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Nicotine replacement therapy: latest guidelines for GPs

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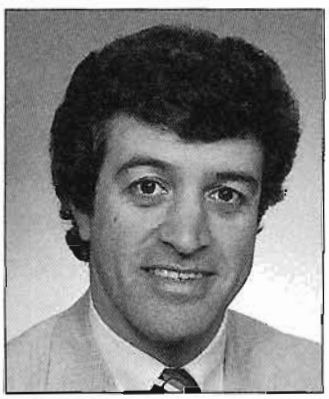
Nicotine replacement therapy has revolutionised smoking cessation in general practice. This article examines the latest recommendations for the use of the nicotine patch, in particular optimal dosage, length of treatment, the role of weaning and the relative benefits of 24-hour and 16-hour patches. Guidelines for optimising the use of nicotine gum and the role of combined patch and gum treatment are discussed. Future treatments, such as the nicotine nasal spray and inhaler, are briefly described.

■ Nicotine replacement products have been available for 11 years in Australia. First the gum and then the nicotine patch have been shown to be effective aids for helping smokers to quit. More recently a nicotine nasal spray has been marketed overseas and a nicotine inhaler has shown promising results.



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This range of products allows doctors to tailor nicotine replacement therapy for each smoker. Therapy can be individualised according to the degree of nicotine dependence, smoking habit, side effects and any personal preferences to achieve an optimal result. Products may be used alone or in combination to this end.

Smoking involves both a pharmacological and behavioural dependence in most cases. Nicotine products alleviate the withdrawal symptoms and cravings associated with addiction to nicotine during the early stages of cessation, allowing the smoker to focus on the psychosocial aspects of stopping smoking. The best results are achieved when nicotine replacement is combined with behavioural advice and follow-up.

A previous review in this journal examined nicotine transdermal patches.[1] This article explores the full range of nicotine replacement products from the general practice perspective (see the Table). The most recent evidence for efficacy and safety is discussed and the latest guidelines for optimal use by general practitioners are described.

Does nicotine replacement work?

The nicotine transdermal patch is highly effective in helping smokers to quit, with long term abstinence rates two to three times those observed with placebo.[2-5] At six months, 22% of smokers using the active patch are successful compared with 9% of placebo users.[2] The nicotine patch is effective for both low and high nicotine dependence.[6] Most importantly, the patch is effective in the general practice setting, when given with only brief or minimal advice.[2,7-9]

Nicotine gum trials have also shown doubling of long term abstinence rates.[3,10] However, while very effective in specialist clinics, the efficacy of the gum in general practice has generally been inconsistent, showing relatively small, if any, differences between nicotine and placebo gum.[4,10-14] This finding reported by several studies is at odds with a recent meta-analysis (an analysis of pooled data from a number of trials) which found that results in primary care were as effective as the clinic setting.[3]

The newer forms of nicotine replacement are also effective. Both the nicotine nasal spray[15] and the nicotine inhaler[16] are about three times more effective than placebo at one year follow-up in a specialist clinic setting.

The nicotine transdermal patch is highly effective, with long term abstinence rates two to three times those observed with placebo.

Is the smoker nicotine dependent?

Nicotine replacement should only be considered for quitters who are pharmacologically dependent on nicotine. Only 75% of quitters experience withdrawal symptoms. A simple guide to whether the patient is nicotine dependent is the following three point check-list:[17]

- does the patient smoke 20 or more cigarettes per day?
- does the patient smoke his or her first cigarette within 30 minutes of rising?
- did the patient have strong cravings or withdrawal symptoms in previous quit attempts?

A more detailed and accurate assessment of the level of dependence can be made with the Fagerström Test for Nicotine Dependence (see the box on page 109).[16] This is a set of six questions which measures nicotine dependence on a scale of zero to 10. It can also help to determine the type and dose of nicotine replacement which may be required.

