ORIGINAL INVESTIGATION

Adherence to and Consumption of Nicotine Replacement Therapy and the Relationship With Abstinence Within a Smoking Cessation Trial in Primary Care

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ABSTRACT

Introduction: Nicotine replacement therapy (NRT) medications have been shown to be effective in increasing smoking cessation rates. There is, however, a lack of good evidence describing how individuals in primary care use these medications and which factors are likely to affect this. The study objectives are to describe adherence and consumption, examine key factors that may determine use, and examine the relationship between consumption of NRT and abstinence from smoking.

Methods: Secondary analysis of data from a randomized controlled trial conducted in smoking cessation services in primary care. Adult smokers (n = 633) starting a quit attempt within smoking cessation clinics were followed for 6 months, with NRT use closely monitored for an initial treatment period of 4 weeks. The main outcomes were 4-week adherence to prescribed NRT, mean daily consumption of NRT over the 4-week period, and abstinence from smoking at 4 weeks.

Results: Levels of adherence to prescribed NRT were high: more than 94% in participants who completed the treatment period. After controlling for possible confounders, prescribing higher doses of patch and oral NRT was associated with higher mean daily consumption of NRT. Using an inhalator to deliver oral NRT was associated with both higher adherence and higher consumption. The amount of NRT consumed predicted future abstinence when reverse causation was accounted for.

Conclusions: Most individuals within a clinical trial in primary care who persisted with a quit attempt adhered closely to their prescription. Prescribing higher doses of NRT led to higher consumption and higher consumption to higher abstinence.

INTRODUCTION

Nicotine replacement therapy (NRT) is considered to be a safe and effective pharmacological intervention for smoking cessation, with increases in consumption directly increasing the likelihood of sustained smoking cessation (Shiffman, 2007). A meta-analysis of the effectiveness of NRT found all forms to be significantly more effective than placebo in aiding abstinence from smoking, with participants using NRT more than 1.5 times more likely to be abstinent (Stead, Perera, Bullen, Mant, & Lancaster, 2008). Despite this well-corroborated link between NRT use and abstinence, there are few studies describing adherence and those typically focus on smoking cessation outcomes, rather than on detailed description of the extent of adherence and the factors that are associated with increased adherence.

This study focuses on two types of NRT use: adherence—the proportion of prescribed NRT that is consumed; and consumption—the total dose of NRT absorbed. These merit being examined separately because they have different implications for practice. There is a common perception that people do not consume sufficient NRT to derive maximum benefit from its use. Assessing consumption in primary care will provide evidence whether this is true. It is the dose consumed that is related to the outcome of cessation (Shiffman, 2007). Understanding (and ultimately, maximizing) adherence to a prescribed optimal dose of NRT is also important because it is the means by which an optimum level of consumption is achieved. The data presented are taken from a smoking cessation trial in primary care (Marteau et al., 2012), but otherwise the care provided was typical of that within the English NHS Stop Smoking Service.

The first aim is to present descriptive data on how individuals in a primary care treatment context use prescribed NRT for the duration of the treatment period. It is important to have high-quality descriptive data to examine whether concerns

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about underdosing are justified. It also allows investigators interested in improving adherence to plan the sample size of future studies. The second aim is to identify factors associated with adherence to and consumption of prescribed NRT, which may inform treatment approaches to facilitate successful use. We focus on two factors that are of particular clinical interest: the nature or makeup of the prescribed dose, and the mode of delivery of NRT. There is evidence that combination treatment, such as a nicotine patch plus an oral or intranasal form of NRT, enhances abstinence over a single form alone (Brose et al., 2011; Stead, et al., 2008). Such combination treatment was used in the current study, and it is important to ascertain whether particular combined forms of medication are associated with enhanced adherence and consumption in routine practice and whether prescribing more NRT leads to increased or decreased use. Because prescribed use of oral NRT requires a higher frequency of action than applying a patch, it may be expected that prescriptions requiring high use of oral NRT will be adhered to less than those requiring low use of oral NRT. A further question concerns whether the chosen mode of delivery of oral NRT product (e.g., inhalator or gum) affects use. There is currently little evidence that adherence to different types varies significantly, although in a trial in which participants were randomized to a given product, Hajek et al. (1999) reported that although gum, nasal spray, and inhalator were all used suboptimally, gum was used as recommended more often. Finally, the ultimate purpose of prescribing NRT and encouraging its use is to increase the probability of smoking cessation, so we also examine the relationship between consumption of NRT and abstinence from smoking. Although there is substantial evidence for this relationship (Jackson, Stapleton, Russell, & Merriman, 1989; Lam, Abdullah, Chan, & Hedley, 2005; Shiffman et al., 2002), research has not been typically able to exclude reverse causation. That is, giving up a quit attempt causes people to stop using NRT rather than people who use more NRT being more likely to achieve abstinence. We therefore examine this association using an approach that controls for reverse causation.

