using it long term.

Using nicotine replacement therapy to reduce cigarette consumption before quitting

NRT is marketed to help smokers reduce the number of cigarettes smoked before quitting (eg, Nicorette Reduce to Stop\(^{101,102}\)). Smoking reduction per se is not a new strategy. In a survey to assess the prevalence of smoking and
smoking cessation behaviours it is estimated that about 50% of smokers are cutting down at any one time, and a sizable proportion (43%) of these smokers reported cutting down as a step towards stopping smoking completely.\textsuperscript{103}

Health benefits are unlikely to be achieved by reduced consumption (rather than complete cessation),\textsuperscript{104} partly because smokers can compensate by smoking their fewer cigarettes differently (eg, by increasing puff volume, blocking vent holes, increasing puff frequency, and smoking more of each cigarette).\textsuperscript{105,106} Therefore, complete cessation remains the ultimate goal. However, reducing cigarette consumption has been shown to increase the self-efficacy for quitting compared with smokers who do not reduce,\textsuperscript{107} and to increase ratings of readiness to quit.\textsuperscript{108} Smokers who report cutting down have a greater interest in making a future quit attempt\textsuperscript{82,109,110} and are more likely to quit.\textsuperscript{103}

Five randomised placebo-controlled trials have tested the use of NRT compared with a placebo in aiding reduction, and have included outcome data on cessation.\textsuperscript{110–113} These trials recruited participants who were unwilling to stop within the next month but wanted to reduce their consumption. The trials have a combined sample size of 2,138 smokers, with treatment periods varying between six and 18 months, and follow-up periods of between six months and two years. Abstinence rates were assessed using seven-day point prevalence abstinence, and were validated for carbon monoxide (CO) in all but one study. Pooling the results at 6–12 months after randomisation shows 16% of those using NRT compared with 9% using the placebo were able to sustain a reduction in consumption of at least 50% of baseline levels at a year.\textsuperscript{114} Significant heterogeneity exists between the studies, so a meta-analysis was not performed. Despite this group of smokers being unmotivated or unwilling to stop when they entered the study, 8% (144 out of 1,709) had stopped smoking at 6–12 months after they were randomised. Those using active NRT were more likely than those using the placebo to achieve abstinence (8% compared with 4%; OR=2.50; 95% CI: 1.69, 3.68).\textsuperscript{114}

The degree of cigarette reduction appears to be an important predictor of making a future quit attempt.\textsuperscript{115} Smokers who reduced their consumption by more than 50% were more likely to make a quit attempt than those with lower levels of reduction (5–50%).\textsuperscript{82,104}

Randomised placebo-controlled trials show that NRT is safe and well tolerated when used concomitantly with smoking.\textsuperscript{82} None of the adverse events experienced by participants was unexpected, and the events that occurred were typical for the type of medication used (eg, hiccups with nicotine gum).

An advantage of the NRT-assisted reduction strategy is that it is likely to attract smokers who are not interested in stopping right away. It provides another option for smokers, especially those who may have tried and failed using other methods. If using this strategy the smoker should aim to reduce consumption by at least 50% in the first six weeks. In the following 18 weeks this reduction can either be maintained or the smoker can continue to reduce or quit completely. NRT should be used as normal once the quit attempt has started. The suggested periods in which the smoker should reduce consumption by at
least 50% (six weeks) and stop smoking (six months) appear in product information, but are not based on empirical evidence.

In a recent review of this strategy, the authors suggested that given the lower probability of cessation in smokers who do not reduce their consumption by at least 50%, little may be gained in continuing the regimen if this goal has not been achieved within the first six weeks. The costs of this strategy would typically be met by the smoker buying NRT over the counter. However, UK guidance on this strategy reported that the annual cost would be about £55 million, making the cost per life year gained £5,000. Only Nicorette gum and the 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.

**Summary:** NRT is safe and effective in aiding smoking cessation. Evidence supports its use in combination with other NRT products, and in cutting down before quitting. NRT is safe to use by smokers with a history of CVD, although consultation with a physician should occur if the smoker has suffered a cardiovascular event within the past two weeks 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 foetus. 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 robust evidence from randomised controlled trials that NRT improves six-month continuous abstinence rates.

**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. However, there is a good rationale for examining the efficacy of antidepressants for smoking cessation, because the link between depression and smoking is well established.

The precise mechanism of action for aiding smoking cessation is unknown, but bupropion is thought to act through 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.
Two pivotal outcome studies were published in the late 1990s about bupropion’s efficacy in helping smokers to quit. The first compared the effect of three different daily doses (100 mg, 150 mg, and 300 mg) with a placebo, and demonstrated a linear effect of an increasing dose on point-prevalence cessation, although there was no significant difference between 150 mg and 300 mg per day at the 12-month follow-up. The second compared the one-year cessation rates in smokers receiving bupropion (300 mg per day), a 21 mg/24 hr nicotine patch, both bupropion and the patch, or a placebo. The continuous abstinence rates were 18%, 10%, 23%, and 6% respectively. All active treatments were significantly better than the placebo, and bupropion was better than the patch alone. There was no added advantage of using a combination compared with bupropion alone. Following these main studies more have been undertaken and published.

The Cochrane review pooled the results of 19 studies, with more than 4,000 smokers, that looked exclusively at the efficacy of bupropion compared with a placebo. The meta-analysis showed that, compared with a placebo, bupropion approximately doubled long-term abstinence rates (OR=2.06; 95% CI: 1.77, 2.40). This gives an effect size of 9% (95% CI: 7%, 11%) and a number needed to treat of 11. A recent meta-analysis of studies reporting the one-year outcome show similar evidence of efficacy (OR=1.56; 95% CI: 1.10, 2.21). Another randomised placebo-controlled trial comparing bupropion with a placebo in 509 smokers that has not been included in the Cochrane review shows similar outcomes (six-month CO-validated continuous abstinence rates were 25% for bupropion and 13% for the placebo, OR=2.2; 95% CI: 1.3, 3.6). Furthermore, bupropion is effective for both men and women.

In a ‘real-life’ setting, bupropion appears to produce respectable long-term abstinence rates. In a prospective observation study undertaken in a UK general practice, 227 smokers who were started on bupropion were followed up after a year. The one-year CO-validated continuous abstinence rate was found to be 22% (95% CI: 17%, 28%).

The efficacy of bupropion has also been examined in smokers with smoking-related disease, a population typically more dependent and harder to treat. Those with stable CVD treated with bupropion compared with a placebo achieved a higher one-year continuous abstinence rate (22% compared with 9%). When used in smokers with mild to moderate chronic obstructive pulmonary disease, bupropion was associated with significantly higher abstinence rates at six months (16% compared with 9%) but not at one year (10% compared with 9%). In another study of 255 smokers with, or at risk of, chronic obstructive pulmonary disease participants were randomised to receive bupropion, nortriptyline, or a placebo. Prolonged abstinence at six months was significantly greater in the bupropion group (28%) compared with the placebo group (15%, p<0.05). Although those receiving nortriptyline also achieved higher abstinence rates (25%), the difference with the placebo group was not significant (p=0.09).

There have not been any randomised controlled trials assessing bupropion’s use in pregnancy. We identified one prospective matched, controlled
observational study of 22 pregnant women using bupropion to stop smoking. Forty-five percent stopped smoking during the course of the pregnancy compared with 14% of the controls.\textsuperscript{126} No serious adverse effects on the pregnancy or foetus were noted.

We identified two randomised controlled trials comparing bupropion with a placebo in adolescents.\textsuperscript{127,128} One compared the efficacy of bupropion with the placebo when combined with nicotine patches in 211 young smokers. This failed to show a benefit in long-term abstinence (OR=1.05; 95% CI: 0.38, 2.92).\textsuperscript{127} The other was a small study (n=22) that also failed to demonstrate the efficacy of bupropion in this group of smokers, although this study was extremely underpowered to detect any difference.\textsuperscript{128}

Bupropion’s use in preventing smoking relapse has also been examined. The results of one study investigating the use of bupropion compared with a placebo for a year showed no difference in continuous abstinence rates between groups one year or two years after quitting.\textsuperscript{129} Another study showed no advantage of using bupropion over a placebo for preventing relapse in patients successfully quitting smoking using a nicotine patch.\textsuperscript{130} Therefore, evidence suggests there is little benefit from using bupropion long term to prevent relapse.

A small number of studies have compared bupropion with other smoking cessation medications. In one of the pivotal studies mentioned earlier bupropion was more effective than the nicotine patch. Combining NRT and bupropion significantly increased the one-year outcome compared with that from using the patch alone (23% compared with 10%).\textsuperscript{131} However, a more recent study did not confirm these results.\textsuperscript{132} Pooling the results failed to demonstrate the superiority of bupropion over NRT (OR=1.14; 95% CI: 0.20, 6.42).\textsuperscript{58} There is no evidence to show the superiority of a combination of NRT and bupropion over NRT alone. Another study randomised 140 navy shipyard workers to receive bupropion, a nicotine patch, or a combination of patch and bupropion, or into a control group (counselling only).\textsuperscript{132} No differences in 12-month abstinence rates were detected in this study. In a Brazilian study, 156 smokers were randomised to receive bupropion, nortriptyline (75 mg per day), or a placebo.\textsuperscript{133} All participants received counselling in addition to their pharmacotherapy. The six-month CO-validated continuous abstinence rates were highest in those using bupropion (42%), followed by nortriptyline (31%) and the placebo (22%). Only bupropion achieved a significant difference compared with using the placebo (p=0.05). There was no significant difference between the abstinence rates achieved with bupropion and nortriptyline.

Bupropion is a safe treatment when used correctly.\textsuperscript{134} There are contraindications to be checked when prescribing this medication. In addition, 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 CVD, without adverse effects on blood pressure or heart rate.
Bupropion is metabolised by the liver, primarily by isoenzyme CYP2B6, so other drugs that affect this enzyme, for example, cimetidine, sodium valproate, and cyclophosphamide, may affect bupropion metabolism. Bupropion inhibits the activity of CYP2D6, so there may be a reduced rate of metabolism of drugs such as beta-blockers and Type 1C anti-arrhythmics. A dose reduction in these medications may be required.

Bupropion is marketed for smoking cessation under its trade name Zyban, and is available in 150 mg sustained-release tablets. The recommended treatment regimen is one tablet (150 mg) daily for the first three days and one tablet twice a day from day 4. A course of 120 tablets should be completed. A reduced dose may be required in elderly smokers, smokers with diabetes, and smokers with renal or hepatic impairment.

The most common side effects that are experienced with bupropion include insomnia and a dry mouth. The medication also has a small, 1 in 1,000, risk of seizure, which is similar to some other antidepressants like fluoxetine, for example. Overall, bupropion is a safe medication when used appropriately.

Summary: Bupropion is safe and effective in aiding smoking cessation.

Strength of evidence: 1++

Evidence statement: There is robust evidence from randomised controlled trials that bupropion improves six-month continuous abstinence rates.

Nortriptyline

Nortriptyline is the only other antidepressant that has demonstrated efficacy in improving smoking cessation outcomes. It is a tricyclic antidepressant that inhibits the reuptake of noradrenaline and serotonin, and is thought to aid cessation through its noradrenergic mechanism, thereby reducing the severity of withdrawal symptoms. The most recent Cochrane review included six randomised controlled trials that compared nortriptyline with a placebo. Pooling the results shows an advantage of using nortriptyline over a placebo in assisting smokers to abstain long term (OR=2.14; 95% CI: 1.49, 3.06). This represents an effect size of 9% (95% CI: 5%, 14%) and a number needed to treat of 11.

When the two studies using nortriptyline in addition to NRT are removed from the meta-analysis, the effectiveness of nortriptyline becomes more apparent (OR=2.79; 95% CI: 1.70, 4.59). These findings are replicated in two other systematic reviews. The authors of one review argue that nortriptyline should be a first-line aid to help smokers quit. 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 nortriptyline is safe and well tolerated; and (3) nortriptyline is inexpensive. The authors of the other review agree that nortriptyline is an effective medication for smoking cessation, and note the advantages of this medication, that is, it is inexpensive and therapeutic blood levels can be monitored. However, they raise some concerns about its safety. The first concern is that although the nortriptyline studies show that it is
safe, it has been tested in only about 500 people. This compares with some 4,000 participants in bupropion studies and 35,000 in NRT studies. The second concern is that there are 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.

The main concern with using nortriptyline, like other tricyclic antidepressants, is its adverse cardiovascular effects. It is contraindicated in those who have experienced a recent myocardial infarction or arrhythmia. It is also contraindicated in patients with severe liver disease or bipolar disorder in a manic phase. In addition, there are several cautions for use, including by people with cardiac disease (particularly with arrhythmia), with a history of epilepsy, who are pregnant, who are breastfeeding, who are elderly, with hepatic impairment, with thyroid disease, with phaeochromocytoma, with a history of mania, with psychoses (may aggravate psychotic symptoms), with a susceptibility to angle-closure glaucoma, and with a history of urinary retention. 