The nicotine transdermal patch

The nicotine patch is the treatment of choice in the busy general practice setting because of its ease of use, simple instructions and low risk of dependence. Unlike the gum, it is consistently effective even with minimal advice, although higher success rates are achieved with more intensive counselling.

The relative safety of nicotine patches has been confirmed in a number of recent studies and the risks of using the patch are less than the risks of smoking.[19,20] In particular, there is no evidence of serious adverse effects even when subjects continue to smoke while using the patch. Many experts now recommend the use of the patch for patients who are in high risk groups, such as those with cardiovascular disease or who are pregnant, and are unable to quit without nicotine replacement therapy.[4,21]

Although there has been considerable research on the nicotine patch over the last few years, many important questions remain unanswered. Current guidelines are based on an empirical approach to the available data.

What is the optimal dose?

Nicotine patches achieve blood nicotine levels about half the smoking level. Progressively higher doses of nicotine replacement produce higher success rates,[22] demonstrating a dose–response effect. The standard full strength patches will be adequate for most mildly to moderately nicotine dependent patients. However, the patch is less effective in the more heavily dependent smokers,[4,5,19] suggesting that higher doses of nicotine than are available in current patches may be required for these smokers. There are no data yet on whether a higher strength patch will be more effective in this group, although trials are currently assessing this. Nicabate delivers the highest blood levels of the patches that are now available (see the Table).

In the meanwhile, it seems rational and safe to increase the starting dose to one and one-third or one and one-half patches for more highly dependent smokers. This may be delivered by cutting the full strength Nicabate or Nicorette patches (Prostep and Nicotinell should not be cut) and applying a full patch with a part-patch or by adding one of the smaller patches normally used for weaning. On the other hand, a weaker starting patch may be more appropriate for people who smoke less than 15 cigarettes per day, smokers weighing less than 45 kg or when relative contraindications apply.

One large study in general practice examined whether an increase in nicotine patch dose after one week (from 15 mg to 25 mg) improved quit rates in smokers who had failed to stop or who were having difficulties.[6,7] There was no long term benefit on cessation rates, perhaps, the authors felt, because the increase was too late.

Nevertheless, cautious dose increases seem reasonable in patients who still continue to experience cigarette cravings or withdrawal symptoms after two or three days of patch use, that is, once steady state levels of nicotine have been established. Nicotine dosage should be fine-tuned to control withdrawal symptoms, just as one would adjust medication in a hypertensive patient according to the blood pressure readings.

What is the optimal treatment length?

The rationale for the use of the nicotine patch is to provide time free of withdrawal symptoms and cravings while the smoker unlearns the habit. How long this takes is unclear and it will be different from one smoker to the next. The manufacturers recommend patch treatment durations from 8 to 16 weeks. However, no studies have directly compared different durations of patch treatment in the one clinical trial. One meta-analysis of 17 patch trials found that extending treatment beyond eight weeks did not appear to increase efficacy.[3] It has been suggested that the high rates of relapse after patch treatment may be because the treatment time with the patch was too short.[14] Taking all this into account, at least eight weeks of patch use seems reasonable, with a longer course for certain subgroups, such as more dependent smokers, or if patients specifically request it.

Nicotine replacement should only be considered for quitters who are pharmacologically dependent on nicotine.

Is weaning necessary?

Although abrupt cessation is the usual advice for stopping smoking, tapering from nicotine patches is widely practised; however, the efficacy of weaning has not been proven. Only one study has compared abrupt versus gradual cessation, and this study found no evidence of any long term advantage for either method.[6] Similarly, meta-analysis of patch studies did not demonstrate any added beneficial effect from weaning.[7] It appears that doctors have the option of weaning or not. Weaning may be important for some subtypes of smokers, especially those who are anxious about abrupt nicotine withdrawal.

The 24- or 16-hour patch?