METHODS

Design

Secondary analysis of data from an open label, parallel group, randomized controlled trial (ISRCTN: 14352545). Full details of the trial and methods are published elsewhere (Marteau et al., 2010, 2012). In the current paper, we report detailed information on adherence and consumption in a subset of trial participants (see section "Analysis").

Recruitment

The trial took place in the English National Health Service's (NHS) Stop Smoking Service in primary care, with participants recruited from 29 primary care practices in two English cities. The services provide a combination of weekly behavioral support and pharmacotherapy to assist smokers to quit. Eligible participants smoked at least 10 cigarettes a day, were prepared to quit soon and were 18 years or older. Only people with a recent (within 3 weeks) stroke, myocardial infarction, severe arrhythmias, uncontrolled hyperthyroidism, and severe renal impairment were excluded. A total of 633 participants were randomized. The full dataset was used as the basis for this secondary analysis.

Interventions

All participants were prescribed a nicotine patch, the dose based on their heaviness of smoking. Those smoking 15 or more cigarettes daily were prescribed 21 mg/24 hr patches and those smoking 10–14 cigarettes daily were prescribed 14 mg patches. Participants also received oral NRT and were randomized to have this additional dose based either on their genotype (presence/absence of OPRM1 mutation) or on their level of nicotine dependence (Fagerström Test for Nicotine Dependence [FTND] below eight, or eight and above). The dose of oral NRT was of either 6 mg or 12 mg a day. For their oral NRT prescription, participants chose their preferred means of delivery (either inhalator, gum, lozenge, or sublingual tablet) and changed this at each clinic session if desired. For oral NRT, the dose was the approximate absorbed dose, not the pack dose. Thus, 2 mg gum, lozenge, and sublingual tablets were counted as providing 1 mg and a 10-mg inhalator cartridge counted as 3 mg.

Procedure

Participants attended seven weekly clinic appointments with a research nurse. Baseline measures were taken during the first clinic. Participants started their quit attempt immediately following the third clinic visit. At this third appointment, the rationale for participants' doses, based on the group to which they had been randomized, was given. The defined treatment period therefore comprised all subsequent weeks, that is, a 4-week period. All participants were also contacted 6 months following their quit date, either by telephone or by post, and completed follow-up questionnaires.

Outcomes and Measures

Adherence to Prescription of NRT Over 4 Weeks

This was the primary outcome of the original trial, defined as the proportion of all NRT prescribed consumed each day, averaged over the 4-week treatment period. Overconsumption was defined as 100% adherence. This was because the therapists' prescription was for a minimum dose to be consumed, but therapists instructed participants "to take as much as needed to avoid lapsing." Consumption was measured using pill counts and participants' self-report, recorded in a daily diary and corroborated by a research nurse at each weekly visit. In line with the analysis plan of the original trial, where there were missing adherence outcome data, the missing data were regarded as representing zero adherence. For participants who completed the treatment period (i.e., the focus of the current analysis), zero adherence was imputed for less than 0.5% of the data.

Consumption of NRT over 4 weeks—mean daily consumption in milligrams absorbed for the duration of the treatment program. *Consumption of NRT over 1 week*—assessed in the same way. *Four-week abstinence from smoking*—using the Russell Standard (West, Hajek, Stead, & Stapleton, 2005), counting participants lost to follow-up as smokers with smoking status verified biochemically by exhaled carbon monoxide as <10 ppm. *Total days of NRT use*—length of NRT use postquit. *Nicotine dependence*—measured by the FTND (Heatherton,

Kozlowski, Frecker, & Fagerstrom, 1991) and the number of cigarettes smoked per day. *Preferred delivery mode of oral NRT*—participants chose but could swap forms of oral NRT, so we classed this as the form used for the longest duration over the course of the treatment period. *Motivation to use NRT*—a composite measure of two 7-point scale items ($\alpha = .81$): "Do you intend to use all your NRT every day in the first 4 weeks of your quit attempt?"; "How likely is it that you will use all your NRT every day in the first 4 weeks of your quit attempt?" *Longest previous period of abstinence*.