Nortriptyline has several common side effects, for example, a dry mouth, light-headedness, shakiness, and blurred vision. Urinary retention, constipation, sexual difficulties, and seizure risk have also been reported. An overdose of nortriptyline is commonly fatal.

Given that other effective medications for smoking cessation are readily available, nortriptyline is regarded as a second-line therapy by some smoking cessation guidelines, and not recommended at all by others. In the review by Hughes et al it is recommended that (page 497) “before a clinician recommends nortriptyline as a second-line treatment, the smoker should have failed some form of NRT and bupropion, either when used across separate quit attempts or when used together.” They also advise that therapeutic drug monitoring be considered and that the dose be tapered at the end of treatment to avoid the withdrawal symptoms that may occur if treatment is stopped abruptly.

**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. Debate remains about whether this drug should be listed as a first- or second-line treatment for smoking cessation.

**Strength of evidence:** 1++

**Evidence statement:** There is robust evidence from randomised controlled trials that nortriptyline improves six-month continuous abstinence rates.

**Varenicline**

Varenicline is the latest medication to be licensed for smoking cessation and was developed especially for this indication. Although 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 alpha-4 beta-2 subtype but it also acts as a full agonist at alpha7 neuronal nicotine receptors. The agonist effect on the nAChR produces the release of dopamine, but less than that seen with nicotine.

Varenicline’s mode of action in aiding smoking cessation is primarily by reducing the severity of tobacco withdrawal symptoms (through its agonist effects), but it also reduces the rewarding properties of nicotine (through its antagonistic effects). The later effect may be beneficial in extinguishing smoking behaviour for the week it is used before quitting and helping to protect against complete relapse if a smoker lapses.

The efficacy of varenicline for smoking cessation has been examined in five published placebo controlled trials, with more than 4,000 smokers of 10 or more cigarettes per day and aged 18-65. Four studies examined the long-term efficacy of a 7–12-week treatment period of varenicline (1 mg twice a day) compared with a placebo. One study investigated the benefit of extended (24 weeks compared with 12 weeks) varenicline use in people who were abstinent at the end of the three-month treatment period. There was a small but significant benefit of using varenicline for the extended period.

Wu et al undertook a meta-analysis of these studies, and the pooled one-year abstinence rates show a clear benefit of varenicline over the placebo (OR=2.96; 95% CI: 2.12, 4.12). About 1 in 8 people receiving a course of varenicline who would not have quit smoking on their own will stop smoking for at least six months. The authors went on to assess the efficacy (one-year abstinence rates) of varenicline compared with bupropion, and showed that the pooled results from three studies favoured varenicline (OR=1.58; 95% CI: 1.22, 2.05). Some indirect comparisons were also reported for NRT, showing that varenicline was superior to NRT when compared with a placebo (OR=1.66; 95% CI: 1.17, 2.36).

Studies have found that varenicline reduced urges to smoke significantly more than the placebo. The reinforcing effects of smoking were also reduced in those smokers receiving active treatment. There is an increase in seven-day point prevalence abstinence over the treatment period, suggesting that smokers who may not have stopped immediately after the quit date are stopping later.

Smokers need to commence varenicline one week before their quit date. The dosage is 0.5 mg once daily for the first three days, increasing to 0.5 mg twice daily (one tablet in the morning and one in the evening) for the next four days, and then 1 mg twice daily for 12 weeks. The US Food and Drug Administration has approved usage up to six months if required for those who are abstinent at 12 weeks.

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. Varenicline has a half-life of about 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 the use of other medications has been observed.

The use of varenicline is not recommended in people under the age of 18 years or pregnant or breastfeeding women. Caution is warranted in those with renal impairment.

The most common side effect associated with varenicline is nausea, which appears to be dose dependent. The titration period before quitting helps limit the occurrence of nausea. Sleep disturbance and constipation were more frequently reported by those receiving varenicline compared with the placebo. However, it should be noted that these symptoms are also withdrawal symptoms and are likely to occur more frequently in the varenicline group because these people are more like to be abstinent. Most of the symptoms are reported as mild and dissipate within a few weeks.

**Summary:** Varenicline is safe and effective in aiding smoking cessation.

**Strength of evidence:** 1+

**Evidence statement:** There is robust evidence from randomised controlled trials that varenicline improves six-month continuous abstinence rates.
Smoking cessation interventions in priority populations

Māori

Māori have a high smoking prevalence rate of 46% (current smokers aged 15 years and over).\(^1\) Māori women have a higher rate of smoking (50%) than Māori men (40%). Māori women of childbearing age (15–39 years) have smoking rates of up to 61%. For Māori men aged 15–39 years, rates are as high as 51%.\(^1\) Furthermore, smoking prevalence among Māori has not declined over time at the same rate as in the general population.\(^1\) Tobacco smoking kills an estimated 4,300 people in New Zealand each year but has a particularly adverse effect on the health of Māori.\(^145,146\)

Smoking accounts for 21% of preventable deaths in Māori females and 22% of preventable deaths in Māori males. It is the single most important cause of lost healthy life years among Māori, and the greatest contributor to the life expectancy gap between Māori and non-Māori.

Beliefs and attitudes about smoking are important in addressing smoking cessation in any population. In a study of 130 Māori smokers, Glover found that the majority of participants reported smoking because of habit (73%), followed by stress (48%) and addiction (39%).\(^147\) The 1996/97 New Zealand Health Survey found that 19% of Māori smokers were either thinking of quitting or doing things to help themselves quit. In Glover's study, most (85%) wanted to quit for health reasons, followed by cost (53%) and for the benefit of their children (52%).\(^147\) In another New Zealand study, wanting to quit for financial reasons was noted to be important for Māori men while quitting during pregnancy was an important reason for Māori women.\(^148\)

There are limited data on smoking cessation interventions in Māori. We identified only two randomised controlled trials that examine the efficacy of smoking cessation interventions in Māori. One examined the efficacy of bupropion in a sample of Māori smokers\(^149\) and the other undertook a subgroup analysis of a mobile phone–based smoking cessation intervention.\(^150\) These are described in more detail below. We have attempted to summarise a variety of other data relevant to smoking cessation for Māori, and although this gives some direction of how services might be structured we are unable to comment on the specific effectiveness of these.

It is generally accepted that smoking cessation interventions for Māori need to address all elements of wellbeing: te taha tinana (the physical body); te taha wairua (the spiritual realm); te taha hinengaro (the psychological realm); and te taha whānau (the family and wider community). This is described in more detail elsewhere,\(^147\) but in summary, smoking cessation interventions for Māori need to address the physical dependency on nicotine, include a behavioural support component, be delivered in a way that is culturally appropriate, and need to be as inclusive as possible of whānau. Qualitative research suggests that a group-based cessation support format may work for some Māori (eg, older people and people living in rural communities).\(^151\) It is, therefore, important that alternative cessation treatment modalities and formats are offered to Māori.
Mass media campaigns

Mass media campaigns that promote smoking cessation among Māori smokers have been evaluated by assessing the call volumes to a quitline during times the campaigns were running.\(^{152}\) The campaign “It’s all about whānau” was designed by Māori especially for a Māori audience, and provided positive messages about quitting as well as more general tobacco control messages such as being ‘smoke free’. Another campaign (“Every cigarette is doing you damage”) focused on the damage caused by smoking. Both of these campaigns included the national quitline number and while they were effective in generating an increase in calls to the quitline, their effect on cessation rates was not examined.

Smoking cessation services

Quitline

The most recent published data (2005) show that 18% of quitline callers identify as Māori, and the majority of these are aged 25–44.\(^{153}\) There is a good uptake of NRT by Māori, as measured by the provision of Quitcards. Abstinence rates from a cohort of smokers calling the quitline have also been examined. Although the seven-day point prevalence abstinence rate (unvalidated) at six months is less than that for non-Māori (17.4% compared with 21.7%) this is not significant (OR=1.18; 95% CI: 0.91, 1.55) once confounding variables are controlled for.\(^{154}\)

Aukati Kai Paipa

Aukati Kai Paipa is a smoking cessation programme that was developed for Māori and delivered by Māori specifically trained in smoking cessation. The target audience was initially Māori women and their whānau. Moreover, it was whānau based, delivered by Māori providers in a culturally appropriate way, and adopted a holistic approach.\(^{155}\) The quit coaches had strong ties to the local community and all received specialist smoking cessation training.

Aukati Kai Paipa was piloted for two years, starting in 1999.\(^{155}\) The smoking cessation component combined behavioural counselling with a supply of NRT. Participants had weekly contact with the quit coaches for 4–12 weeks, and thereafter monthly contact for 6–8 months. NRT, in the form of patches or gum, was offered to all participants, although they could choose not to use this and receive just counselling. The programme used the Stages of Change Model and motivational interviewing, and to enter the programme smokers had to be considering stopping or ready to stop.

About 3,200 smokers took part in the pilot phase. Most were middle-aged, female, and in good health. They smoked 15 cigarettes per day (median) and about half (51%) had a high or very high level of addiction (measured by daily cigarette consumption and time to first cigarette in the morning).
The self-reported two-day point prevalence abstinence was measured at three, six, and 12 months. Those lost to follow-up were not included in the data analysis. Abstinence was not biochemically verified. The abstinence rate at 12 months was 23% (322 out of 1,400). Further analysis showed that those who used NRT were more likely to achieve long-term abstinence than those who did not use any NRT. Interestingly, the level of dependence was not a predictor of abstinence. Those who had quit in the past or cut down before quitting were more likely to achieve abstinence at 12 months than those who had not. Living with a smoker was a negative prognostic factor.

The evaluation highlighted a general lack of access to smoking cessation services, and low levels of knowledge about medications to aid quitting.\textsuperscript{155}

\textit{Noho Marae}

Noho Marae smoking cessation programmes are a residential intervention developed initially in Taranaki. Smokers stay on the marae for up to a week and stop smoking with the aid of various behavioural strategies. It is very intensive, and generally adopted by highly motivated smokers. Glover evaluated this programme using a quasi-experimental design,\textsuperscript{147} and high success rates have been reported anecdotally.\textsuperscript{156}

\textit{STOMP}

A New Zealand randomised controlled trial showed that a smoking cessation intervention delivered via mobile phones (STOMP) was effective in increasing short-term abstinence rates compared with a control group. This study targeted young Māori and enrolled 355 Māori smokers (and 1,350 non-Māori smokers). A separate analysis was undertaken to assess the effectiveness in Māori compared with non-Māori.\textsuperscript{157} This showed no significant differences in outcome between the two ethnic groups, providing evidence that this intervention has potential public health benefit. Unfortunately, the intervention as a whole did not show an effect at six months.\textsuperscript{150}

\textit{Bupropion}

Bupropion is a medication proven to aid smoking cessation.\textsuperscript{118} Most of the studies investigating its efficacy have taken place in white North American or European smokers. However, a New Zealand study examined its effectiveness in a sample of Māori smokers.\textsuperscript{149} This study recruited and randomised (2:1 randomisation) 134 Māori participants smoking at least 10 cigarettes per day to a seven-week course of bupropion SR (Zyban) or a placebo. At six months after the quit date the continuous CO-verified abstinence rates were significantly higher in the group using bupropion compared with those using the placebo (30% compared with 11%; relative risk = 2.72; 95% CI: 1.12, 6.61). These findings are comparable to studies of other population groups and provide good evidence for the use of bupropion in Māori. The adverse events reported were similar to those already documented (eg, insomnia, headache, and skin reactions). Most were mild and self-limiting.
**Other general information**

There has been some discussion about ethnic differences in the rate of nicotine metabolism and the role that this might play in the establishment and maintenance of tobacco dependence. Lea et al have found that Māori are more likely to have the gene variant associated with a slow nicotine metabolism, and have suggested that this may contribute to the high smoking rates seen in Māori. However, the rate of nicotine metabolism is only one of several determinants of tobacco dependence. These findings might have a consequence for treatment, but there are no definitive data to suggest how these might alter clinical practice.

A paper on purchasing smoking cessation services for Māori made five recommendations: (1) assess target groups; (2) develop and deliver training in nicotine dependency and smoking cessation methods; (3) develop smoking cessation resources; (4) identify and contract providers; and (5) develop mass media campaigns promoting quitting. The paper recommended that Māori have access to a range of services developed, managed, and delivered by Māori.

