Effectiveness of a nicotine patch in helping people stop smoking: results of a randomised trial in general practice

Imperial Cancer Research Fund General Practice Research Group

Abstract

***Objective*—To assess the effectiveness of 12 weeks' treatment with a 24 hour transdermal nicotine patch in helping heavy smokers to stop smoking; also to assess the value of a specially written support booklet about smoking cessation and patch use compared with a simple advice pamphlet.**

***Design*—Double blind placebo controlled randomised trial with a 2×2 factorial design.**

***Setting*—19 general practices in Oxfordshire.**

***Subjects*—1686 heavy smokers aged 25-64 (mean cigarette consumption 24/day; mean duration of smoking 25 years).**

***Main outcome measure*—Sustained cessation for the last four weeks of the 12 week treatment period, confirmed by saliva cotinine estimation (226/262 cases; 86·3%) or expired carbon monoxide concentration (36/262; 13·7%). Patients lost to follow up (155/1686; 9%) were assumed to have continued to smoke.**

***Results*—Cessation was confirmed in 163 patients (19·4%) using the nicotine patch and 99 patients (11·7%) using the placebo patch (difference 7·6% (95% confidence interval 4·2% to 11·1%); $p < 0·0001$). There was no significant advantage in using the more detailed written support material. The most important adverse effect of the patch was local skin irritation, which occurred in 15·8% (133/842) and 5·1% (43/844) of patients using the nicotine and placebo patches respectively, was graded as severe in 4·8% (40) and 1·1% (nine), and was stated as a reason for withdrawal from the trial in 9·5% (80) and 2·8% (24).**

***Conclusion*—Nicotine patches are effective in a general practice setting with nursing support, but the extent to which this effect is sustained cannot be assessed until the results of longer term follow up are known.**

Introduction

Nicotine withdrawal symptoms make it difficult for heavy smokers to stop smoking.[1] There is good evidence that nicotine replacement in chewing gum reduces withdrawal symptoms and increases the rate of smoking cessation when used by people attending specialised smoking cessation clinics.[2] However, the effectiveness of the gum in general practice is questionable, probably because patient motivation and support are less than in specialised clinics and compliance with its recommended use is poor.[2,3]

Use of transdermal nicotine patches entails only once a day application and does not include chewing unpleasant tasting gum. Patches supply nicotine at a continuous rate over 16 or 24 hours. Two recent and fairly large randomised trials on volunteers recruited to specialised smoking clinics in the United States[4] and Denmark[5,6] have been encouraging. The Transdermal Nicotine Study Group tested 24 hour patches for three months and in 502 subjects reported 26% and 12% abstinence rates at six months in the nicotine and placebo groups respectively. The Danish study enrolled 289 patients in a trial of 16 hour patches, also used for three months, and reported 12 week cessation rates of 41% in the nicotine group and 10% in the placebo group, falling to 24% and 5% at six months, 17% and 4% at one year, and 12% and 3% at two years. This group also reported a very low incidence of side effects from patch use.

Only one general practice trial has been reported.[7,8] This enrolled 199 patients from 21 general practices in Switzerland to use a 24 hour patch for three months and reported three month and one year cessation rates of 36% and 17% in the intervention group and 23% and 11% in the placebo group. The extent to which this degree of success can be achieved in a group of 1686 heavy smokers recruited and supported in 19 general practices in the United Kingdom is reported here.

Subjects and methods

A double blind placebo controlled randomised trial was carried out in 19 practices in Oxfordshire. A total of 1686 patients aged 25-64 were randomised to one of the following four treatment groups: (*a*) nicotine patch with a standard, 16 page Health Education Authority pamphlet on smoking cessation; (*b*) nicotine patch with a 46 page booklet giving specific and more detailed information on smoking cessation with the help of patches; (*c*) placebo patch with a standard Health Education Authority pamphlet on smoking cessation; (*d*) placebo patch with a 46 page booklet giving specific and more detailed information on smoking cessation with the help of patches.