Analysis

For most analyses presented, our focus is on only those individuals who continued to attempt to quit smoking for the duration of the 4-week treatment period. We excluded those lost to contact and people who abandoned their quit attempt prior to the end of the treatment period of 4 weeks. NRT was dispensed weekly and is not indicated outside of a cessation attempt, so no further weekly prescriptions were given to these participants, although prescriptions were issued to those smoking still trying to attain abstinence. It is only by looking at usage up to the point at which a quit attempt stops that we can obtain a true measure of adherence and consumption of those in treatment. However, we also present descriptive data for the complete sample. This provides an indication of the general levels of adherence expected in individuals who attempt to quit.

We examined the association between type and amount of NRT prescribed and both adherence and daily consumption of NRT using analysis of variance and post-hoc testing (Games–Howell procedure) to test differences between group means. When violations of parametric assumptions were found, we used Kruskal–Wallis analysis of variance tests and post-hoc testing with Mann–Whitney tests and reported median values and interquartile ranges. We adjusted for possible confounders using multiple regression analysis, forcing entry of all predictors and possible confounders and applying the same model to adherence and consumption outcomes. Predictors were binary variables of high/low patch and high/low oral NRT, plus binary terms representing each type of oral NRT product (lozenge, sublingual tablet, gum, or inhalator, with inhalator as referent group). The potential confounders arose because the trial design determined the dose prescribed. We included number of cigarettes smoked per day, trial arm, genotype (OPRM1 mutation absent/present), and FTND because these tailored the prescribed dose of NRT, and multiplicative interaction terms (trial arm × FTND, trial arm × genotype) were also to be included but were discarded because they led to unacceptable multicollinearity (Variance Inflation Factor [VIF] values >23, tolerance values <.05). We controlled for participants' motivation to use the prescribed NRT as we considered this likely to be an important predictor of actual use.

We used logistic regression to examine whether the amount of NRT consumed was associated with an increased likelihood of achieving abstinence adjusting for potential confounders (trial arm, genotype, cigarettes smoked per day, and FTND). Multiplicative interaction terms were discarded due to multicollinearity (VIF > 19, tolerance < .06). We also controlled for longest previous quit attempt, as this is an important predictor of cessation. Because some people abandoned their quit attempt prior to the end of treatment and were not prescribed medication, this inevitably created an association between consumption of medication and abstinence. We followed Shiffman's procedure to overcome this (Shiffman, 2007). We confined the analysis to participants abstinent after 1 week of quitting and assessed the association between consumption of medication during that first week and subsequent abstinence at 4 weeks.

RESULTS

Description of Adherence and Consumption of NRT

From 633 individuals who were randomized, 539 (85.2%) attended the clinic at 1 week. 419 participants (66.2%) completed the 4-week behavioral support program. Descriptive data are given in Table 1.

Adherence

The complete sample used 90.7% of their prescribed NRT over the 4 weeks of treatment. The respective figure was 94.5% in participants who continued their quit attempt until 4 weeks.

Consumption

The complete sample consumed 20.7 mg/day of NRT over the 4 weeks of treatment. In participants who continued their quit attempt until 4 weeks, the respective figure was 24.8 mg/day. (NB: The following analyses were conducted only for participants who completed the treatment period [$n = 419$]).

Effects of Dose of Patch and Oral NRT on Adherence and Consumption

Adherence

Participants were assigned 14 or 21mg patch and either 6mg or 12 mg of oral NRT and the percentage adherence compared (Table 2). Adherence was high in all four groups but significantly greater in the "high patch/low oral" group than both the "low patch/low oral" and "high patch/high oral" groups, $H(3) = 14.12$, $p = .002$; $U = 8145.00$, $p = .019$.

Consumption

As expected given the lack of consistent effects on adherence, people who were prescribed more NRT consumed more NRT. The differences in consumption among groups were significant, $F(3,425) = 48.62$, $p < .001$, with post-hoc testing revealing differences ($p < .01$) among all cells other than "high patch/low oral" and "low patch/high oral," where the prescribed dose was very similar at 27 mg and 26 mg, respectively.

