Dependence potential of nicotine replacement treatments: Effects of product type, patient characteristics, and cost to user

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Abstract

Objective. To assess the extent of long-term use of different nicotine replacement treatment products in smokers attending routine smoking cessation treatment and to examine the effect of nicotine replacement treatment cost on its long-term use.

Method. 1518 consecutive patients prescribed nicotine replacement treatment at the East London Smokers' Clinic between January 2000 and November 2002 were followed up at 1-year.

Results. The rates of long-term use ranged from 2% for patch to 13% for nasal spray. Long-term use of nicotine replacement treatment was significantly more likely in more dependent smokers. Treatment cost, and whether it was provided free of charge, had no significant effect on its long-term use.

Conclusions. Long-term use of nicotine replacement treatment is not uncommon. Its occurrence seems positively related to speed of nicotine delivery of individual products. For self-selected highly dependent smokers, long-term use of nicotine replacement treatment may be a necessary precondition for maintaining long-term abstinence. The findings have financial and clinical implications for providers of smoking cessation services.

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Introduction

The recommended duration of nicotine replacement treatment (NRT) use is currently up to 3 months (USDHHS, 2000), but some patients continue to use the medication for longer. A household purchase survey suggested that among smokers who buy NRT over the counter (OTC), 0.1% of those who purchase nicotine patches and 1% of those who purchase nicotine gum use their NRT for a year or more (Shiffman et al., 2003a). Higher long-term use rates were reported in volunteers taking part in studies of smoking cessation medications. This can be expected, as compared to smokers who purchase NRT OTC, trial volunteers obtain more support and are likely to maintain abstinence and use the medication for longer. Between 1% and 8% prevalence of long-term use (for at least 1 year) was reported for nicotine chewing gum (Hajek et al., 1988; Blondal, 1989; Hughes et al., 1991; Hatsukami et al., 1993; Nides et al., 1995; West et al., 2000a) and between 3% and 11% for nasal spray (Sutherland et al., 1992; Hjalmarson et al., 1994; Blondal et al., 1999; West et al., 2000a).

The occurrence of long-term NRT use in 'real-life' smokers who attend routine smoking cessation treatment outside clinical trials and who are not carefully selected and screened is not known. There are also no published data on long-term use of the newer NRT products, i.e. nicotine lozenge, nicotine inhalator, and nicotine sublingual tablets. Finally, it is not known what influence the cost of NRT to the user has on its long-term use.

These issues have important financial and clinical implications for planning and operation of smoking cessation services. In some US states and in a number of other countries, NRT is available free to the users, or heavily subsidised, and in this context any information of the effect of removing the cost to user for long-term NRT utilisation is of interest. The existing

clinical practice guidelines provide little or no advice to clinicians on how common long-term NRT use is, what type of smoker is likely to become a long-term user, and how to handle such cases (USDHHS, 2000; West et al., 2000b; National Institute for Clinical Excellence, 2002). Relevant information which can guide clinical practice is needed.

The UK government initiated smoking cessation clinics within the National Health Service in 1999 and the clinics are currently treating some 500 000 smokers per year (Department of Health, 2005). During the lifetime of the smoking cessation service, there were changes in the way NRT was priced, until it became free of charge to most users in 2002 (Department of Health, 2000). We report the prevalence and predictors of long-term use of all the existing forms of NRT in a large cohort of smokers attending for smoking cessation treatment, and assess the effect of patient characteristics and of NRT cost on its long-term use.