The nicotine patch used was Nicotinell TTS. All patients used an initial 30 cm^2 patch for the first four weeks, reducing to 20 cm^2 for four weeks and then 10 cm^2 for four weeks. The patches delivered 21 mg, 14 mg, and 7 mg nicotine per 24 hours respectively. The total treatment period was 12 weeks. Patients were advised to stop smoking completely from the first day.

RECRUITMENT

Patients aged 25-64 years registered with each practice were contacted by letter asking if they smoked 15 or more cigarettes per day and, if so, whether they would be interested in joining the trial. A list was drawn up of all patients in the age range and ordered by day (ignoring month and year) of birth. Invitation letters were sent sequentially until the practice quota of recruits was complete. Recruitment continued from June 1991 until March 1992. The proportion of patients in the eligible age range invited from each practice ranged from 15% to 100% (median 32%), depending primarily on the size of the practice. Patients who were interested in participating were

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asked to return a reply slip. Some patients contacted their surgery on the basis of letters received by friends and relatives. Those patients were given or sent a fact sheet and reply slip similar to the formal invitation letter. Of the patients recruited, 997 (59·1%) were recruited by invitation letter and 667 (39·6%) as a result of direct contact with the surgery before they had received an invitation. For 22 patients (1·3%) the source of recruitment was not known.

The trial was coordinated by five trial nurses, who were each responsible for specific practices. Patients who expressed an interest in participating were contacted by the nurse and invited to make an appointment with her. At this appointment she explained what was entailed and gave the patient a further appointment to see his or her own general practitioner one week later. Altogether, 1772 patients kept an appointment with the nurse and 1686 (95·1%) were recruited. The general practitioner confirmed that the patient wished to participate, checked the patient's eligibility, and issued the patch and support material.

RANDOMISATION

Randomisation was carried out by prior random allocation of study numbers to each intervention group and by sequential allocation of a study number to patients on entry. Prepared precoded packages containing the patches were handed to the patients by the general practitioner. The packaging and appearance of the two types of patch were identical. It was not possible to blind the nurse or patient to the support material provided. This consisted of a 16 page pamphlet issued by the Health Education Authority, entitled *So You Want to Stop Smoking?* or a 46 page booklet entitled *Smoker's Quit Plan*,[9] adapted specifically to help the patients use nicotine patches.

EXCLUSION CRITERIA

The main exclusion criteria for the trial were known skin hypersensitivity to nicotine, a severe skin condition likely to make patch use impossible, untreated peptic ulcer, life threatening arrhythmia, active cancer, a cerebrovascular or cardiovascular event within six months, lactation, and existing or planned pregnancy. Patients were warned that they should not use other forms of nicotine, such as cigars, pipes, or nicotine chewing gum, during the trial and that medication with centrally acting α activity (such as clonidine) was contraindicated.

FOLLOW UP

Patients were reviewed by the trial nurse one week, four weeks, eight weeks, and 12 weeks after beginning patch use. All follow up contacts were conducted in the patient's own general practice. At these contacts (which were scheduled for 10-15 minutes but often overran) adverse effects and compliance with the patch were recorded, further supplies of the patch were issued, and advice and encouragement were given. Patients received enough patches to last until their next scheduled visit, plus an extra week's supply. At each visit the patient's exhaled carbon monoxide concentration was measured with a Bedfont Smokerlyser portable monitor.

Patients who did not attend for their scheduled three month visit were contacted by telephone and encouraged to attend. Those who were unwilling to attend were asked for as much information as possible by telephone. Patients who reported at their 12 week visit that they had not smoked for the previous four weeks were asked to provide a saliva sample at least 10 days after they had used their last patch. Cotinine, a metabolite of nicotine, was assayed in this saliva sample by gas chromatography in the department of preventive medicine at St Bartholomew's Medical College, London. A concentration of 113·5 nmol/l (20 ng/ml) or less was taken as biochemically validated evidence of non-smoking.[10] Seventy five patients did not provide a saliva sample for analysis. These patients were counted as confirmed non-smokers if their exhaled carbon monoxide reading at the three month visit was ≤ 10 ppm.[11] Overall 226 patients (86·3%) in whom smoking cessation was confirmed had their non-smoking validated by cotinine measurement and 36 (13·7%) had their non-smoking validated by exhaled carbon monoxide measurement.