All four types of nicotine patches should be applied in the morning and deliver nicotine at the same rate – approximately 1 mg per hour. Three patches are designed for 24-hour application (Nicabate, Nicotinell and Prostep) and one (Nicorette) is for 16-hour use only and should be removed at bedtime.

The 24-hour patches deliver higher blood nicotine levels throughout the day and night. The higher morning nicotine levels are designed to relieve early morning withdrawal but the raised nicotine levels through the night are associated with more sleep disturbances. If disturbed sleep is a persistent problem, 24-hour patches can be removed at bedtime. The 16-hour patch is said to mimic the smoker's pattern of nicotine intake more closely.

The 24-hour and 16-hour patches have been shown to be equally effective in assisting smokers to quit.[2] However, the 24-hour patch may be more effective in the more dependent smoker because it delivers higher blood nicotine levels.

Nicotine gum

Nicotine gum is of uncertain value in general practice because of its low efficacy in this setting, the need for detailed instruction, poor compliance and problems with dependence. However, the gum may be useful when skin reactions or cost preclude the use of the patch or when a more flexible dosing schedule is preferred. Nicotine gum can be used for smoking triggers or high risk situations if taken 20 to 30 minutes before they occur. After cessation, nicotine gum can be kept available in case of unexpected triggers and cravings, and may help

Table. Nicotine replacement products

Product	Nicotine absorbed per unit	Time to peak blood level	Average blood nicotine	Time period for use	Duration of full course	Poisons schedule‡	RPBS benefit
Nicotine patches*							
Nicabate 21 mg	21 mg	4 h	17 ng/mL	24 h	10 weeks	S4	Yes
Nicotinell 30	21 mg	8 to 10 h	13 ng/mL	24 h	12 weeks	S4	Yes
Prostep 30 mg	22 mg	9 h	11 ng/mL	24 h	6 to 8 weeks	S4	Yes
Nicorette 15 mg	15 mg	8 h	8 ng/mL	16 h	16 weeks	S4	Pending
Other products							
Nicorette 2 mg gum	0.9 mg	30 min	10 ng/mL	30 min	13 weeks	S3	No
Nicorette 4 mg gum	1.2 mg	30 min	19 ng/mL	30 min	13 weeks	S4	No
Nasal spray†	NA	5 min	16 ng/mL	NA	NA	NA	NA
Inhaler†	NA	30 min	NA	NA	NA	NA	NA

* Only full strength nicotine patches included. † Not yet available in Australia. ‡ S4: available on prescription only; S3: available over the counter from a pharmacist. § For patches, based on 'NSW list price' to wholesaler plus average wholesaler markup of 13% plus average pharmacy markup of 40% plus $6.20 dispensing fee. Prices in other states may vary slightly.

There is no evidence of serious adverse effects with the patch even when subjects continue to smoke while using it.

to prevent relapse.

The main problem with the gum is that patients do not use enough pieces or do not continue to use the gum for an adequate length of time.[23] In an Australian study, only 25% of gum users reported levels of use sufficient for a pharmacological effect.[11] It is very important to encourage patients to use adequate amounts of the gum for a full three-month period. One suggested starting schedule is to use 10 to 14 pieces per day if the smoking rate has been 20 cigarettes per day, 14 to 18 pieces for 30 cigarettes, and 18 to 22 pieces to replace 40 cigarettes.[24] The dose should be increased if it is not sufficient to relieve cravings or withdrawal symptoms.

The gum has been shown to be most effective if taken on a regular, fixed schedule to build up good blood nicotine levels, rather than taken only when cravings are present.[25] It is most important to give detailed instructions for use of the gum (see the patient handout on page 112). Many of the side effects from nicotine gum are from incorrect use. Patients should be encouraged to persist with the gum, despite the initial unpleasant taste. Results are also greatly improved by providing behavioural advice and ongoing support.