**Summary:** Few studies assess the outcome of smoking cessation interventions for Māori smokers. There is insufficient evidence to show that a mobile phone-based intervention increases long-term abstinence rates in the general population. It did, however, have a positive effect on short-term outcome, and there was no difference between Māori and non-Māori in the subgroup analysis. There is good evidence from one randomised controlled trial that bupropion is effective in aiding cessation in Māori smokers who were motivated to quit.

No evidence supports 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 Māori, although the findings of various reports suggest these interventions must be acceptable to Māori. The recommendations made by Glover in 1997 remain relevant.

**Evidence statement:** With the exception of bupropion (strength of evidence = 1+), there is insufficient evidence on specific interventions for smoking cessation in Māori to draw any conclusions.

**Pacific peoples**

Pacific people in New Zealand have a high smoking prevalence rate of 36% (current smoking, 15 years of age and over), with 39% of Pacific males and 33% of Pacific females current smokers. Pacific women of childbearing age (15–39 years) have smoking rates of up to 47%. For Pacific men aged 15–39 years, rates are as high as 60%. Information on smoking prevalence among different Pacific population groups is limited. Smoking prevalence in Pacific people has remained stable since the 1990s whereas the prevalence in the general population has slowly declined.
No specific trials have examined the effectiveness of smoking cessation interventions for Pacific peoples. Interventions for a minority group may need to be especially tailored for that group in order to be effective, and culturally appropriate models or examples may increase a smoker’s acceptance of treatment. Therefore, more research into attitudes and knowledge in New Zealand may be required in order to develop more appropriate cessation interventions for Pacific peoples.

**Evidence statement:** There is insufficient evidence on smoking cessation interventions for Pacific peoples to draw any conclusions.

**Asian peoples**

Smoking prevalence in Asian peoples living in New Zealand is lower than that for most other ethnic groups at 12%. Smoking prevalence varies by sex, with 18% of Asian males and 4% of Asian females currently smoking. Asian men aged 20–24 years have the highest smoking prevalence (31%). Although smoking prevalence rates among New Zealand Asian peoples is lower than among other ethnic groups, subgroups in the Asian population have high rates. In New Zealand Asian males, smoking prevalence is highest in Japanese, Korean, and Vietnamese, followed by Cambodian, males. Asian females are generally less likely to smoke than Asian males, but Japanese women have the highest rates among Asian women.

There are very few trials of smoking cessation interventions specific to Asian populations. It is unknown how relevant these studies may be to New Zealand Asian populations. Attitudes and perceptions of smoking are likely to differ depending on a person’s country of origin. However, the attitudes and perceptions of smoking among New Zealand Asian peoples are unknown. Also, the Ministry of Health’s *Asian Public Health Project Report (2003)* stated that many Asian people have difficulties accessing language- and culture-appropriate health information and services.

**Summary:** There is insufficient evidence on Asian-specific cessation interventions to make any conclusions. Cessation interventions based on non-Asian population research is likely to be inappropriate. Culturally appropriate services may be more effective than mainstream smoking cessation services for Asian populations.

**Evidence statement:** There is insufficient evidence on smoking cessation interventions for Asian peoples to draw any conclusions.

**Pregnant and breastfeeding women**

Data from 2006 show the prevalence of smoking in women of childbearing age (15–39 years) ranges from 26–29%. However, rates are highest in Māori (39–61%) and Pacific women (27–47%) compared with Pākehā women (22–27%). Smoking during pregnancy is associated with risks to the pregnancy (eg, premature delivery, spontaneous abortion, placenta previa, and placental abruption), the newborn (eg, low birth weight), and the infant (sudden infant death
syndrome, otitis media, and learning difficulties). The proportion of pregnant women who continue to smoke throughout pregnancy has decreased in line with the decrease in smoking prevalence in the total population. While about 20% of adult female smokers stop smoking when they become pregnant, they tend to be less-dependent smokers and have better resources to help them quit. Conversely, women who 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. However, the majority of these women would like to stop smoking.

Helping pregnant women to stop smoking has benefits for the mother and the child. Cessation efforts should be encouraged at any time throughout the pregnancy and into the post-partum period.

A meta-analysis undertaken by the Cochrane group showed that interventions among pregnant women result in a 5% (95% CI: 4%, 7%) increase in absolute long-term success compared with that of control groups (mostly usual care) (odds ratios were not reported). 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 or their partners. Another well-conducted randomised controlled trial failed to demonstrate the benefit of a home-based motivational interviewing intervention. A cluster-randomised controlled trial of self-help materials also failed to show any efficacy in helping pregnant women to quit smoking. Furthermore, it seems that to be effective, interventions need to be delivered by people whose sole purpose is to help people stop smoking, as opposed to cessation treatment being an additional task of an already busy healthcare professional. Studies that have used midwives to deliver smoking cessation interventions have not been successful. Possible reasons for this 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. However, all midwives should be providing brief advice to stop smoking, although evidence suggests that few provide this advice. There is some evidence that brief interventions from midwives, nurses or doctors can improve cessation rates in this group of smokers. The provision of advice to stop smoking is not associated with increased stress in pregnant women who smoke. This may be contrary to the belief of some healthcare professionals.

The use of NRT to aid smoking cessation in pregnancy has been examined in only a few studies. The evidence is borderline (a 5% increase in abstinence rates; 95% CI: 0%, 11%). However, given its efficacy in the non-pregnant population there is no reason to believe that it should not help pregnant women. Nevertheless, several factors should be considered. The use of nicotine during pregnancy is not without risk, but it is undoubtedly safer than smoking because NRT contains only nicotine and none of the other substances in cigarette smoke that are known to be harmful in pregnancy (eg, carbon monoxide). Therefore, a
risk–benefit assessment is advised before using NRT in pregnancy. In the UK the contraindication for NRT use in pregnancy has been replaced with a caution. This gives women who are finding it difficult to quit the permission to use this medication if they wish. A significant proportion of pregnant women who smoke may be interested in using NRT. A survey conducted in the UK found that 68% of pregnant smokers would accept an NRT product. Another UK study reported that 35% would definitely or probably use NRT to help them stop smoking. However, NRT is not a panacea and women should be encouraged to seek behavioural support to aid their quit attempt. More detailed information on the use of NRT in pregnancy can be found on page 37.

A small number of high quality studies have tested programmes aimed at reducing a relapse to smoking in the post-partum period. The evidence shows no benefit from these interventions. However, most interventions have focused on the traditional skills-based approach to preventing relapse (see the section on relapse prevention, page 66) and it may be that this approach on its own is not enough.

If the rates of smoking in pregnancy are to continue to fall, smoking cessation systems and interventions need to be implemented into all maternity care settings. Maternity workers need to be skilled in asking about smoking, advising those who smoke to quit, and referring those who want help in stopping to appropriate smoking cessation treatment providers.

At a practical level, midwives in New Zealand generally do not come into contact with pregnant women until the second or third trimester. Therefore, the role of the GP in advising and assisting pregnant women who smoke is very important.

**Summary:** Evidence supports the effectiveness of interventions to help pregnant women to stop smoking. 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:**
- There is evidence from randomised controlled trials that multi-session behavioural interventions to help pregnant women stop smoking improve six-month continuous abstinence rates.
- There is mixed evidence on whether NRT improves six-month continuous abstinence rates in pregnant women.
- There is insufficient evidence that bupropion, nortriptyline, or varenicline aid smoking cessation in pregnancy to draw any conclusions.
Young people

Young people have a high overall smoking prevalence rate of 27%, but this varies considerably by ethnicity and sex. Young Māori women (aged 15–19) have the highest prevalence (60%), followed by young Pacific men (aged 15–19) (46%).

Evidence shows the prevalence of smoking in 15-year-olds has decreased over the past decade.

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

A recent systematic review undertaken by the Cochrane collaboration identified only 15 randomised controlled trials that examined smoking cessation interventions in a total 3,605 young smokers. Young smokers were defined as people aged under 20 years who had smoked on average at least one cigarette a week for at least the last six months. The review included studies testing a wide range of interventions, including pharmacotherapies and behavioural support programmes based on models such as the Stages of Change and motivational enhancement. A group of studies reporting on the Not on Tobacco programme used social cognitive theory for the theoretical basis of the intervention. As with other Cochrane reviews only those studies with at least six-month cessation outcomes were included, and analyses were performed on an intention to treat basis.

Interventions were grouped by type and results entered into meta-analysis. Two studies examined interventions based on the Stages of Change Model, which essentially delivered material appropriate to the young smokers’ stage of change and compared results with those of a control group (health education). Both these studies reported 30-day point prevalence abstinence and neither attempted to validate self-reports. At 12 months, more participants in the intervention groups had stopped smoking than had participants in the control groups (OR=1.70; 95% CI: 1.25, 2.33).

The remaining studies assessed in this review all used interventions that aimed to enhance motivation (eg, motivational interviewing) and cognitive behavioural therapy, and an older study based the intervention on an educational approach (eg, using facts, scare tactics, and attitudinal changes). The combined results of the three trials that used motivational interviewing show a positive outcome (OR=2.05; 95% CI: 1.10, 3.80). However, the authors urge caution when interpreting the results because the studies included other behavioural components and not motivational interviewing alone.
The Not on Tobacco intervention deserves further mention. This study recruited 673 young smokers from 84 schools across three US states (Florida, North Carolina, and West Virginia). The intervention involved small same-gender groups that met for 50 minutes once a week and discussed nicotine dependence, the 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 with 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 six-month follow-up, and it is unclear whether this measure is meaningful. We identified one further abstract with results from an Alabama site are similar to those described above, so are unlikely to change the results of the meta-analysis.

Two studies examined the effectiveness of pharmacotherapies. One study randomised 120 young smokers to nicotine patches or gum or a placebo and found no advantage of NRT over the placebo. The other study found no benefit of bupropion over the placebo when combined with nicotine patches in 211 young smokers (OR=1.05; 95% CI: 0.38, 2.92). Pharmacotherapies are not usually recommended for use in people under the age of 18, not so much because of specific safety concerns but usually because of a lack of clinical data. No evidence suggests that these medications are harmful. In recognition of this the Medicine and Healthcare Products Regulatory Authority has recommended that NRT can be used in smokers 12 years and older who want to stop smoking. The US guidelines recommend that bupropion may be used in adolescent smokers when deemed appropriate by a clinician. Unlike bupropion, which has been available for more than a decade, there is less clinical data and experience with the use of varenicline in young smokers. Although there is no logical reason why varenicline could not be used by young people, its general use in young smokers cannot yet be recommended. Further details on the use of pharmacotherapies in young smokers can be found in earlier in this review (see page xx).

One New Zealand study targeted recruitment at older adolescents (people aged 16 years or over) and young adults (although there was no upper age limit) for a text message mobile phone–based smoking cessation intervention. The study had no difficulty recruiting participants, including 472 adolescents (16–19-year-olds). This was a six-month programme of regular personalised messages, including cessation advice, support, and distraction. The intervention was found to double self-reported quit rates at six weeks. However, the six 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 six 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).
Summary: Overall, little data confirms the effectiveness of interventions specifically aimed at helping young people to quit smoking. Furthermore, many studies have methodological problems such as the definition of abstinence, the length of follow-up, and a lack of biochemical validation of abstinence. Those studies that did undertake validation\textsuperscript{127,189} demonstrate the significant proportion of young people who misreport their smoking status, which raises concerns about the validity of studies that rely on self-reporting.\textsuperscript{185} 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 who want to quit.

The US guidelines recommend that healthcare professionals provide advice to stop smoking to young smokers and assist those interested in stopping.\textsuperscript{4} 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.

Strength of evidence: 1+

Evidence statements:

- There is insufficient evidence concerning whether behavioural interventions aimed specifically at smoking cessation in young people improve six-month continuous abstinence rates. However, results from randomised controlled trials suggest that behavioural interventions show promise and further research is warranted.
- There is insufficient evidence that the use of pharmacotherapies in young people improves six-month continuous abstinence rates.

Hospitalised smokers

Relevance of helping hospitalised smokers to quit

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 often directly relevant to the reason for hospitalisation, the smokefree environment in hospital provides few smoking cues, and some people will have less desire to smoke when feeling ill. Hospitalisation, therefore, is an important opportunity to help people to stop smoking.

The adverse effects of smoking on cardiovascular health are well established.\textsuperscript{190} Stopping smoking is one of the best things smokers with CVD can do to improve their current and future health. The reduction in total mortality after stopping smoking in people with CVD is estimated to be 36\% (RR=0.64; 95\% CI: 0.58, 0.71), which is greater than the reduction in risk achievable with medical treatments such as statins.\textsuperscript{191}
Patients with CVD who stop smoking appear to achieve better outcomes than those with respiratory illness who stop smoking.\textsuperscript{90} It may be that stopping smoking might be harder for respiratory patients because of co-morbidities more common in this group such as depression (which is also a negative prognostic factor for smoking cessation), or the more insidious nature of disease progression compared with the life-threatening and sudden crisis of an acute myocardial infarction.\textsuperscript{192}

To be effective, smoking cessation interventions (ie, interventions aimed at helping smokers to stop as opposed to brief advice to stop) delivered within hospitals need to be more than a short, one-off session delivered by a busy healthcare professional.