COMPLIANCE

At each visit patients were asked to return used and unused patches and to report difficulties with patch use. Nurses were asked to count and record the patches used and unused and to make a written comment on departures from recommended use. At the end of the 12 week period non-compliance was defined as more than five days' total missed use during the treatment period or a clear violation of protocol as assessed from the written comments—for example, not wearing patches at night.

ADVERSE EFFECTS

Initial assessment of the probability that adverse events were related to patch use was made by the responsible nurse, primarily on the basis of the temporal relation of symptoms to patch use according to a written protocol. Severe adverse events were reported to and reassessed by the principal investigators (DM or GF). All adverse effects thought possibly or probably to be related to patch use are reported here. Events categorised as unlikely to be related to patch use—for example, pregnancy—are not reported. Assessment of the severity of adverse events (mild, moderate, or severe) was also made by the study nurse. Criteria for assessing the severity of skin lesions were the extent and severity of erythema, eschar formation, and oedema.

WITHDRAWAL SYMPTOMS

Withdrawal symptoms were categorised on a five point scale—none, slight, moderate, moderately severe, and severe. The proportions of patients reporting reactions in the two highest categories (moderately severe and severe) at the one week follow up are reported for all attenders, for all patients reducing their cigarette consumption by more than 80%, and for all patients reporting complete cessation during the first week and who had an expired carbon monoxide concentration of ≤ 10 ppm.

ANALYSIS

Results were analysed on an intention to treat basis. Patients lost to follow up (n=155; 9·2%) were assumed to have continued to smoke. Proportions were compared by χ^2 test or Fisher's exact test when cell frequencies were small. Means were compared by analysis of variance (non-parametric version was used when appropriate).

Results

PATIENT CHARACTERISTICS

The characteristics of patients recruited to each group are shown in table I. Patients were long term heavy smokers, who on average smoked 24 cigarettes per day and had been smoking for 25 years. There were no important or statistically significant differences between the groups.

COMPLIANCE

More than half the patients (966; 57·3%) stopped using the patch before the end of the 12 week study

period—462 (54·9%) in the nicotine patch group, 504 (59·7%) in the placebo patch group. Most patients withdrawing (778/966; 80·5%) did so without specific reason, but 15·4% (149/966) withdrew because of an adverse event probably or possibly related to patch use. Of the 720 patients still using the patch at the end of the study, only 260 (36·1%) had adhered strictly to the protocol. The remainder had not used the patch strictly according to the guidance given by the nurse. Reasons included difficulty with making the patch stick and missing occasional days.

SMOKING CESSATION

Smoking cessation rates for the four groups are given in table II. Overall, 24·5% of patients using the nicotine patch (206/842) and 14·2% of those using the placebo patch (120/844) reported that they had not smoked for the last four weeks of the treatment period. Smoking cessation was confirmed in 19·4% of patients using the nicotine patch (163/842) and 11·7% of patients using the placebo patch (99/844), a difference of 7·6% (95% confidence interval 4·2% to 11·1%; $p<0·0001$). Some of these confirmed quitters had missed appointments or smoked during the early weeks of the treatment. Documented continuous abstinence for the 11 weeks from the first follow up visit to week 12, supported by a carbon monoxide measurement of ≤ 10 ppm at the four and eight week visits and confirmed at 12 weeks, was achieved by 121 (14·4%) patients in the nicotine group and 73 (8·6%) patients in the placebo group, a difference of 5·7% (2·7% to 8·8%; $p<0·001$). The proportion of patients for whom reported cessation was not confirmed at week 12 was similar (about one in five) in both the nicotine and placebo patch groups. Failure to confirm cessation was due to failure to provide a saliva sample or to attend for carbon monoxide measurement (30/64; 47%) or to a high cotinine or carbon monoxide reading (34/64; 53%).