Blood nicotine levels from the 2 mg and 4 mg gum are approximately one-third and two-thirds, respectively, the level from smoking. Because of the higher blood nicotine levels, the 4 mg gum is more effective than the 2 mg gum for more highly dependent smokers[26] and should be used for smokers with a score of seven or more points on the Fagerström Test for Nicotine Dependence.[23] The 4 mg gum may be more effective than the currently available nicotine patches in this group of smokers.[4]

Although gradual withdrawal after three months is recommended, up to 25% of successful quitters continue to use the gum after one year with a daily usage of six or seven pieces per day.[27] Although this is not desirable, the gum is safer than smoking and may be likened to methadone use in narcotic addiction. Strategies for weaning long term gum users include

Pack sizes available	Average retail price[8]
7	$36.10
7/28	$36.27/$121.37
14	$81.19
7/28	$36.10/$118.27
30/105	$10.00/$25 to $30
105	$40
NA	NA
NA	NA

The Fagerström Test for Nicotine Dependence

1. How soon after you wake up do you smoke your first cigarette?

Within 5 minutes	3
Within 6 to 30 minutes	2
Within 31 to 60 minutes	1
After 60 minutes	0

2. Do you find it difficult to refrain from smoking in places where it is forbidden – for example, in church, at the library, or in a cinema?

Yes	1
No	0

3. Which cigarette would you hate most to give up?

The first one in the morning	1
All others	0

4. How many cigarettes a day do you smoke?

10 or less	0
11 to 20	1
21 to 30	2
31 or more	3

5. Do you smoke more frequently during the first hours after waking than during the rest of the day?

Yes	1
No	0

6. Do you smoke if you are so ill that you are in bed most of the day?

Yes	1
No	0

Proposed scoring cut-off

Points	Nicotine dependence
0 to 2	Very low
3 to 4	Low
5	Medium
6 to 7	High (heavy)
8 to 10	Very high

Source: Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. Br J Addiction 1991; 86: 1119-1127. Reproduced with permission courtesy of Carfax Publishing Company, Abingdon, Oxfordshire, UK.

The standard full strength patches will be adequate for most mild to moderately nicotine dependent patients.

reducing the daily dose by one piece per week, cutting gum pieces in half, replacing with chewing gum or the use of nicotine patches.