Method

Sample and clinical treatment

The sample comprised 1518 consecutive patients using nicotine replacement treatment who set a quit date at the East London Smokers' Clinic between January 2000 and November 2002. The clinic uses Withdrawal-oriented treatment (Hajek, 1989), a combination of medication and behavioural support, which is the prevailing model of treatment within the UK Stop Smoking Service. Patients select their preferred NRT product and are advised to use it in accordance with manufacturer's instructions for up to 3 months. They are seen weekly over 6 weeks with the last session scheduled at 4 weeks after their quit date. Patients continue to receive NRT as needed via their doctors or pharmacists, collecting prescription forms at the clinic, or buying NRT over-the-counter. The clinic treatment is free, but the medication had incurred different levels of cost to the patient. Until April 2001, NRT was sold to patients for up to 1 year at a cost of $17 per 1-week supply.[1] From April 2001 NRT has been provided 'on prescription' for up to 1 year, contingent on continuing abstinence. Approximately 70% of clinic patients are entitled to receive this free of charge, while the rest paid a prescription charge of US $11 for each 1-week supply.

Measures

Patients filled in the clinic assessment questionnaire collecting data on demographic and smoking characteristics including Fagerstrom Test of Nicotine Dependence (FTND) (Heatherton et al., 1991), and Motives for Smoking (West and Russell, 1985), and they also provided expired-air carbon monoxide readings at each of the seven weekly treatment sessions.

As part of the Clinic routine practice, all patients abstinent at the end of the 6-week treatment programme were contacted by telephone 1 year after their quit date. Duration of NRT use was recorded. Clients reporting continuous abstinence (no smoking at all for the whole year) were invited to attend the clinic to validate their abstinence by expired air carbon monoxide reading (less than 10 ppm) as per UK smoking cessation services monitoring requirement (Department of Health, 2001). Clients lost to follow-up were considered smoking.

Approval for the audit of Clinic data was obtained from the East London Research Ethics Committee, and clients gave written informed consent on their first visit to the clinic.

Statistical analysis

To assess the differences in demographics and smoking characteristics between groups (1-year abstainers still using NRT, 1-year abstainers not using NRT, and 1-year smokers) we used analysis of variance (ANOVA) with post-hoc analysis (pairwise comparison with Bonferroni correction) and Pearson's Chi-squared. Univariate ANOVA and then logistic regression were used to assess the predictors of long-term NRT use. Intention to treat analysis was undertaken and significance levels for all tests were 2-tailed (alpha = 0.05).

Results

Table 1 provides sample characteristics. These were typical of smokers seeking treatment in UK service, i.e. middle aged highly dependent smokers mostly from lower socio-economic groups (Chesterman et al., 2005).

Five percent of the sample (76 of 1518 patients) used NRT 1 year after their quit date. All remained continuously abstinent throughout the year. Table 2 shows the number and proportion of long-term NRT users for each of the six NRT products. The long-term use of spray was significantly more common than patch use while the use of the other products was intermediate (see Table 2). Long-term NRT users comprised 27% of validated continuous 1-year abstainers.

Long-term NRT users were similar to treatment failures in dependence and in smoking for withdrawal relief, with both groups differing significantly from NRT-free abstainers (see Table 3). Of the 23 demographic and smoking variables taken at baseline, six were associated with long-term NRT use in univariate analyses (FTND, previous NRT use, educational status, employment, and smoking for withdrawal relief, weight control, and to help concentrate). These were entered into a logistic regression model with long-term NRT use versus NRT-free abstinence as dependent variables. Long-term NRT users were more likely to smoke for relief of withdrawal and to be more dependent smokers (see Table 4).

Six hundred smokers set a quit date before NRT became available on prescription, and 918 afterwards, when the personal cost of long-term use was significantly reduced. The proportion of long-term NRT users did not change significantly after NRT became available on prescription (4% versus 6%, $\chi^2 = 2.82$, $df = 2$, $p = 0.24$). There was also no significant difference in long-term NRT use between people entitled to

Table 1
Sample characteristics

	N [a]	Mean	S.D.
Age	1500	48	14
Cigarettes per day	1475	23	10
Number of previous quit attempts	1434	3	6
Carbon monoxide in expired air (ppm) [b]	1510	23	11
FTND	1397	5	2
% female	1518	56%	
% in paid employment	1461	31%	
% completed education by age 16	1518	60%	
% smoking within 30 min of waking	1464	86%	

Data were collected at the East London Smokers' Clinic between January 2000 and November 2002.