The rate of confirmed smoking cessation was slightly but not significantly higher in patients using the 46 page booklet (139/842; 16·5%) than the 16 page pamphlet (123/844; 14·6%) (difference 1·9% (95% confidence interval −1·5% to 5·4%); $p=0·30$). This small advantage was seen equally in the nicotine and placebo patch groups. There was no interaction between type of patch and support material.

The overall rate of confirmed cessation in the patients recruited by invitation letter and by direct contact was 14·8% (148/977) and 16·9% (113/667) respectively (difference 2·1% (95% confidence interval −1·5% to 5·7%); $p=0·28$).

WITHDRAWAL SYMPTOMS

At the end of the first week 1568 patients (93% of those recruited) attended for follow up. Of these, 479 (30·5%) had stopped smoking completely, and in the remaining 1089 the mean cigarette consumption had fallen from 24·2 (SD 7·9) to 7·0 (7·0) cigarettes per day. Table III shows the proportion of patients reporting moderately severe or severe withdrawal symptoms in the nicotine and placebo groups for three sets of patients: those reporting complete cessation confirmed by a low carbon monoxide reading, those reporting a reduction of more than 80% in the number of cigarettes smoked (including those reporting complete cessation), and all patients attending. Data were incomplete for 24 patients, who were excluded from the table.

Craving for cigarettes was fairly common (reported by 36·3% of patients (560/1544)) and affected significantly fewer patients in the nicotine group (31·1% (244/784) *v* 41·6% (316/760)). Consistently fewer patients in the nicotine group than in the placebo group reported irritability, moodiness, tenseness, and difficulty in concentrating, but there was no difference between the groups in the proportion of patients reporting hunger.

ADVERSE EFFECTS

The two most common adverse effects of the patch were sleep disturbance and skin reactions. Table IV shows the degree of severity of these adverse effects and the frequency with which they led to withdrawal from the trial. Sleep disturbance was the most common event and was nearly three times as frequent in the nicotine group as in the placebo group (20·4% (172/842) patients *v* 7·5% (63/844); relative risk 2·7 (95% confidence interval 2·1 to 3·6)). Patients in the nicotine group were particularly likely to complain of wakefulness and dreaming. However, these symptoms seldom caused discontinuation of patch use. Conversely, skin reactions were frequently cited as a reason

TABLE I—*Characteristics of people recruited to each trial group*

	Nicotine patch		Placebo patch	
	16 Page pamphlet (n=422)	46 Page booklet (n=420)	16 Page pamphlet (n=422)	46 Page booklet (n=422)
Age, sex, recruitment:				
No (%) of women	230 (54·5)	219 (52·1)	241 (57·1)	239 (56·6)
Mean age (years) (SD)	42·3 (9·8)	42·5 (9·8)	42·9 (10·1)	42·9 (9·9)
No (%) recruited without invitation letter*	167 (40·0)	163 (39·3)	158 (38·2)	172 (42·9)
Smoking:				
Mean No of cigarettes/day (SD)	24·1 (7·7)	24·9 (8·8)	24·1 (7·5)	24·3 (8·4)
Mean duration of smoking (years) (SD)	25·1 (9·8)	24·9 (10·1)	25·2 (10·2)	25·3 (9·9)
Mean dependency score (SD)†	14·5 (4·4)	15·2 (4·9)	14·7 (4·6)	15·0 (4·7)
Median No of previous attempts to quit (range)	2 (0-30)	2 (0-50)	2 (0-50)	2 (0-30)
No (%) having first cigarette within 30 minutes of waking	319 (75·6)	319 (76·1)	302 (71·7)	325 (77·0)
Follow up:				
No (%) followed up at three months	379 (89·8)	382 (91·0)	388 (92·0)	382 (90·5)

*Missing values: recruitment n=22; first cigarette n=2. †Modified Horn-Russell score.[12]

TABLE II—*Proportion of people reporting smoking cessation at three month follow up*