A Cochrane review identified 16 studies and categorised them according to levels of intensity: (1) a single contact in hospital less than 15 minutes’ duration; (2) one or more contacts in hospital, each more than 15 minutes’ duration; (3) any number of contacts in hospital with less than one month of outpatient follow-up for smoking cessation; and (4) any number of contacts in hospital with at least one month of outpatient follow-up for smoking cessation.\textsuperscript{90} Only the last category showed a significant effect, increasing six months’ abstinence 9% (95% CI: 6%, 12%) with an odds ratio of 1.82 (95% CI: 1.49, 2.22) compared with the results for the 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.

There has been concern about the use of NRT in smokers with a history of CVD.\textsuperscript{87} However, NRT is generally safe to use for these smokers to use (for more detail see page 39).\textsuperscript{91}

**Summary:** Evidence supports 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 statements:**

- There is robust evidence from randomised controlled trials that high-intensity behavioural interventions that include at least one month of follow-up contact improve six-month continuous abstinence rates in hospitalised patients.
- There is evidence from randomised controlled trials that NRT improves six-month continuous abstinence rates.
Preoperative smoking cessation

About 5–10% of the population have a surgical procedure in any given year. Complications are common, especially following major procedures: cardiac and respiratory complications occur in about 10% of all cases. Compared with non-smokers, smokers have an increased risk of cardiopulmonary complications, poorer wound and bone healing, a greater chance of being transferred to other hospital departments, and a longer hospital stay. The risk of developing complications depends on both the acute and chronic effects of smoking. Acute effects arise from the effects of substances such as carbon monoxide, which binds to haemoglobin and reduces its oxygen-carrying capacity, while chronic effects are the result of underlying disease such as atherosclerosis or chronic obstructive pulmonary disease, for example.

The preoperative period is thus an opportunity to advise on smoking cessation, not just for the immediate peri-operative period but permanently. Available evidence confirms that interventions aimed at assisting smokers to stop before surgery are effective. A Cochrane review identified four studies that met its inclusion criteria.

Results could not be pooled because of significant heterogeneity between the studies. All studies showed short-term efficacy. Only two studies measured longer-term abstinence rates, and there was no difference between the intervention and control groups.

Preoperative smoking cessation has been shown to decrease post-operative risks such as wound infection, delayed wound healing, and post-operative pulmonary and cardiac complications. Moller et al showed that wound complications were less frequent in the intervention group compared with in the control group (5% compared with 31%; RR=0.17; 95% CI: 0.05, 0.56), whereas Sorensen and Jorgensen’s study showed no significant difference (33% compared with 27%). Likewise, the Moller et al study found fewer cardiopulmonary complications (2% compared with 12%), but this was not seen in the Sorensen and Jorgensen study. Combining all complications, again Moller et al’s study showed a significant difference (18% compared with 52%), but Sorensen and Jorgensen’s study showed no difference (41% compared with 43%).

The timing of cessation appears to be important in determining the risk of post-operative complications. While difficult to achieve in acute situations, cessation at around eight weeks before surgery appears to be optimal, and is feasible for elective surgery when waiting lists are often long. It has been postulated that stopping immediately before surgery may increase respiratory complication risks due to a temporary increase in sputum production and ineffective sputum clearance. However, this does not explain why respiratory complication rates are the same in smokers, since they too have reduced cilia function and impaired alveolar immunity.
As noted, a problem common to many smoking cessation studies is a reliance on self-reported smoking status. Patients may misrepresent their true smoking status, particularly when the surgery is correcting a smoking-related disease (eg, coronary artery bypass grafting). This may explain why some studies have an increased complication rate among patients who claimed to have stopped smoking or reduced the number of cigarettes smoked. Other studies group reducers and abstainers together, but it is likely that cutting down has less benefit on post-operative recovery than abstinence.

There is a lack of evidence for the efficacy of preoperative smoking cessation interventions on long-term abstinence. Cessation interventions that are effective in the non-hospitalised population should, however, 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 preoperatively may have committed to abstain only for a short period (similar to women who stop throughout their pregnancy but re-start smoking afterwards).

**Summary:** All smokers should be encouraged to stop smoking, and supported in their attempt before surgery. While stopping smoking at any time is likely to be beneficial compared with continuing to smoke, the earlier a person stops, the lower the post-operative risk they are likely to face. There is insufficient evidence that temporary abstinence increases the risk of complications.

**Strength of evidence:** 1+

**Evidence statement:** There is evidence from randomised controlled trials that preoperative smoking cessation interventions improve short-term abstinence rates. However, there is insufficient evidence to draw any conclusions regarding six-month continuous abstinence rates.

**People who use mental health services**

People with mental illness have particularly high smoking prevalence rates. Te Rau Hinengaro: The New Zealand Mental Health Survey found a higher prevalence of current smoking in people with any mental illness (32%; non-institutionalised) compared with in people without mental illness (21%).

There is evidence that tobacco companies have targeted ‘marginalised groups’ including people with mental illness. For example, free samples of cigarettes have been provided to mental health institutions and the tobacco industry actively formed alliances with organisations that provided services to people with mental illness.

The problems faced by people who use mental health services in stopping smoking are described in detail in Mental Health Literature Review: New Zealand Smoking Cessation Guidelines Project. Encouraging people with mental illness to stop smoking is often overlooked or not seen as an important intervention. Smokers with mental illness typically have lower abstinence rates than those without mental illness. Differences in demographics and smoking history between smokers in the population without mental illness and people with mental health issues.
the population with mental illness may account for this. For example, smokers with mental illness tend to be more-dependent smokers\textsuperscript{205–208} and have a higher cigarette consumption\textsuperscript{208,209} A depressed mood is a tobacco withdrawal symptom,\textsuperscript{210} and the onset of major depressive episodes following cessation have been reported.\textsuperscript{211} Furthermore, a depressed mood is a predictor of relapse.\textsuperscript{212}

One hypothesis for why people with mental illness may smoke more than people without mental illness is that smoking may alleviate some psychiatric symptoms.\textsuperscript{213} However, stopping smoking appears to improve psychiatric symptoms such as anxiety and stress\textsuperscript{205,214} and depressive symptoms,\textsuperscript{215} and lead to a general improvement in mental health.\textsuperscript{216} Smoking may also reduce the side effects of some neuroleptic medications.\textsuperscript{217} It is also reported that nicotine may improve cognitive function,\textsuperscript{217} although 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 population without mental illness.\textsuperscript{4} These recommendations are echoed in a recent systematic review.\textsuperscript{218}

Another systematic review of ‘healthy living’ interventions in adults with a diagnosis of schizophrenia identified seven smoking cessation studies.\textsuperscript{219} Five of these reported six-month abstinence rates of 12–18\%, while two reported no successful abstainers. The authors observed that those programmes that provided group-based or individual behavioural support with pharmacotherapy achieved higher abstinence rates than those that did not. However, the majority of these studies were of a non-randomised design with small sample sizes and of variable methodological quality, making results difficult to interpret.

We identified one randomised controlled trial (n=78) that examined the effect of a single session of motivational interviewing compared with the effect of psychoeducational and minimal-control interventions in prompting smokers with schizophrenia to seek smoking cessation treatment.\textsuperscript{220} The motivational interviewing and psychoeducational interventions both lasted 40 minutes and included advice to quit and referral to a smoking cessation treatment programme. The minimal-control intervention lasted 5 minutes. Significantly, more participants who received motivational interviewing contacted the smoking cessation treatment provider within a month (32\%) compared with those in the psychoeducational group (11\%) and minimal-control group (0\%).

There is limited evidence about who should deliver smoking cessation treatment to people with mental illness. The results of a small (n=66) randomised trial comparing treatment integrated with psychiatric care with treatment provided outside psychiatric care suggested that the integrated care approach may achieve greater cessation success.\textsuperscript{221} However, the repeated seven-day CO-verified point prevalence rate for nine months of follow-up failed to reach statistical significance (12\% for integrated care compared with 3\% for standard care, p=0.2). Participants in the integrated care group were more likely to
receive nicotine patches and gum, and were more likely to receive combination therapy. The authors conclude that cessation treatment delivered in an integrated approach may be more likely to engage smokers and encourage compliance with medication.

**Pharmacotherapy**

There is no doubt that pharmacotherapies increase long-term smoking cessation success rates. 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. It is likely that these smokers may benefit from more aggressive pharmacological treatment, including higher doses and a longer length of treatment, compared with smokers without mental illness. A small, single blind randomised controlled trial assessed the efficacy of extended use of NRT in people with a diagnosis of schizophrenia. Fifty smokers entered a three-month open label smoking cessation treatment programme that consisted of group-based behavioural support and nicotine patches. At the end of treatment 36% (n=18) were abstinent and were randomised to receive another six months of a placebo or an active patch. Significantly more people relapsed (eight out of nine) in the placebo group than in the group receiving active patches (three out of nine; p<0.01).

Williams et al reported on a case series of 12 patients with schizophrenia treated with nicotine nasal spray. Despite all patients receiving behavioural support and most using another form of pharmacotherapy, the authors observed significant gains in clinical outcome when nasal spray was added to the treatment regimen. The medication was well tolerated and the users responded positively to this delivery system. The authors concluded that behavioural support and combination pharmacotherapy that includes nicotine nasal spray might be a promising treatment for people with schizophrenia.

We identified two randomised placebo-controlled trials of bupropion for smoking cessation in people with schizophrenia. The first trial randomised 32 people with a diagnosis of schizophrenia to bupropion of 300 mg/day or a placebo. All participants received group-based behavioural support. At the end of the 10-week treatment period significantly more people in the bupropion group than in the group receiving the placebo achieved seven-day CO-verified point prevalence abstinence (50% compared with 12.5%, p<0.05). Although the seven-day point prevalence abstinence rates remained higher in the bupropion group at six months the difference was not significantly different (p=0.29). There was no difference between the groups on the effect of positive symptoms of schizophrenia. However, the bupropion group had a 15% reduction in negative symptoms. There were no significant differences in the number of adverse events between the two groups, and the authors concluded that bupropion is safe for use in this population of smokers. Interestingly, it was discovered that atypical antipsychotic drugs (eg, clozapine, risperidone, and olanzapine) seemed to augment the effect of bupropion more so than typical
antipsychotic drugs. In fact, no participants who were assigned bupropion or the placebo and were maintained on typical antipsychotic medications quit smoking, although the relatively small sample size precludes any definitive conclusions. However, it has been reported in other studies that clozapine seems to reduce smoking. The other study randomised a sample of 53 adult smokers with a diagnosis of schizophrenia to a 12-week course of bupropion or a placebo in combination with cognitive behavioural therapy. The results showed a significant benefit of bupropion over the placebo at the end of treatment (a seven-day point prevalence abstinence rate of 16% compared with 0%, p<0.05), but not after 12 weeks.

**Effect of stopping smoking on mood and medication side effects**

Most people with mental health disorders do not experience a worsening in the symptoms of their illness when they stop smoking. Smoking cessation can precipitate a relapse of depression in some people, but this is rare and is not a sufficient reason to not provide support to people to stop smoking; rather it is a reason for monitoring their mental health closely. In the studies reviewed by Bradshaw et al none showed any adverse effects of stopping smoking on psychiatric symptoms or side effects from medication. Moreover, three studies showed an improvement in some of the negative symptoms associated with schizophrenia. The literature review for the US guidelines also concluded that although some smokers may experience a worsening of symptoms related to their mental illness this is not the norm. George et al found no increase in extra-pyramidal side effects or on individual blood levels of antipsychotic medications. Similarly Evins et al found no worsening of clinical symptoms of schizophrenia. In an open label trial of bupropion for smoking cessation in people with schizophrenia there were no adverse effects on the symptoms of schizophrenia.