[a] N varies due to missing data.
[b] Average of up to 3 baseline readings.

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[1] Patients in receipt of free prescriptions were entitled to 1 or 4 weeks free NRT for a limited period during this time.

Table 2
Incidence of long-term use of different NRT products

Product	N started treatment	N (%) long-term users
Transdermal patch	800[a]	15 (2%)
Sublingual tablet	267	18 (7%) *
Lozenge	49	4 (8%)
Inhalator	143	11 (8%)
Chewing gum	115	10 (9%)
Nasal spray	144	18 (13%) **
Total	1518	

Data were collected at the East London Smokers' Clinic between January 2000 and November 2002.

[a] Includes 80 clients who used a combination of patch plus another NRT product. The details of the second product were not recorded but none of the 80 became long-term user of NRT.

* Proportion significantly different from patch use, $p=0.025$.

** Proportion significantly different from patch use, $p=0.001$.

free prescriptions and those who paid for their prescriptions (5.7% versus 4.3%, $\chi^2=4.22$, $df=2$, $p=0.12$).

Comment

Long-term use of NRT among smokers attending specialist smoking cessation clinic ranged from 2% for patches to 13% for nasal spray. It was not influenced by NRT cost or whether patients paid for their prescriptions or not. Long-term use of nicotine replacement was predicted primarily by the degree of nicotine dependence.

There are several limitations to our findings. Data were not available on the consumption of NRT or the self-reported reasons for long-term use. Previous studies have reported that NRT consumption in long-term users is mostly modest and that they ascribe extended use to an effort to avoid relapsing to smoking rather than as simply compulsive use (Shiffman et al., 2003b), but future studies should examine these issues more

Table 4
Logistic regression model for factors predicting long-term NRT use among continuous abstainers

	Beta	Wald	Significance	Odds ratio	95% C.I. for odds ratio
Smoking for withdrawal relief	0.67	4.62	$p=0.03$	1.95	1.06–3.60
Fagerstrom Test of Nicotine Dependence	0.18	5.61	$p=0.02$	1.20	1.03–1.40
Previous NRT use	0.53	2.93	$p=0.09$	1.71	0.93–3.14
Smokes to help concentrate	0.01	0.01	$p=0.93$	1.01	0.80–1.28
Smokes for weight control	0.36	1.241	$p=0.27$	1.432	0.76–2.69
Educational status	−4.11	1.80	$p=0.18$	0.66	0.36–1.21
Employment	0.30	0.92	$p=0.34$	1.35	0.73–2.50

Data were collected at the East London Smokers' Clinic between January 2000 and November 2002.

closely. The findings relating to the important issue of the effects of medication costs on their long-term use are only observational. Although the lack of effect remained after controlling for baseline participant characteristics, the change in pricing policies may have led to a change in the type of smokers accessing the treatment in ways not recorded by our baseline questionnaire. The sample may have been too small to detect a modest effect. Finally, the treatment approach used within the UK services may generate rates of long-term use different from other treatment approaches, although this is unlikely. Most clinicians using NRT follow very similar guidelines (e.g. US and UK guidelines; USDHHS, 2000; West et al., 2000b).

A previous randomised study suggested that prolonged use of NRT is positively related to speed of nicotine absorption (Hajek et al., 1999; West et al., 2000a). The current results are consistent with this observation. Our data also confirm the previous finding (Hajek et al., 1988) that long-term NRT users are close to treatment failures and different from other

Table 3
Comparisons of long-term NRT users, NRT-free abstainers, and patients who did not manage long-term abstinence in baseline variables