Future treatments

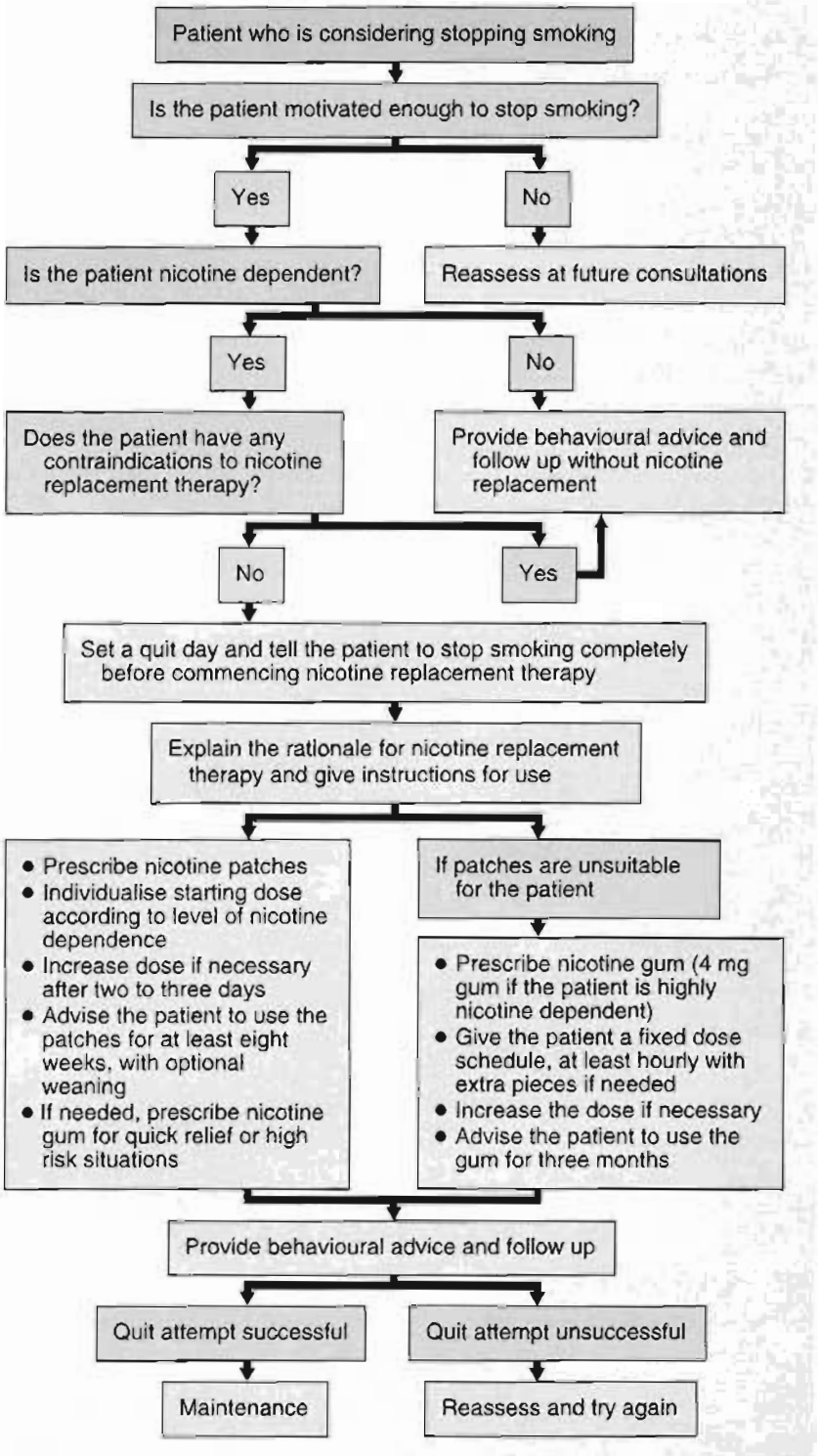
The nicotine nasal spray is now available in several countries overseas, including the United Kingdom. It delivers nicotine to the nasal mucosa as a mist from a small bottle with a pump mechanism. The spray most closely resembles nicotine delivery from a cigarette, with a rapid rise to a peak blood level at five minutes followed by a slower decline. The spray has been shown to significantly reduce cravings and withdrawal symptoms and is most effective for highly dependent smokers.[15] It may be of value in situations where a faster relief of symptoms or a more flexible control over nicotine dosing is required.

The nicotine inhaler is a plastic tube with a nicotine containing sponge which is inhaled like a cigarette.[16] Like the nasal spray it is well tolerated and the dose of nicotine delivered can be titrated by the smoker, although blood levels rise more slowly. It is better able to mimic the oral, tactile and sensory aspects of smoking.

Combination therapy

The combination of fast and slow delivery systems provides the opportunity to tailor nicotine replacement for the individual needs of smokers. A logical combination consists of a nicotine patch to provide a steady fixed dose of nicotine, supplemented as needed by the patient with a faster acting preparation, such as gum, spray or inhaler, for more immediate relief of symptoms or for assistance with high risk situations. Combinations can provide higher blood nicotine levels and may increase quit rates.

Guidelines for smoking cessation using nicotine replacement therapy



It has been suggested that high rates of relapse after patch treatment may be due to inadequate duration of treatment.

PATIENT HANDOUT

Instructions for using nicotine gum

First

Stop smoking completely

How do I use the gum?

Chew the gum several times slowly until you taste it or feel tingling. 'Park' the gum in the cheekpouch for one to two minutes or until the taste disappears. Repeat this cycle for 30 minutes and then throw the gum away.