Smoking tobacco causes induction of the liver enzyme cytochrome P450 (CYP1A1, CYP1A2). This is mainly the effect of the polycyclic aromatic hydrocarbons present in tobacco smoke, not an effect of the nicotine. CYP1A2 is responsible for the breakdown of several medications, and medications metabolised by this enzyme will be metabolised faster in smokers than in non-smokers. On a person's cessation of smoking, these enzymes return to a normal level of activity, but this may mean that several medications are metabolised more slowly, so a dosage adjustment may be needed. Relevant medications are shown in Table 7. There have been case reports of clozapine toxicity following smoking cessation. However, because of genetic variation in the activity of the CYP1A2 enzyme not all smokers will show a clinically significant change in blood levels. It has been suggested that a stepwise 10% reduction in dose per day be undertaken until the fourth day of cessation. As a general rule therapeutic drug monitoring should be carried out following smoking cessation and dosage adjustments should be made accordingly.
Table 7: Drugs affected or not affected by smoking or smoking cessation

<table>
<thead>
<tr>
<th>Drug affected by smoking</th>
<th>Effect of smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caffeine</td>
<td>Increased clearance (by 56%)</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Decreased serum concentrations (by 24%)</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Decreased plasma concentrations (by 28%)</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Possible anti-estrogenic effects</td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>Increased clearance (by 61%)</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Decreased plasma concentrations (by 47%)</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Decreased serum concentrations (by 70%)</td>
</tr>
<tr>
<td>Heparin</td>
<td>Increased clearance</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Decreased serum concentrations</td>
</tr>
<tr>
<td>Insulin</td>
<td>Decreased subcutaneous absorption; possible higher insulin requirements in smokers</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Decreased oral bioavailability</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Increased clearance (by 98%)</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Increased oral clearance (by 77%)</td>
</tr>
<tr>
<td>Tacrine</td>
<td>Decreased mean plasma concentrations (three-fold)</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Increased metabolic clearance (by 58 to 100%); within seven days of smoking cessation, theophylline clearance falls by 35%</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Decreased plasma concentrations (by 13%); no effect on prothrombin time</td>
</tr>
</tbody>
</table>

Stopping smoking can result in the opposite effect to those noted above. Healthcare workers should be aware of the potential for increased blood levels of some of these medications when smoking is ceased. Blood levels of some medications (eg, clozapine, theophylline) may need to be monitored.

**Drugs not affected by smoking or smoking cessation**
- Benzodiazepines (diazepam, lorazepam, midazolam, chlordiazepoxide)
- Bupropion
- Ethinyl estradiol (levonorgestrel)
- Glucocorticoids (prednisone, prednisolone, dexamethasone)
- Paracetamol
- Quinidine

**Drugs on which the effect of smoking or smoking cessation is unclear**
- Nortriptyline

Summary: Few randomised controlled trials have assessed the outcome of smoking cessation interventions for smokers with mental illness. Many studies have methodological problems such as a 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. It is suggested that combination pharmacotherapy might be associated with a superior outcome. Most smokers will not experience a worsening in the symptoms of their mental illness when they stop smoking. Components of tobacco smoke cause the induction of some liver enzymes. Smoking cessation may, therefore, affect the metabolism of several medications.

Strength of evidence: 1+

Evidence statements:

• There is insufficient evidence concerning whether specialised smoking cessation services aimed specifically at smoking cessation in people with mental illness improve six-month continuous abstinence rates.

• There is evidence from two randomised controlled trials that bupropion improves short-term abstinence rates, and that it has a good safety profile in this group.

People who use addiction treatment services

Evidence for smoking cessation in people who use addiction treatment services

Te Rau Hinengaro: The New Zealand Mental Health Survey found particularly high smoking prevalence rates in people with any substance use disorder – 56.2% in non-Māori and 67.5% in Māori. 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 have more medical problems, and, therefore, may be more likely to experience greater difficulty quitting than smokers who do not use drugs.

However, a 2006 review of research articles on smokers with alcohol problems found that despite higher nicotine dependence they did not have more difficulty quitting on a given attempt than smokers without alcohol problems. Overall, the smokers with alcohol problems were less likely to quit over their lifetime, leading the authors to hypothesise that they may make fewer quit attempts, although no studies prove whether this was true.

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 with other drugs, and drug substitution with tobacco. However, it has been suggested it would be best to provide a consistent message and to treat the underlying addiction with quitting all such dangerous substances.
Two major reviews of smoking cessation treatment with addiction service users have been reported. The first, a systematic review included all 24 published studies of drug users in recovery up to 2000. This found that over a variety of treatment approaches quit rates in inpatients had not been higher than 12% after at least six months’ after treatment. Quit rates in outpatients who were drug-free could reach 25% at 1-year after treatment, but in those maintained on methadone cessation rates fell below 12% at six months or longer. The second review, a meta-analysis of 18 randomised controlled trials up to September 2003 included individuals in both treatment and recovery. For those in treatment, the post-treatment point prevalence quit rates were 12% in intervention and 3% in comparison conditions (RR=2.03; 95% CI: 1.21, 3.39). For participants in recovery, quit rates were 38% in intervention and 22% in comparison conditions (RR=1.77; 95% CI: 1.37, 2.30). However, the studies demonstrated more difficulty maintaining cessation with long-term quit rates in intervention and control groups of 7% and 6% (RR=1.00; 95% CI: 0.64, 1.57) in treatment and 20% and 15% (RR=1.31; 95% CI: 0.92, 1.86) in recovery. This study identified several issues with the quality of included studies, but did find stronger effects among studies that provided NRT.

A further analysis of one of the included studies found that, as expected, those who were less dependent (as measured by the Fagerstrom Test for Nicotine Dependence score) and those with less overall opiate use were more likely to succeed in quitting. Other studies have found that those with a longer duration of sobriety are more likely to quit.

We found three more recently published randomised controlled trials comparing different treatment modalities. One study of patients being treated for alcohol dependence randomised participants to intensive behavioural counselling plus NRT or brief advice only. Short-term differences in quitting (30.0% compared with 5.1% CO validated at two weeks, p<0.001) were not maintained to six months (9.3% compared with 2.3% CO validated, a non-significant difference). A further study in smokers with past alcohol dependence found no significant difference in cessation rates between those assigned the 21 mg nicotine patch and those assigned the 42 mg nicotine patch (16.9% and 9.2% respectively 36-week CO-validated point prevalence quit rates).

A randomised controlled trial of cessation for the methadone-maintained recruited from treatment programmes compared minimal support (the 4As approach (ask, advise, assist, arrange) and self-help materials) with intensive support, with both groups receiving NRT if desired. Overall, the study demonstrated low quit rates, even after treatment. The six-month CO-validated point prevalence quit rates showed no difference between the groups (5.2% intensive and 4.7% minimal, OR=1.12; 95% CI: 0.45, 0.83).

A subgroup analysis of smokers (n=94) within a larger randomised controlled trial of topiramate as a treatment for alcohol dependence, looked at 12-week validated quit rates for treatment with topiramate compared with a placebo (OR=4.97; 95% CI: 1.1, 2.3). In this study a 1% increase in drinking abstinence led to an increase of 4% in the odds of smoking abstinence in the topiramate group compared with the placebo group (OR=1.04; 95% CI: 1.01,
However, the study was not designed to look at smoking cessation and there was no long-term follow-up. Therefore, further research in this area is warranted.

**Effects of smoking cessation on treatment for other substance use disorders**

In the meta-analysis described above abstinence rates from other substances were similar in smoking cessation treatment and control groups after treatment, and were higher at long-term follow-up in the treatment group. This led the authors to conclude that smoking cessation may help, and certainly does not hinder, long-term sobriety even if cessation is not achieved. Smoking cessation can precipitate a relapse of a substance use disorder in a minority of clients. However, this should not be seen as a reason not to encourage quitting in all clients, but rather a reason for close monitoring and intensive support.

**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, this effect is not sustained in the long term. There is no evidence that particular types of intervention may be effective in this group, although a meta-analysis suggests NRT-based interventions may be more effective in the short term.

**Strength of evidence:** 1+

**Evidence statements:** There is evidence from randomised controlled trials that cessation interventions do not improve six-month continuous abstinence rates for people with substance use disorders.

**People who make repeat attempts to stop smoking**

Unfortunately, most smokers who attempt to stop smoking will not achieve long-term abstinence. Furthermore, a failed quit attempt, especially if relapse occurs shortly after the quit day, may predict future failed attempts. However, previous failure is likely to indicate greater tobacco dependence and other factors, such as a history of mental illness, that are negative predictors of abstinence. It is also important to note that many other factors are associated with a failed quit attempt, for example, 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. Although two-thirds had relapsed, 65% said 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.\textsuperscript{249} Some studies investigating the use of pharmacotherapies in repeat quitters found little to no effect on long-term cessation.\textsuperscript{98,250–252} One study investigated the use of telephone support for repeat quitters, but failed to show a benefit.\textsuperscript{253} However, other studies demonstrate that pharmacotherapies such as bupropion and NRT have equally good outcomes on active treatment despite previous failure with pharmacotherapies.\textsuperscript{247,254,255}

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. Client preference, ease of use, and contraindications should guide the treatment selection of pharmacotherapy.\textsuperscript{247}

There is some debate about the length of time a client should be made to wait between quit attempts. For example, guidance issued by NICE suggested that the UK National Health Service would not usually fund a quit attempt within six months of a quit attempt.\textsuperscript{85} However, only limited data support this. 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.\textsuperscript{266}

**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 who have tried pharmacotherapies in the past but failed. However, treatment choice should be guided by client preference and will be limited by product contraindications.

**Strength of evidence:** 1+

**Evidence statements:**

- 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.
- There is insufficient evidence to recommend a minimum time between quit attempts.
Relapse prevention

Given the current 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.

One of the problems in reviewing the literature in this area is defining when initial treatment ends and the relapse prevention intervention begins. Some studies have randomised participants before the quit date. In some studies, the relapse prevention treatment begins immediately or soon after the quit date, and in others it begins once the smoking cessation treatment has finished.

Typically, relapse prevention programmes have used a skills approach whereby recent ex-smokers are taught to recognise high-risk situations and then taught skills to try to resolve the temptation. Other programmes have used cue-exposure techniques, aversive smoking, exercise, extending the duration of the treatment period, and ongoing pharmacological treatment.

The Cochrane review identified 40 studies that met its inclusion criteria. More than half of these included participants who had already stopped smoking. Nine specifically examined the efficacy of interventions aimed at women who had stopped smoking. In studies that recruited people who had recently stopped, eight tested behavioural interventions and three examined the efficacy of pharmacological approaches.

Meta-analyses of published studies with long-term follow-up have not provided any evidence for the effectiveness of relapse prevention programmes. Pooling the results from studies examining the efficacy of interventions in women who had stopped smoking during their pregnancy gave an overall odds ratio of 1.08 (95% CI: 0.92, 1.27).

Behavioural approaches in people who had stopped smoking without any assistance (n=2,878) showed no effect (OR=1.14; 95% CI: 0.94, 1.38). The same result was derived in smokers who had received some sort of help to stop smoking (OR=1.00; 95% CI: 0.80, 1.25). The pooled results of two studies testing the success of nicotine gum compared with placebo gum to help prevent relapse showed a borderline beneficial effect (OR=1.30; 95% CI: 1.06, 1.61), increasing long-term success rates 4% (95% CI: 1%, 7%). Two trials of bupropion have failed to show a benefit over the use of a placebo (OR=1.25; 95% CI: 0.86, 1.81).

Although there is little positive news regarding relapse prevention, several factors 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 a lack of originality in the interventions tested with most focusing on a skills-based approach. The possibility that this approach does not work must be considered. Alternatively, the approach may work, but the skills may not be taught effectively. Finally, many of the interventions were brief and one-off. Given the nature of tobacco dependence, this may not be
enough. If we are to increase the number of recent ex-smokers abstaining for a year or more we need to develop and test innovative approaches to relapse prevention. Suggestions include approaches that maintain motivation to remain abstinent, maintain awareness about the hazards of a lapse and how it can lead to a complete relapse, support the ongoing opportunistic use of NRT, support ongoing social support, and support contingency contracting.

The question remains about what should be done until evidence for effective relapse prevention is available. Commonsense advice can be provided, but extensive resources should probably not be used to fund relapse prevention programmes that will not be evaluated. For now, it may be better to channel resources into encouraging more smokers to make a quit attempt and providing cessation support for those who want it.

**Summary:** Despite several studies, there is no conclusive evidence for the efficacy of specific interventions for preventing relapse.

**Evidence level:** 1+

**Evidence statement:** There is inconsistent evidence on relapse prevention interventions to draw any conclusions.
Other treatments and interventions

Cytisine

Cytisine is a product that may be effective and inexpensive in helping smokers to stop smoking. Cytisine is an alkaloid found in plants such as golden rain (Cytisus laburnum), which is native to Europe but grows in the southern parts of New Zealand. A Bulgarian pharmaceutical company (Sopharma) manufactures cytosine and markets it as Tabex. Cytisine was introduced in several Eastern European countries as a smoking cessation medication in the late 1960s and it remains in use today in countries such as Bulgaria and Poland. Its use in smoking cessation stems from the fact it is a nicotine analogue, acting as a partial nicotinic acetylcholine receptor agonist. It has a high affinity for the alpha-4 beta-2 receptor subtype, which is thought to be the main receptor that mediates the central effects of nicotine. In fact, the newly developed drug varenicline was derived from, and is similar in structure and function to, cytisine.