	Abstainers		Smokers at 1 year (N=906–1233)[+]	Difference between groups
	Using NRT at 1 year (N=58–76)[+]	NRT-free at 1 year (N=165–209)[+]		
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	
Age	49 (12)	51 (14)[a, **]	47 (14)[b, **]	$F=5.9$, $p=0.003$
% women	61%	54%	56%	NS
% completed education by age 16	53%[b, *]	68%[a, c, *]	60%[b, *]	$\chi^2=6.5$, $df=2$, $p=0.04$
% in paid employment	47%[a, *]	34%	31%[c, *]	$\chi^2=8.8$, $df=2$, $p=0.01$
Previously used NRT	67%[b, *]	51%[a, c, *]	61%[b, *]	$\chi^2=8.7$, $df=2$, $p=0.01$
FTND	5.6 (2.1)[b, **]	4.7 (2.1)[a, c, **]	5.3 (2.2)[b, **]	$F=7.4$, $p=0.001$
Smokes for withdrawal relief	63%[b, **]	40%[a, c, **]	53%[b, **]	$\chi^2=15.1$, $df=2$, $p=0.001$
Smokes to help control weight	40%[b, *]	24%[a, c, *]	28%[c, **]	$\chi^2=6.2$, $df=2$, $p=0.04$
Longest previous abstinence (weeks)	35.3 (79)	55.3 (175)[a, **]	25.1 (73)[b, **]	$F=8.1$, $p<0.001$

Data were collected at the East London Smokers' Clinic between January 2000 and November 2002.

[a] Differs from smokers.

[b] Differs from NRT free abstainers.

[c] Differs from long-term NRT users.

* $p<0.05$.

** $p<0.01$.

[+] Ns differ due to missing data.

treatment successes in their level of dependence. Smokers differ in the time course of post-cessation withdrawal symptoms (Piasecki et al., 1998), and the more dependent smokers who are likely to be affected by protracted withdrawal discomfort may require prolonged withdrawal relief medication.

Long-term use of NRT currently contradicts the product labelling. A need has been highlighted for regulators to review current licensing restrictions (McNeill et al., 2001; Hajek, 2006). Medications for the management of other chronic conditions are available on prescription for indefinite periods.

Among general public and some health professionals there exist concerns about NRT safety. However, there are no known health risks associated with NRT use (National Institute for Clinical Excellence, 2002; Silagy et al., 2004) with the exception of allergic skin reaction to patches (Greenland et al., 1998). One small case-control study reported an effect of long-term NRT use on glucose metabolism, but it compared long-term NRT users with non-smokers so it is not clear whether the findings were due to nicotine or the effects of smoking (Eliasson et al., 1996). In the Lung Health Study a large number of smokers ($n = 3094$) were provided with nicotine gum to help them quit. At the 5-year follow-up 14% of those who managed to quit, and 5% of those who did not, reported using NRT. NRT use was associated with no serious adverse events (Murray et al., 1996). After over 20 years of worldwide use by millions of smokers, no serious side effect of either short-term or long-term NRT use have been reported and there exist few theoretical reasons to expect any such risk. Few medications, if any, seem to be as safe as NRT and there is no doubt that any hypothetical risk is insignificant compared to risks of smoking (Sims and Fiore, 2002).

It is reassuring that the reduction in the cost of NRT to the patient and even providing it free of charge had no major effect on the occurrence of its long-term use. Where NRT is provided free of charge, the financial implications of its long-term use, and a somewhat unclear boundary between its therapeutic and recreational use, need to be considered. Health care providers may be interested in the current UK approaches which are either to carry on prescribing, or to prescribe NRT for 3 months and to advise patients who want to continue its use to buy it OTC.

The current results can provide some guidance on dealing with patients who use NRT beyond the 'approved' 3 months. Clinicians should be aware that a quarter of successful ex-smokers treated in intensive treatment programmes can be expected to use NRT throughout the first year of abstinence and indeed may not be successful without it. Extended use of NRT has no known negative effects and patients who are worried should be reassured. The main clinical challenge is to prevent relapse back to smoking.

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