How often?

Chew at least one piece hourly. Use extra pieces if needed for cravings.

How much?

Use at least eight to 12 pieces a day. You can use up to 30 pieces of 2 mg gum or 15 pieces of 4 mg gum a day.

For how long?

Start tapering the gum after three months.

Other tips

Allow 20 to 30 minutes for the gum to work. Do not eat or drink while the gum is in your mouth or for 15 minutes before using the gum.

In one study, the combined use of patch and gum gave better relief from withdrawal symptoms than either product alone.[28] Another trial demonstrated that the combination was effective in the short term in improving cessation rates, although a long term benefit was not demonstrated.[29] However, whether Australian patients will accept the concept or cost of combined therapy remains to be seen.

Recommendations for treatment

The flowchart on page 111 summarises the guidelines for prescribing the currently available nicotine replacement therapies in the general practice setting. It is important to assess the smoker's motivation first, because only

The main problem with the gum is that patients do not use enough pieces or do not use it for an adequate length of time.

20% of smokers are ready to quit at any one time.[10] Then assess nicotine dependence, as described earlier, because not all quitters will require nicotine replacement therapy. Set a quit day and tell the patient to stop smoking completely before commencing treatment. Arrange follow-up visits to provide further support and advice.

Nicotine replacement therapy should be provided wherever possible with brief behavioural counselling, such as the *Smokescreen for the 1990s* programme.[31] This smoking cessation programme was developed in the School of Community Medicine at the University of New South Wales and over 4,000 general practitioners throughout Australia have been trained in the programme since 1985. It provides cognitive and behavioural strategies for helping smokers to quit in combination with nicotine replacement and follow up (see the box on this page).

Smoking is a chronic lifestyle problem with a high rate of relapse no matter what quitting strategy is used. Therefore, most attempts will fail.

Practice points

- The nicotine patch is the nicotine replacement therapy of choice in general practice.
- The patch is a safe and effective aid to quitting for nicotine dependent smokers.
- The nicotine dose from the patch should be individualised for each smoker and titrated to adequately relieve withdrawal symptoms.
- Patches should be used for at least eight weeks and weaning is optional.
- Nicotine patches are most effective when combined with behavioural advice and follow up.
- Nicotine gum is less effective than the patch in general practice.
- Nicotine gum should be provided with detailed instructions and used in adequate amounts. It works best on a regular, fixed dosing schedule.
- The combination of nicotine patch and gum may be more effective for some smokers than either treatment alone.
- Newer forms of nicotine replacement therapy such as the nasal spray and inhaler may allow treatment to be better tailored for the needs of individual smokers.
- Most quit attempts will be unsuccessful and smokers should be encouraged to keep trying.

Further information

For further information about the *Smokescreen for the 1990s* programme, contact:

The Healthy Lifestyle Centre
St Vincent's Hospital
Victoria Street
Darlinghurst NSW 2010
Phone: (02) 361 2625
Fax: (02) 361 2464

Be prepared to reassess and treat the smoker on a repeated basis because most successful ex-smokers have tried three to five times before finally quitting.

Conclusion

Nicotine replacement products are safe and effective aids to helping nicotine dependent smokers quit. The nicotine patch is the treatment of choice in the general practice setting and at least doubles quit rates. It should be prescribed in doses adequate to prevent cravings and withdrawal symptoms for at least eight weeks, with optional weaning. Nicotine gum is less effective in general practice and should be provided with detailed instructions for use and a fixed dosing schedule of at least eight to 12 pieces per day. Nicotine gum may be added to the patch for greater flexibility of nicotine dosing and higher blood levels. The future availability of the nicotine nasal spray and inhaler will allow doctors to tailor therapy further, according to individual need. The best results are produced when nicotine replacement products are provided with behavioural advice and follow up. ■

References are available on request to the editorial office.