Several efficacy trials of cytisine have been published in Eastern Europe, but these have gone largely unnoticed in Western countries. A recently published meta-analysis showed that pooling the results of these studies produced an odds ratio after 3–6 months of 1.83 (95% CI: 1.12, 2.99). Finally, a rigorous cohort follow-up study demonstrated long-term validated continuous abstinence rates of 14%, suggesting an active treatment ingredient. This compares with rates of about 4% found in untreated smokers attempting to stop in countries such as the US and UK, and 15–20% in clinical trials of NRT with intensive behaviour support.

Like nicotine, cytisine is toxic in animals when ingested in large amounts. Preclinical studies showed an increase in liver transaminase concentrations in animals given a dose of 1.35 mg/kg for a period of 90 days. However, a Bulgarian case report is of a psychiatric patient who survived two suicide attempts that involved digesting very large numbers of cytisine tablets. Symptoms of nicotine intoxication are observed in cytisine overdose. The toxic effects are similar to those found with nicotine and include nausea, vomiting, pupil dilation, tachycardia, general weakness, clonic convulsions, and paralysis of respiration. When used in its therapeutic dose (1.5–9 mg per day) cytisine is reported to be well tolerated with few reported adverse effects. This is similar to what is seen with NRT. The most prominent effects are nausea, dry mouth, constipation, and nausea, affecting up to 10% of users. By way of comparison, nausea is experienced in up to 30% of varenicline users. Changes in taste and appetite and a mild elevation in arterial blood pressure are also reported. Altogether, the discontinuation rate due to side effects in the recent cohort study was 16%. This is comparable to other current medications such as bupropion and oral NRT products. Although the medication has been used for some 40 years in several countries, the lack of good quality studies is a limitation.
On the basis of the experimental data, it is recommended that cytisine should not be taken by pregnant women because of the potential risk to the foetus. It is also recommended that the drug should not be administered during breastfeeding.

The reason for cytisine being contraindicated in arterial hypertension and ‘advanced atherosclerosis’ is not clear. Cautions for use in smokers with certain diseases are listed in the product information. These cautions are stated primarily because there is insufficient clinical experience with cytisine administration in smokers with these conditions and it is recommended that cytisine be provided after the potential benefit has been weighed against the possible risks. Some NRT product licences have similar cautions. Cytisine does not affect a person’s ability to drive or operate machines. There are no known clinically significant drug interactions of cytisine with other drugs.

Summary: The evidence suggests cytisine could be a useful smoking cessation aid. However, more robust research is needed.

Strength of evidence: 1-

Evidence statement: There is evidence from one randomised controlled trial that suggests that cytisine improves six-month continuous abstinence rates. Evidence from studies with shorter follow-up periods and recent highly positive results of a similar medication corroborate the statement above.

Glucose

Glucose is known to reduce appetite, and it is because of this effect that its role in helping smokers to quit has been investigated. The relationship between smoking and appetite is interesting, but complex. Caloric restriction, for example, increases cigarette consumption, and restricting food intake while trying to stop smoking is associated with an increased risk of relapse. Conversely, smoking acutely reduces hunger, and in some studies has been found to decrease the desire for and consumption of sweet tasting foods.

Using glucose to help smokers stop was first proposed by West et al in 1990. It was initially hypothesised that due to the hunger-suppressing effects of smoking and other physiological mechanisms (eg, the effects of smoking on glucoregulation), hunger may become a cue for smoking. Glucose might alleviate the urge to smoke by satisfying the need for carbohydrates and satiating appetite. More recently, it is thought that glucose may exert an effect on withdrawal relief through a complex pathway involving serotonin, tryptophan, and insulin. Drugs that increase the release of serotonin reduce appetite. Nicotine stimulates the release of serotonin in parts of the brain whereas smoking cessation leads to a reduction in serotonin levels. The production of serotonin depends on tryptophan, and the entry of tryptophan into the brain is indirectly influenced by insulin. Glucose increases plasma insulin levels that lead to a reduction in blood levels of large amino acids that compete with tryptophan for uptake into the brain. Therefore, a relative decrease in these
amino acids would result in a greater uptake of tryptophan into the brain, leading to an increase in serotonin.

Two randomised studies, one published and one unpublished, by West and colleagues have examined the effects of glucose on abstinence.\textsuperscript{271,272} One showed a benefit from using glucose tablets over a placebo in short-term (four-week) abstinence rates. However, the effect on the longer-term outcome disappears. However, in a subsample who used glucose or a placebo in addition to routinely used smoking cessation medications (NRT or bupropion), six-month abstinence rates favoured glucose (18%) over the placebo (13%). However, this positive finding is based on post hoc analyses and needs to be confirmed by future studies. Several investigators have looked at the effect of glucose on tobacco withdrawal symptoms; results have been mixed.

Glucose seems to improve abstinence only when used in combination with NRT or bupropion. On the available evidence, it is unlikely to be an effective smoking cessation agent when used on its own. Glucose is generally safe, but cannot be used in those with diabetes. A simple urine dipstick test for glucose should, therefore, be undertaken before giving smokers large quantities of glucose.\textsuperscript{273} It is not clear what risks the short-term use of glucose presents for dental health. Smokers may be concerned about additional weight gain when using glucose but results seem to show no significant difference in post-cessation weight gain between participants on glucose and participants on a placebo.

**Summary:** Evidence from one good quality randomised controlled trial suggests glucose on its own does not improve six-month continuous abstinence rates.\textsuperscript{272} This trial suggests that glucose may improve the efficacy of other smoking cessation medications (bupropion or NRT).

There is evidence that glucose improves short-term abstinence, and the effect seems stronger when used with NRT or bupropion.

**Strength of evidence:** 1+

**Evidence statement:** Evidence from one good quality randomised controlled trial, directly applicable to the UK, shows that glucose on its own increases short-term (one-month) but not long-term (six-month) continuous abstinence rates. Post hoc results suggest that it may increase the efficacy of other smoking cessation medications.

**St John’s wort**

St John’s wort (Hypericum perforatum L.) extracts are known to have antidepressant properties, and have been used for many years to treat mild to moderate depression, anxiety, and sleep disorders. St John’s wort’s antidepressant effects have led some to believe it might be a useful aid for smoking cessation. The link between smoking and depression has been long recognised. There is a higher prevalence of smoking among people who have a history, or current diagnosis, of depression, smokers who are depressed find
it more difficult to quit than smokers who are not, some smokers become depressed when they stop smoking, and post-cessation depression is related to relapse. Antidepressants such as bupropion and nortriptyline have a proven efficacy in aiding smoking cessation, although this is not a property of all antidepressants. St John’s wort has been shown to attenuate nicotine withdrawal symptoms in an animal study and in a single study in humans.

In a review of natural and complementary therapies for substance use disorders St John’s wort was identified as a potential treatment for nicotine withdrawal. Two small studies suggest that St John’s wort, at doses up to 600 mg per day, has no effect on smoking cessation.

Summary: There is no evidence that St John’s wort is helpful for smoking cessation. Further evidence from good quality studies is required.

Strength of evidence: 1-

Evidence statement: There is insufficient evidence on St John’s Wort to draw any conclusions.

Lobeline

Lobeline is a partial nicotine agonist and comes from a plant, Lobelia inflate, (also known as Indian Tobacco). It is structurally similar to nicotine, which is why it was used as a smoking cessation aid. However, the US Food and Drug Administration banned the sale of this product in 1993 due to the lack of good quality data. Despite this, the product is still available online and may appeal to some smokers.

A Cochrane review has been undertaken, but none of the studies available met the inclusion criteria, mostly because studies with a long-term outcome lacked a control group. The review identified controlled trials that reported on the short-term outcome but none showed any advantage of lobeline over a control.

Summary: There are no good quality studies that adequately assess the efficacy of lobeline in aiding smoking cessation.

Evidence statement: There is insufficient evidence on lobeline to draw any conclusions.

Clonidine

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, and has been shown to reduce the symptoms of tobacco withdrawal, and increase abstinence rates.
A Cochrane review of clonidine use for smoking cessation identified 21 studies, many with only short-term follow-up. Six studies met the inclusion criteria, with the pooled results showing an odds ratio of 1.89 (95% CI: 1.30, 2.74). However, clonidine has multiple adverse effects, such as postural hypotension, dizziness, and a dry mouth. Other reported symptoms include those that are also typical of nicotine withdrawal (depression, constipation, and sleep disturbance). Clonidine causes sedation, although this could be beneficial in those with very intense symptoms of tobacco withdrawal. Patients with a history of depression or occlusive peripheral vascular disease are advised not to use clonidine.

Treatment with clonidine is usually from 2–3 days before quitting to the first 3–4 weeks after quitting. It can be taken orally (0.1 mg per day gradually increased to 0.4 mg per day) or through a transdermal patch (0.1–0.3 mg per day). The dose has to be reduced over several days to avoid a hypertensive crisis and hypoglycaemia in people with hypertension and diabetes respectively.

Summary: There is evidence that clonidine is helpful for smoking cessation, but because of its extensive adverse effect profile it is not recommended for use.

Strength of evidence: 1+

Evidence statement: There is robust evidence from randomised controlled trials that clonidine improves six-month continuous abstinence rates.

Anxiolytics

Medications used for treating anxiety have been examined as possible smoking cessation aids. A Cochrane review of anxiolytics identified one trial for diazepam, meprobamate, metoprolol, and oxprenolol and two for buspirone that met the inclusion criteria.

Buspirone is an atypical anxiolytic that is believed to act through its serotonergic and dopaminergic activity. However, there seems to be no clear effect on tobacco withdrawal symptoms, and pooled results from two long-term studies comparing buspirone with a placebo showed no benefit of using buspirone for smoking cessation (OR=0.71; 95% CI: 0.34, 1.48). Diazepam and meprobamate were not found to aid smoking cessation. Little evidence of effectiveness was demonstrated for three beta-blockers (propanolol, metoprolol, and oxprenolol). There are no good long-term studies of ondansetron, a 5-HT3 antagonist thought to affect the reinforcing properties of nicotine. In addition, there may no longer be a rationale for the use of anxiolytics, as anxiety seems to decrease rather than increase after cessation of smoking.

Summary: There is no evidence that anxiolytics are helpful for smoking cessation.

Strength of evidence: 1+
**Evidence statement:** There is evidence from randomised controlled trials that anxiolytics do not improve six-month continuous abstinence rates.

**Nicobrevin**

Nicobrevin is a product that was developed in Germany in the late 1960s and has been marketed for smoking cessation in several countries for some years. It is composed of four main ingredients each with an action claimed (without supporting evidence) to facilitate smoking cessation: (1) menthyl valerate to help through sedative and anxiolytic effects; (2) quinine to relieve withdrawal; (3) camphor; and (4) eucalyptus oil to relieve ‘airway symptoms’.

The Cochrane review\(^2\) identified two studies\(^2\) 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 the short-term outcome but both studies pose methodological problems, so the data from these studies must be considered carefully.

**Summary:** No data are available on the effects of Nicobrevin on long-term smoking cessation. Two trials suggest that Nicobrevin may have an effect on the short-term outcome but both studies pose methodological problems.

**Strength of evidence:** 1-

**Evidence statement:** There is insufficient evidence on Nicobrevin to draw any conclusions.

**NicoBloc**

NicoBloc is marketed in several countries as a smoking cessation aid and is often sold through community pharmacies. It comes in a liquid form, containing a sugar compound that is dropped onto the filter of a cigarette. It then dries and forms an occlusive barrier to nicotine and tar, thereby reducing the delivery of these substances to the smoker. At its ‘full dose’ it is said to trap up to 99% of tar and nicotine (one drop traps 33%, two drops trap 66%, and three drops trap 99%) without affecting the taste or smoker’s satisfaction of the cigarette.

This product’s proposed mechanism of action is that of a gradual reduction of cigarette consumption and nicotine intake. NicoBloc aims to stop the compensatory smoking that usually occurs with a 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 they apply to the filter.

This substance has been used by a large number of smokers and two cohort follow-up studies report success rates of 42–58% at the end of a course of treatment (six weeks).\(^1\) However, the study methodology and outcome criteria are not well 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 a placebo.\(^2\)
Summary: One small, well-designed randomised double blind placebo controlled trial showed no benefit of NicoBloc over the placebo.

Strength of evidence: 1-

Evidence statement: There is insufficient evidence on NicoBloc to draw any conclusions.

Rongoā Māori
We found no published studies investigating the effectiveness of traditional Māori medicine (rongoā Māori) for aiding smoking cessation.

Evidence statement: There is insufficient evidence on rongoā Māori to draw any conclusions.