	Nicotine patch			Placebo patch		
	16 Page pamphlet (n=422)	46 Page booklet (n=420)	Total (n=842)	16 Page pamphlet (n=422)	46 Page booklet (n=422)	Total (n=844)
No (%) with cessation confirmed	77 (18·2)	86 (20·5)	163 (19·4)	46 (10·9)	53 (12·6)	99 (11·7)
No (%) with cessation reported but not confirmed	15 (3·6)	28 (6·7)	43 (5·1)	12 (2·8)	9 (2·1)	21 (2·5)
No (%) reported still smoking or lost to follow up	330 (78·2)	306 (72·9)	636 (75·5)	364 (86·3)	360 (85·3)	724 (85·8)

Cessation confirmed: nicotine *v* placebo $\chi^2=18·1$ (df=1), $p<0·0001$; 16 page pamphlet *v* 46 page booklet $\chi^2=1·06$ (df=1), $p=0·30$.

TABLE III—*Proportion of patients attending for one week follow up reporting "severe" or "moderately severe" withdrawal symptoms*

	No (%) of patients abstaining only†		No (%) of patients reporting >80% reduction in number of cigarettes smoked‡		All patients (No (%))	
Symptoms	Nicotine patch (n=277)	Placebo patch (n=182)	Nicotine patch (n=548)	Placebo patch (n=433)	Nicotine patch (n=784)	Placebo patch (n=760)
Craving	59 (21·3)	53 (29·1)	141 (25·7)	140 (32·3)*	244 (31·1)	316 (41·6)***
Irritability	43 (15·5)	32 (17·6)	90 (16·4)	94 (21·7)*	138 (17·6)	162 (21·3)
Moodiness	34 (12·3)	30 (16·5)	75 (13·7)	81 (18·7)*	116 (14·8)	135 (17·8)
Tenseness	35 (12·6)	30 (16·5)	77 (14·1)	78 (18·0)	115 (14·7)	141 (18·6)*
Difficulty in concentration	35 (12·6)	27 (14·8)	60 (10·9)	69 (15·9)*	90 (11·5)	123 (16·2)**
Hunger	99 (35·7)	64 (35·2)	205 (37·4)	148 (34·2)	267 (34·1)	252 (33·2)

Nicotine *v* placebo: *$p<0·05$; **$p<0·01$; ***$p<0·001$. †Verified by carbon monoxide concentration ≤ 10 ppm. ‡Including abstainers.

TABLE IV—*Skin lesions and sleep disturbance related to patch use*

	No (%) with skin lesions		No (%) reporting sleep disturbance	
	Nicotine patch (n=842)	Placebo patch (n=844)	Nicotine patch (n=842)	Placebo patch (n=844)
Mild	18 (2·1)	8 (0·9)	45 (5·3)	10 (1·2)
Moderate	75 (8·9)	26 (3·1)	95 (11·3)	40 (4·7)
Severe	40 (4·8)	9 (1·1)	32 (3·8)	13 (1·5)
Total	133 (15·8)	43 (5·1)***	172 (20·4)	63 (7·5)***
Causing withdrawal	80 (9·5)	24 (2·8)***	7 (0·8)	2 (0·2)

Nicotine *v* placebo: ***p < 0·0001.

for discontinuation (80 (9·5%) and 24 (2·8%) patients in nicotine and placebo groups respectively). Skin reactions were three times more common in the nicotine patch group (15·8% (133 cases) *v* 5·1% (43); relative risk 3·1 (2·2 to 4·3)). Most were categorised as of either mild or moderate intensity and were restricted to the patch site. Severe skin reactions occurred in 40 (4·8%) patients using the nicotine patch and nine (1·1%) patients using the placebo patch (relative risk 4·5; 95% confidence interval 2·2 to 9·1).

Other adverse effects reported are shown in table V.

TABLE V—*Other adverse events related to patch use*

	Nicotine patch (n=842)	Placebo patch (n=844)
No (%) with headache	75 (8·9)	75 (8·9)
No (%) with nausea and vomiting	19 (2·3)	27 (3·2)
No (%) with other gastrointestinal disturbance*	45 (5·3)	43 (5·1)
No (%) with mouth problems†	15 (1·8)	15 (1·8)
No (%) with chest pain	4 (0·5)	1 (0·1)

Nicotine *v* placebo: all symptom groups NS.
*Diarrhoea, constipation, flatulence, abdominal pain.
†Abnormalities of taste or salivation, dry mouth, sore mouth, mouth ulcers.