Effects of Preferred Oral NRT Delivery Mode on Adherence and Consumption

Adherence

Gum, lozenge, and tablet oral NRT products were adhered to less than inhalator (Table 2). Differences were detected among groups, $H(3) = 20.84$, $p < .001$, with post-hoc testing revealing that adherence to oral NRT differed between inhalator and each of the other products, $U = 5027.00$, $p = .017$. We assessed adherence to combination NRT (patch plus oral NRT) and found that adherence was higher for participants given patch plus inhalator than for patch plus gum or lozenge, $H(3) = 20.44$, $p = <.001$, $U = 3688.00$, $p = .002$.

Table 1. Description of Adherence to Prescribed Dose and Consumption of NRT

	Participants who completed treatment period (n = 419)	All randomized participants (n = 633)
Adherence to prescribed dose[a]		
One-week percentage of prescribed NRT used		
Mean (*SD*)	88.1 (18.8)	72.5 (35.7)
Median (IQR)	95.5 (16.3)	91.9 (24.0)
Four-week percentage of prescribed NRT used		
Mean (*SD*)	88.7 (16.4)	66.0 (37.7)
Median (IQR)	94.5 (13.2)	90.7 (38.7)
Participants using 100% of prescribed NRT over 4-week period, %(n)	10.3 (43)	6.8 (43)
Participants using >90% of prescribed NRT over 4-week period, %(n)	66.1 (277)	43.8 (277)
Participants using >80% of prescribed NRT over 4-week period, %(n)	83.8 (351)	56.9 (360)
Participants using 0% of prescribed NRT over 4-week period, %(n)	0.2 (1)	13.3 (84)
Total days of NRT use from start of treatment		
Mean (*SD*)	75.1 (52.7)	64.2 (54.2)
Median (IQR)	56.0 (56.0)	45.0 (63.0)
Prescribed dose and consumption in milligrams		
Daily mg NRT prescribed, mean (*SD*)	26.7 (3.8)	26.8 (3.9)
Daily mg NRT consumed over 1-week period, mean (*SD*)	24.7 (7.4)	20.4 (11.0)
Daily mg NRT consumed over 4-week period, mean (*SD*)	24.8 (6.8)	20.7 (10.2)

Note. IQR = interquartile range; NRT = nicotine replacement therapy; *SD* = standard deviation.
[a]For each participant, mean percentage adherence was calculated. We present the average and variability of those figures to indicate typical levels in the population.

Table 2. Adherence to Prescribed Dose and Consumption of NRT by Nature of Medication

Dosage				
Four-week percentage adherence to prescribed dose, median (IQR)				
	Low patch (14 mg)		High patch (21 mg)	
Low oral (6 mg)	92.89 (15.33)		96.39 (11.30)[a]	
High oral (12 mg)	93.68 (15.71)		91.16 (14.78)	
Four-week mean daily consumption in milligrams, mean (*SD*)				
	Low patch (14 mg)		High patch (21 mg)	
Low oral (6 mg)	18.03 (5.33)		25.59 (5.67)	
High oral (12 mg)	23.77 (4.05)		29.34 (7.29)[b]	
Oral NRT product				
Four-week percentage adherence to prescribed dose, median (IQR)				
	Gum (n = 110)	Lozenge (n = 71)	Tablet (n = 88)	Inhalator (n = 140)
Percentage of oral NRT used only	84.88 (32.25)	85.12 (27.85)	90.74 (24.86)	96.03 (20.34)[c]
Percentage of total NRT used	91.58 (17.24)	93.41 (14.27)	95.13 (13.64)	96.77 (9.61)[d]
Four-week mean daily consumption in milligrams, mean (*SD*)				
	Gum (n = 110)	Lozenge (n = 71)	Tablet (n = 88)	Inhalator (n = 140)
Oral NRT consumption only	6.89 (4.08)	6.57 (3.09)	6.57 (2.91)	9.36 (5.26)[e]
Total NRT consumption	23.66 (6.82)	23.73 (6.45)	23.85 (5.62)	26.95 (7.31)[f]

Notes. IQR = interquartile range; NRT = nicotine replacement therapy; *SD* = standard deviation. Footnotes indicate differences between groups.
[a]Adherence greater (p < .05) than in both "low patch/low oral" and "high patch/high oral" groups but not "low patch/high oral."
[b]Consumption greater (p < .01) than in all other groups.
[c]Adherence greater (p < .05) than in all other groups.
[d]Adherence greater (p < .01) than for patch plus gum or lozenge.
[e]Consumption greater (p < .01) than in all other groups.
[f]Consumption greater (p < .001) than in all other groups.