Hypnosis
Hypnosis is one of the most widely advertised and best-known alternative treatments for smokers. It has been used by smokers for many years, and is said to work by placing the smoker in a heightened level of attention during which suggestions regarding the risks of smoking, the benefits of quitting, and the determination and commitment to stop can be imparted. The most commonly used technique (Spiegel's single-treatment session) typically combines post-hypnotic suggestion with self-hypnosis. Smokers are taught to repeat to themselves five suggestions: they have a responsibility to their body; they need their body to live; smoking is poisonous to their body; they owe their body protection; and they owe it to their body to stop smoking. There are other versions of hypnosis, for example, those that provide more-intensive treatment combining elements such as an initial assessment session (an assessment of mental status and smoking history, a discussion about smoking, reasons for quitting, and setting a quit day), more hypnotherapy sessions, and self-hypnosis.

The Cochrane review of hypnotherapy for smoking cessation included nine studies in its meta-analysis. The methods of hypnosis varied in intensity (from a single session to a nine-week programme) and duration (from 30 minutes to seven hours in total). There was no benefit in smokers receiving hypnotherapy compared with 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 caution. Hypnosis is a safe intervention, although it may worsen symptoms in those experiencing mental illnesses such as schizophrenia and bipolar disorder. Hypnosis may also result in the emergence of unpleasant memories in people experiencing post-traumatic stress disorder, and caution is advised in those with major depression and borderline personality disorder.
Summary: In randomised trials controlling for attention, hypnosis does not increase long-term quit rates. However, it may be better than no treatment at all.

Strength of evidence: 1+

Evidence statement: There is evidence from a meta-analysis of randomised controlled trials that hypnotherapy does not improve six-month continuous abstinence rates more than attention control does. There is evidence that hypnotherapy may be more effective than no treatment.

Acupuncture

Acupuncture is one of the most widely used complementary treatments. It is used to treat a variety of illnesses with varying degrees of effectiveness. Reviews have concluded that acupuncture is effective for nausea and vomiting (particularly that occurring post-operatively and induced from chemotherapy) and dental pain. Evidence is unclear for chronic pain. Acupuncture is ineffective for weight loss or smoking cessation.

Acupuncture has been part of traditional Chinese medicine for centuries. It is believed that a person’s state of health and wellbeing is influenced by a vital energy known as qi (pronounced ‘chee’). This energy must move between organs, along channels called meridians, in the correct strength and quality to maintain health. The insertion of needles at different points is said to change the energy flow along the meridians and so treat different illnesses. The contemporary belief is that acupuncture might exert its effect on anatomical and physiological points, such as junctions of peripheral nerves, by increasing blood flow or releasing endorphins and neurotransmitters.

The basis for using acupuncture to aid smoking cessation arose from observations made in a group of Chinese opiate addicts treated with electroacupuncture (electrical stimulation to acupuncture needles) who were said to suffer less severe withdrawal symptoms. One of the proposed mechanisms of action for this effect is through the release of endorphins and neurotransmitters such as dopamine, serotonin, and noradrenaline, which have all been shown to have a role in tobacco dependence and withdrawal.

There are two main treatments for smoking cessation. The first typically involves inserting needles at points on the ear (eg, the lung and hunger auricular points) or on the face while 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 may also be applied. The second involves inserting needles into points in the ear and securing them in place for a length of time (eg, 1–3 weeks). These can then be pressed whenever the person has an urge to smoke. Instead of needles small beads or seeds can be used. These are usually taped in place, and 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 a low-level laser. Although there is no sensation on the skin, laser acupuncture is said to stimulate traditional acupuncture points in a similar way as other techniques.

Many studies investigating the efficacy of acupuncture for smoking cessation are marred by methodological problems that make it difficult to interpret the results. The Cochrane review of acupuncture and related interventions for smoking cessation is the most recent and comprehensive systematic review.\(^{268}\) Like the other Cochrane reviews, it uses strict criteria for the inclusion of studies into the meta-analysis. When the results of studies comparing acupuncture with sham (placebo) acupuncture were pooled, there was no evidence of any benefit of acupuncture over the placebo in aiding long-term smoking cessation (OR=0.99; 95% CI: 0.68, 1.44). Only a few studies compared acupuncture with other smoking cessation treatments. No differences were demonstrated between acupuncture and a one-week supply (105 pieces) of 2 mg nicotine gum and behavioural approaches. One study showed no difference in adding acupuncture or sham treatment to smoking cessation counselling. There is no evidence that any acupuncture technique is better than another. Although acupuncture is said to have some effect on withdrawal symptoms there is no evidence from randomised controlled trials to support these claims.

The US guidelines carried out a series of meta-analyses of various interventions for smoking cessation and reached similar conclusions.\(^{4}\) Five studies that investigated the efficacy of acupuncture compared with ‘control acupuncture’ were included. There was no difference in the estimated abstinence rates between the two treatments (8.9% compared with 8.3% for acupuncture and control respectively).

When acupuncture is practised competently, there are very few adverse events. Pain from the skin punctures is the most commonly reported side effect, while other common side effects include bleeding, bruising, fainting, fatigue, and light-headedness. Although extremely rare, there are documented reports of serious adverse events such as pneumothorax, cardiac tamponade, hepatitis B, and spinal lesions. Slightly less serious events include broken or forgotten needles.

**Summary:** Acupuncture does not increase long-term quit rates more than placebo treatment.

**Strength of evidence:** 1+

**Evidence statement:** There is evidence from meta-analyses of randomised controlled trials that acupuncture, acupressure, laser therapy, and electrostimulation do not improve long-term abstinence rates compared with the use of a placebo.

**Allen Carr’s Easyway method**

Allen Carr’s book *The Easy Way to Stop Smoking* (first published in 1985) is one of the best-known approaches to helping smokers quit. Allen Carr’s Easyway is a commercial organisation providing face-to-face smoking cessation
treatment. According to its website, it treated more than 35,000 smokers worldwide in 2005 with a success rate of more than 90%. The method claims to remove the smoker’s conflict of will, cause no bad withdrawal pangs, be instantaneous and easy, be equally effective for long-term heavy smokers and light smokers, and not result in weight gain, and that the person will not miss smoking. Smokers are typically seen once, either in groups of up to 25 people or individually. The sessions last for 4–5 hours, with shorter ‘booster’ sessions available if required by patients.

Underpinning the treatment is the hypothesis that smokers continue to smoke because they are afraid to quit, fearing the loss of something they enjoy. The treatment, delivered through a structured lecture and discussion, aims to remove the belief that smoking provides pleasure and to increase the confidence of the smoker that they can stop smoking without suffering any great loss. In the parlance of contemporary clinical psychology, it can be classified as a form of cognitive therapy.

There is little published literature about the efficacy of this smoking cessation method. There are no randomised controlled trials. Cohort studies report the outcome of using the Allen Carr technique in workplace settings as one-year abstinence rates of 36–40%. These rates need to be interpreted with caution, because the investigators relied on self-reported abstinence, which was not biochemically validated, and smoking status was not clearly defined. Randomised controlled trials are needed to assess the true efficacy of this method.

Summary: There have been no randomised controlled trials of the Allen Carr method to determine its effectiveness.

Strength of evidence: 2-

Evidence statement: There is insufficient evidence on the Allen Carr method to draw any conclusions.

Rapid smoking

Aversive treatments for smoking cessation reached their height of popularity in the 1970s and early 1980s. With the advent of NRT and other pharmacological treatments for smokers, the interest in aversive techniques declined, and they are now rarely used. Nevertheless, there is a large body of literature on rapid smoking in particular, and the US guidelines consider the method effective. A recent Cochrane review, although more guarded, also found signs of efficacy.

The general aim and rationale of aversive treatments for smoking cessation is to link smoking with an unpleasant stimulus to reduce its desirability. The first version of aversion therapy for smokers involved blowing warm stale smoke in subject’s faces while they smoked. Among other methods, unpleasant electric stimulation was also tried. The approach that eventually became the treatment of choice was ‘rapid smoking’, which was first proposed in 1968. It has also become the most extensively examined behavioural treatment for
smoking cessation. Smoking cigarettes rapidly produces swift increases in plasma nicotine levels, which lead to a degree of ‘nicotine overdose’ and unpleasant central symptoms such as nausea. In addition, there are also irritant sensory effects of the tobacco smoke on the oral mucus membranes, throat, and airways. The standard method of rapid smoking requires the smokers to puff on their own brand of cigarette once every six seconds. The treatment session continues until the patient has smoked a certain number of cigarettes or until they cannot tolerate further smoking. After a five-minute rest period where participants have a chance to recover and reflect on the experience, the procedure is repeated. This pattern continues until the patient cannot tolerate any further treatment. The timing of treatment could vary from consecutive days to weekly intervals. During the intervals between sessions patients are instructed not to smoke and to concentrate on the unpleasant sensations rapid smoking has caused.

Rapid smoking is not a ‘stand-alone’ treatment because most studies combined it with cognitive behavioural components, and regular support from the therapist coordinating the sessions. Most of the relevant literature is from the early days of smoking cessation research, with methodology considered poor by today’s standards. For example, a self-reported reduction in cigarette consumption is often used as an outcome and is rarely biochemically validated; when abstinence is measured it is not clearly defined; studies often lack a good control group; sample sizes are very small; and follow-ups are not blind to subject allocation. A therapist effect is sometimes noted, and as in all behavioural treatments, it is difficult to blind subjects and investigators.

The US guidelines carried out a series of meta-analyses of various interventions for smoking cessation. The authors concluded that there was an beneficial effect of rapid smoking (OR= 2.0; 95% CI: 1.1, 3.5), although this method was not considered to be a first line treatment, but instead one that may be used in smokers for whom other methods had been unsuccessful or if they wanted to try it. The meta-analysis undertaken in the Cochrane review arrived at a similar outcome, showing that the six-month abstinence rates for rapid smoking compared with a control were 36% compared with 22% (OR=1.98; CI: 1.36, 2.90). Furthermore, the intensity of aversive stimulation was marginally related to outcome (OR=1.66; CI: 1.00, 2.78). In addition to smoking cessation outcome studies, ‘modern’ studies have assessed the effect of rapid smoking on withdrawal. These showed some evidence of an effect of rapid smoking on reducing craving.

Although rapid smoking is safe when used in the majority of healthy smokers, harmful effects are always possible. Two main concerns regarding the use of this procedure are the risks of nicotine poisoning and cardiovascular events. The likelihood of nicotine poisoning is extremely unlikely. However, given that smoking in this fashion increases the heart rate, systolic blood pressure, and carboxyhaemoglobin, the possibility of an adverse cardiac event is of greater concern. ‘Real-life’ data from the 1970s, however, estimates that more than 30,000 smokers had used the procedure, and there were no reports of serious adverse events. No reports of significant adverse events related to the use of this procedure have emerged.
Even if rapid smoking has a positive effect on withdrawal and cessation outcome, this method is unlikely to become a mainstream cessation method.

**Summary:** Studies show a significant effect of rapid smoking. However, a cautionary note was added to the findings from the Cochrane review, because a funnel plot of included studies was asymmetric due to the relative absence of studies with negative results. Also, most trials used methodologies that were ‘state of the art’ at the time, but that would not be up to current standards. The review concluded that rapid smoking cannot be considered a proven method, but there are sufficient indications of promise to warrant further evaluation. Other strands of evidence suggest the method may have an active ingredient. These include the evidence for a dose–response effect and the finding from recent studies that rapid smoking has an positive effect on craving.

**Strength of evidence:** 1-

**Evidence statement:** There is evidence from randomised controlled trials that rapid smoking improves six-month continuous abstinence rates.

### Competitions and incentives for smoking cessation

The provision of a reward for stopping smoking has been used as an incentive in several settings. Workplaces, for example, have used financial incentives to encourage employees to stop smoking. Rewards have been in the form of cash payments, and salary bonuses.

The Cochrane collaboration sought to investigate the effect of competitions and incentives on long-term quit rates, as well as the relationship between the provision of incentives and participation rates. The authors identified 15 randomised controlled trials that met Cochrane inclusion criteria. Several of these studies offered incentives for attendance on and completion of the programme. Other studies offered payments for verified abstinence at various time points or over a predefined period. All but one of the studies provided smoking cessation treatment in addition to the incentives.

None of the studies showed any effect of incentives or competitions on long-term abstinence. The studies included in the review were often underpowered and had methodological flaws.

One of the key findings, as may be expected, was that these interventions might work, but 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 who are less motivated to quit or who find it harder to quit. A more obvious disadvantage of
these programmes is that a proportion of participants claiming to be smokers will be non- or ex-smokers at the time of their entry into the programme. Workplaces may be less susceptible to this falsification, but large incentives may still be a motivating factor for deception.