No symptom was significantly more common in the nicotine than placebo patch group, although four of the five patients reporting chest pain were in the nicotine group. No action was taken by the nurse or doctor in three of these cases. In one case pain had lasted only three minutes and in another it occurred only in smoky rooms. However, in the fourth patient, who was previously diagnosed as suffering from unstable angina, glyceryl trinitrate was prescribed. The one patient in the placebo group complained of mild sharp chest pain, and no action was taken.

ASSESSMENT OF BLINDING

On questioning, none of the nurses thought that they could guess which was the active patch and which the placebo patch. At the end of the 12 week treatment period 743 patients attending for follow up were asked to guess which patch they had received. More of those using the nicotine patch (275/389; 70·7%) than the placebo patch (172/354; 48·6%) guessed correctly (difference 22·1% (95% confidence interval 15·2% to 29·0%); p < 0·0001).

Discussion

From a methodological perspective this study was very successful. The process of randomisation worked efficiently, and the extent of follow up achieved was high. Although a greater proportion of patients in the nicotine patch group guessed correctly the arm of the trial to which they had been allocated, it seems unlikely that this would have had an important influence on the outcome. One reason for the ability of the patients to guess their treatment may have been the side effects associated with the nicotine patch. Skin lesions and sleep disturbance were both about three times more common than in patients wearing placebo patches. However, other adverse effects reported by patients, such as headache and gastrointestinal effects, occurred equally in the nicotine and placebo groups.

The smoking cessation rate achieved was lower than in other patch trials. Previous trials have usually been based on volunteers recruited to special smoking cessation clinics,[4,5] which tend to recruit highly motivated people and often can offer a higher degree of counselling and support than is available in general practice. The trial reported by Abelin *et al* was general practice based, but fewer than 20 patients were recruited from each practice.[7] As our trial was based mainly on invitation of a random sample of general practice patients and recruited at least 50 patients from each practice, possibly we obtained a less motivated but more representative sample of the heavy smoking general practice population. About half of the patients were still using the patches at the end of the three month treatment period, which is a smaller proportion than in previous trials.[4,5,7] In the trial by Abelin *et al* about 80% of patients completed treatment. But compliance in our patch trial was much better than in our nicotine gum trial in general practice, in which only about 10% of patients completed three months of treatment.[3]

The monthly reduction in nicotine dose received by all treated patients in our trial may also have tended to lower the cessation rate. In the trial reported by Abelin *et al* participants who succeeded in abstaining switched to the next smallest patch for the next month whereas those relapsing switched to the largest.[7] In the study of Tonnesen *et al* patients used 30 cm² patches for the 12 week treatment period, followed by a choice of abrupt withdrawal or gradual reduction over four weeks.[5]

Our criteria for confirmed cessation were strict. Validation of cessation was based primarily on cotinine measurement rather than the less reliable exhaled carbon monoxide concentration used in most studies.[4,5,7] In addition, Abelin *et al* deemed subjects as "abstinent" even if they smoked occasionally (up to three cigarettes per week),[7] and the main measure of smoking cessation reported by Tonnesen *et al* allowed occasional lapses.[5]

The level of nursing support which we provided was almost certainly less than that provided in special smoking clinics. However, the cessation rate in the placebo group indicates the importance of basic nursing support. By the end of the final three month assessment participants were scheduled to have been seen (for 10-15 minutes) on four previous occasions by the nurse and one occasion by the general practitioner. This support was an integral part of the intervention assessed in our trial. Sustaining cessation is a very important part of a smoking cessation programme, and the level of support necessary to achieve this is a research question which deserves to be addressed.

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STUDY PARTICIPANTS

General practitioners in the trial were Peter Burke, Andrew Chivers, John Clements, Martin Dawes, Ian Eastwood, David Ebbs, Rickman Godlee, Richard Harrington, Karen Kearley, Neil MacLennan, David Mant (joint principal investigator), Janet Murray, Mary Nichols, Helen van Oss, David Stern, Richard Stevens, David Thurston, Robin Wilson, and Stephen Wood.