**Summary:** Incentives or competitions as part of smoking cessation programmes do not increase long-term abstinence rates.

**Evidence level:** 1+

**Evidence statement:** There is robust evidence from randomised controlled trials that incentives and competitions do not improve six-month continuous abstinence rates.

### Quit and Win contests

Quit and Win contests as a means of promoting smoking cessation have been used since the 1980s. The first published report of such interventions, by the Minnesota Heart Health Programme, entered biochemically confirmed quitters into a large prize draw and achieved a 35% one-month quit rate.

Since then, such competitions have been used in tobacco control programmes. In 1994, an international Quit and Win competition was undertaken, involving 13 countries with an average 12-month continuous abstinence rate of 21%.

A Cochrane systematic review of this topic identified four trials for inclusion. All had relatively small sample sizes (about 300–600 participants). Three were non-randomised controlled trials that showed a difference in 12-month abstinence rates (8–20%). However, the fourth study, a randomised controlled trial, failed to show any difference between intervention and control groups.

Although evidence from non-randomised trials shows some smokers benefit from these interventions, the impact on the prevalence of smoking among the whole population is low. It is estimated that fewer than 1 in 500 smokers will quit as a result of this type of intervention.

**Summary:** Evidence from non-randomised controlled studies suggests Quit and Win contests increase long-term quit rates, but the population impact is low.

**Evidence level:** 1-

**Evidence statement:** There is insufficient evidence from randomised controlled trials of the efficacy of Quit and Win contests to draw any conclusions.

### Exercise to aid smoking cessation

Studies have investigated the use of exercise in aiding smoking cessation. Evidence shows that exercise may help alleviate the symptoms of tobacco withdrawal. There is a good rationale for interventions that reduce withdrawal symptoms, because some symptoms have been shown to predict
relapse (e.g., urges to smoke\textsuperscript{212,302} and depression\textsuperscript{303}). Exercise might be helpful for several reasons. It may provide an alternative reinforcer to smoking or it might simply be a distraction from smoking. It may also help by increasing self-esteem, and may have a positive effect on managing post-cessation weight gain.\textsuperscript{304}

The Cochrane review on exercise interventions for smoking cessation identified 11 randomised controlled trials with adequate follow-up. All but one of these studies examined the effect of exercise in combination with standard smoking cessation treatment and compared outcomes with a control condition that also received smoking cessation treatment. In three of the studies, the smoking cessation outcome was higher in the intervention group than in the control group. In all other studies, no significant differences were observed. Methodological problems exist between the studies that make some of the results difficult to interpret. These are common to many studies of behavioural intervention and include such factors as small sample size, varied durations and intensities of the exercise intervention, the inconsistent measurement of physical activity and whether it was supervised or not, and the varied adherence to the treatment programme. In addition, the design of the control condition was not always optimal.

Although little evidence supports the use of exercise as a stand-alone smoking cessation intervention, smokers should not be discouraged from adopting exercise during their cessation attempt. One study reported that pregnant smokers expressed a high level of interest in exercise to help them quit.\textsuperscript{305} Finally, it is worth noting that there is also the question of when the exercise intervention should be implemented: before or while stopping smoking. No data suggest that one approach is better than the other.

**Summary:** Evidence does not show that exercise can increase smoking cessation rates. However, some evidence suggests that exercise may alleviate some of the symptoms of tobacco withdrawal.

**Evidence level:** 1+

**Evidence statement:** There is insufficient evidence on exercise to aid smoking cessation to draw any conclusions.

**Partner support**

Support is an important factor when stopping smoking. This may be provided by a smoking cessation specialist, other people who are stopping smoking at the same time, or family and friends. Having a partner who smokes is a negative prognostic factor, as is not having a partner. Studies that have sought to examine the efficacy of increasing partner support on smoking cessation outcome have, overall, not demonstrated any long-term benefit.\textsuperscript{306} The Cochrane review on enhancing partner support to improve smoking cessation identified nine studies for including into the meta-analysis.\textsuperscript{307} The pooled results show no significant benefit of increasing partner support on long-term (6–9 months) abstinence rates (OR=1.08; 95% CI: 0.81, 1.44). However, most
have relied on general educational methods as the main component of the intervention, so it may be that education is not sufficient to foster the appropriate degree of support needed. Also, these studies, like many others that examine behavioural interventions, suffer from methodological problems such as inadequate sample sizes and participants and investigators are not blinded to the intervention or control.

There has been interest in the use of ‘buddy support’ within smoking cessation treatment programmes. This is where social support is provided by another member of the smoking cessation programme (ie, another smoker who is quitting). A review undertaken on this topic identified methodological problems in the literature, but, nonetheless, suggested that using a buddy system within the context of a smoking cessation clinic might be of some benefit.\textsuperscript{308} However, the results of a randomised controlled trial testing the effectiveness of the buddy system within this clinical setting showed no benefit.\textsuperscript{309}

**Summary:** No evidence supports the implementation of interventions to enhance partner support to increase smoking cessation rates. However, the interventions tried may not have been enough to alter the degree of support.

**Strength of evidence:** 1+

**Evidence statement:** There is insufficient evidence on enhancing partner support to draw any conclusions.

**Biomedical feedback**

Smokers can often see few of the adverse effects of smoking on their bodies until the damage has reached a stage where it causes physical disease. Furthermore, smokers often experience little immediate change in health when they stop smoking. It has been reasoned that if smokers could see the damage smoking was doing to their bodies, then they would be more likely to quit. There are various ways smokers can receive feedback on the physical effects of smoking. This might be by the measurement of smoke exposure (eg, a measurement of carbon monoxide in breath, or cotinine in saliva or urine), an assessment of smoking-related harm (eg, a lung function test), or an assessment of the risk of developing a smoking-related disease (eg, a genetic susceptibility to the adverse effects of tobacco smoke). The effect of these assessments on the smoking cessation outcome has been the subject of two systematic reviews by the same authors.\textsuperscript{310,311}

The Cochrane review on biomedical risk assessment as an aid for smoking cessation identified eight randomised controlled trials that met the inclusion criteria, although these were of variable quality.\textsuperscript{311}

Three studies access the effect of CO measurement on the smoking cessation outcome. The pooled results failed to show an effect (OR=10.7; 95% CI: 0.83, 1.39). There was also no effect from undertaking spirometry (OR=1.21; 95% CI: 0.60, 1.41) or a combination of spirometry and CO measurement. A single study assessed the effect of genetic testing (ie, the susceptibility of lung
cancer), but showed no effect on the smoking cessation outcome (OR=0.80; 95% CI: 0.93, 1.65). One study showed a positive outcome of using ultrasonography of the carotid and femoral arteries to demonstrate the existence of atherosclerotic plaques. Participants (n=155) were randomised to an intervention group (with participants receiving ultrasonography and smoking cessation counselling, and, if one or more plaques were present, a photograph of the ultrasound result) or a control group (with participants receiving smoking cessation counselling only). At the six-month follow-up the unvalidated seven-day point abstinence rates were higher in the intervention group (OR=3.15; 95% CI: 1.06, 9.31). However, participants in this study were relatively light smokers, so caution is needed when interpreting these results.

**Summary:** There are too few data to provide a sense of whether measurement of biomedical risk is helpful in aiding smoking cessation.

**Strength of evidence:** 1-

**Evidence statement:** There is insufficient evidence on biomedical risk assessment to draw any conclusions.
Cost-effectiveness of smoking cessation treatments

There is relatively little New Zealand–specific data on the cost-effectiveness of smoking cessation treatments. Previous New Zealand reviews have been based on international evidence that shows the overwhelming cost-effectiveness of smoking cessation treatments, both behavioural and pharmacological.

Cost information is often presented 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, because the earlier in life a person stops smoking the more life years they are expected to gain. It is noted that the LYS measure is a conservative measure of effectiveness, because it considers only mortality as an outcome. Another measure, quality-adjusted life years saved (QALYs), is more inclusive, because it includes all benefits (eg, the improvement in health) from stopping smoking, not just the 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 accurate than LYS.

Many smoking cessation treatments look at only the short-term outcome or, at best, smoking cessation rates at one year. However, with known relapse rates estimations can be made. For example, it is expected that 60–65% of four-week abstainers will have relapsed by a year. The relapse rate after a year is about 35%. Therefore, subtracting this percentage from one-year abstinence rates will give the proportion of lifelong ex-smokers.

Published New Zealand studies have examined the cost-effectiveness of television advertising campaigns in generating calls to Quitline by Māori, although the data are expressed simply as the cost of generating calls to Quitline. The study assessed calls during a two-year period (2002 and 2003), over which time there were almost 15,500 new calls from Māori who smoke. This represents about 8% of all Māori adults who smoke. The total cost of the advertising campaign driving these calls was $304,560, giving the cost per call $30–$48.

The UK smoking cessation guidelines (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. 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 was undertaken to determine the cost-effectiveness of the stop smoking services. In the one-year period (1 April 2000 to 31 March 2001) the NHS had contributed £21.4 million to the set-up, running, and monitoring of the service. This figure did not include the costs of medication provided on prescription, and only NRT was provided by a voucher system (similar to the New Zealand Quit Card scheme). In the same period, 126,800 people made an attempt to stop smoking with 48% abstinent at the end of four weeks of treatment. Simply
calculating the cost per person treated gives a reasonable figure of £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 one-year abstinence rate is about 17%, which equates to 11% of all people using the services becoming lifelong ex-smokers. Accounting for discounted LYS 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. Even under a ‘worst case scenario’ the cost per LYS was still under £3,000.

NICE has a benchmark cost-effectiveness figure of £20,000 as being acceptable for NHS expenditure. The figures above demonstrate that smoking cessation services, in general, are extremely cost-effective.

The cost-effectiveness of medications to aid smoking cessation have also been established. In 2002, NICE assessed the cost-effectiveness of NRT and bupropion. This assessment took into account all factors associated with the costs of treatment and benefits of stopping, and concluded that both treatments were among the most cost-effective of all healthcare interventions. The discounted cost per LYS was calculated at £1,700 (range £1,000–£2,400) for NRT and £1,100 (range £640–£1,500) for bupropion. An evaluation of the cost-effectiveness of the strategy where NRT is used to reduce consumption before quitting shows that this method is very cost-effective compared with no quit attempt, but not as cost-effective as using NRT for abrupt quitting.

An economic evaluation of the New Zealand Quitline NRT service was undertaken in 2004. The cost per quitter (using a conservative 9% 12-month abstinence rate) was estimated to be $4,272. The cost per QALY was shown to range between $4,983 and $6,794, which is in line with the international data quoted above.

Nortriptyline is an inexpensive medication, but little work has been reported on its cost-effectiveness. One randomised controlled trial compared smoking cessation with bupropion, nortriptyline, and a placebo, and calculated the cost-effectiveness at one year. Nortriptyline was more cost-effective than bupropion, although this difference was not statistically significant. Wilson notes that nortriptyline may be more cost-effective than bupropion given its lower cost per day ($0.37 compared with $6.67). A seven-week course of bupropion costs about $330. There has been some debate within New Zealand about the decision by the Pharmaceutical Management Agency of New Zealand (Pharmac) not to subsidise bupropion, which is partly based on the cost-efficacy comparison with nortriptyline.
NICE has not completed an analysis for varenicline. However, it will also be a cost-effective treatment. Using cost-effectiveness estimates for bupropion and data from outcome studies comparing bupropion and varenicline, Stapleton calculates the cost per LYS for varenicline to be about £900.\textsuperscript{327} Despite the small differences between individual medications, they all compare 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).\textsuperscript{328} Furthermore, in a paper comparing the cost-effectiveness of four interventions to prevent CVD (smoking cessation, aspirin, anti-hypertensives, and statins), smoking cessation was the most cost-effective.\textsuperscript{329} It is also noted that medications such as aspirin and anti-hypertensives are typically used for the remainder of the person’s life, compared with smoking cessation treatments, which are used for only a short period.\textsuperscript{330}
Appendix 1: Search strategy

Terms used for the MEDLINE searches are shown below.

**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 Maori: (maori.mp)
Smoking cessation for Pacific peoples: (pacific.mp)
Smoking cessation for Asian peoples: (asian.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)
Rimonabant: (((Receptor, Cannabinoid, CB1/) or (rimonabant.mp.) or (Receptors, Cannabinoid/))
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.))
Allen Carr’s Easyway: ((allen carr$.mp.) or (easy way.mp.))
Hypnosis: ((hypnosis.mp. or Hypnosis/) or hypnotherapy.mp.))
NicoBloc: (((nicobloc.mp. or (accu drop.mp.) or (take-out.mp.))
Nicobrevin: Nicobrevin.mp
Rongoa Maori: rongoa maori.mp
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