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Targeting heavy smokers in general practice: randomised controlled trial of transdermal nicotine patches

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Abstract

***Objectives*—(*a*) To evaluate the efficacy of transdermal nicotine patches as an aid to stopping smoking when used as an adjunct to brief advice and support in a general practice setting; (*b*) to see whether an increase in nicotine patch dosage enhances the rate of initial cessation.**

***Design*—Randomised double blind placebo controlled parallel group study with one year of follow up.**

***Setting*—30 general practices in 15 English counties.**

***Subjects*—600 dependent heavy smokers (≥15 cigarettes daily) who were well motivated to give up.**

***Interventions*—Brief general practitioner advice, booklet, and 16 hours per day patch treatment for 18 weeks with brief support and follow up at one, three, six, 12, 26, and 52 weeks.**

***Main outcome measures*—Self reported complete abstinence for up to one year with biochemical validation at all follow up points.**

***Results*—Nicotine patches reduced the severity of craving and adverse mood changes in the first weeks of withdrawal and doubled the rate of initial cessation at week 3 (nicotine group 36% of patients (144/400), placebo group 16·5% of patients (33/200)) and of continuous abstinence throughout one year (nicotine group 9·3% (37), placebo group 5·0% (10)). A dose increase at week 1 among patients experiencing difficulty in quitting increased the proportion who achieved abstinence at week 3. There were no adverse systemic effects attributable to nicotine, but the incidence of moderate or severe local irritation or itching at the patch site was 16·4% (63 patients), compared with 3·8% (seven) with placebo.**

***Conclusion*—Transdermal nicotine patches used as an adjunct to brief advice and support in a general practice setting are an effective aid to long term cessation of smoking in highly dependent smokers.**

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Introduction

Cigarette smoking has long been recognised as the major single cause of preventable disease and premature death in developed countries.[1] According to estimates by Peto *et al* between a third and a half of smokers will die from smoking if they do not give it up. Those who die aged 35-69 lose an average of 23 years of life.[2] Although many smokers succeed in stopping without any formal help or treatment, there are many more who fail despite trying hard to stop.

Nicotine replacement therapy with nicotine chewing gum is established as an effective aid to stopping smoking,[3,4] and transdermal nicotine patches have recently become available for clinical use in several countries.[5] A number of placebo controlled trials have shown that nicotine skin patches are effective at reducing craving for cigarettes and increasing the rates of short term cessation[6-10] but only two, carried out at specialist clinics, have assessed and shown efficacy over a longer term.[11,12]

It is important to evaluate the patches in general practice, where the efficacy of nicotine gum has been less consistent.[4,13] A potential advantage of the skin patch is the ease of securing good compliance with minimal instruction. This makes it suitable for use as an adjunct to brief interventions targeted at many smokers. We report the outcome for up to one year of follow up of the first 600 subjects of a multicentre controlled trial in general practice.

Subjects and methods

The study was designed to evaluate the efficacy of nicotine skin patches (*a*) in alleviating withdrawal symptoms, (*b*) in enhancing initial cessation in the first three weeks of attempting to stop smoking, and (*c*) in preventing relapse in the first three months after stopping (weeks 3-12) and to examine the overall effect of these factors on increasing the rate of long term cessation for up to one year. Additional aims were to examine the effect of increasing patch nicotine dosage in those who seemed to respond inadequately to the standard dose and to compare the effects of gradual versus abrupt withdrawal of transdermal nicotine on the relapse rate after three months of abstinence from smoking. However, the size of the study sample was determined to address the four main questions and we were aware that statistical power might not be adequate for definitive answers to the two subsidiary points of interest.

The sample size of 1200 was planned to detect differences between the low rates of sustained abstinence expected after one year, and the study had a 95% chance to detect a difference of 10% versus 5% ($p < 0{\cdot}05$, one sided test). Thus both α and β were set at