Consumption

The use of an inhalator was associated with significantly higher consumption than that for each of the other oral products, $F(3,405) = 7.05$, $p < .001$, Games–Howell $p < .01$. The total dose of NRT consumed was also higher for patients using patch plus inhalator versus patch plus other oral NRT products, $F(3,405) = 12.57$, $p < .001$, Games–Howell $p < .001$.

Factors Associated With 4-Week Adherence and Consumption

Adherence

We examined whether dosage of prescribed NRT and delivery mode of oral NRT increased adherence (Table 3). We therefore entered binary variables of high/low patch and high/low oral NRT, plus binary terms representing each type of oral

NRT product (lozenge, sublingual tablet, gum with inhalator as referent group). We also controlled for potential confounders. Each contrast within the model corresponds to percentage points of adherence to NRT over the 4-week treatment period. Using gum rather than inhalator was associated with 5.3% lower adherence to NRT. For each cigarette smoked daily at baseline, adherence to NRT reduced by 0.26%.

Consumption

We also examined whether dosage of prescribed NRT and delivery mode of oral NRT increased consumption, using the same model as described for adherence. Prescribing 21 mg patches in preference to 14 mg patches was associated with a 7.0 mg/day increase in actual dose consumed, and prescribing 12 mg instead of 6 mg absorbed equivalent dose of oral NRT was associated with a 4.3 mg/day increase in consumption. Using lozenge, sublingual tablet, or gum was associated with lower consumption of NRT of between 2.5 and 3.3mg/day than with inhalator. The pattern of results using 1-week consumption was similar.

Consumption as a Predictor of Subsequent Abstinence

We accounted for reverse causation by including only the 285 participants abstinent for 1 week and assessed the association between their adherence during that week and abstinence at 4 weeks (Table 4). Higher consumption of NRT was associated with a nonsignificant increase in abstinence (p = .093; Model 1). However, the trial design meant that higher doses were prescribed to participants who were at higher risk of relapse through having higher levels of nicotine dependence. When potential confounders were controlled for in Model 2, this relationship was statistically significant (p = .042). In this model, each additional mg/day consumed was associated with increased odds of abstinence of 5%.

Table 3. Regression Models of Variables Associated With 4-Week Adherence and 4-Week Mean Daily Consumption

	Adherence		Consumption	
Included	*B* (beta)	*SE*	*B* (beta)	*SE*
Intervention arm	.17 (.01)	1.62	.07 (.01)	.58
OPRM1 genotype	−2.06 (−.05)	2.32	−.40 (−.02)	.83
FTND	.96 (.13)	.51	.21 (.07)	.18
Patch dose (high)	4.30 (.11)	2.33	6.99 (.41)***	.83
Oral dose (high)	−2.32 (.06)	2.56	4.28 (.25)***	.91
Lozenge use	−2.17 (−.05)	2.40	−2.95 (−.16)**	.85
Tablet use	−1.94 (−.05)	2.22	−2.54 (−.15)**	.79
Gum use	−5.34 (−.14)*	2.09	−3.28 (−.21)***	.75
Cigarettes per day	−.26 (−.14)*	.12	−.04 (−.05)	.04
Motivation	.69 (.09)	.40	.45 (.07)	.29
Model summary				
Adjusted R^2	.03		.29	
F for model	2.40**		17.50***	

Note. Beta = standardized regression coefficient; *B* = unstandardized regression coefficient; FTND = Fagerström Test for Nicotine Dependence; *SE* = standard error of unstandardized coefficient.
* = $p < .05$, ** = $p < .01$, *** = $p < .001$.

Table 4. Regression Model of 1-Week Mean Daily Consumption as a Predictor of Subsequent 4-Week Abstinence

	Model 1		Model 2	
Included	*B* (*SE*)	Odds ratio (95% *CI*)	*B* (*SE*)	Odds ratio (95% *CI*)
Mean daily consumption at 1 week	.03 (.02)	1.03 (.99, 1.07)	.05 (.02)*	1.05 (1.01, 1.10)
Intervention arm	–	–	.18 (.29)	1.20 (.68, 2.13)
Genotype	–	–	.38 (.41)	1.47 (.66, 3.29)
FTND	–	–	−.21 (.09)*	.81 (.68,.97)
Cigarettes per day	–	–	.01 (.02)	1.01 (.96, 1.06)
Longest previous quit	–	–	.05 (.09)	1.05 (.89, 1.24)
Model summary				
Nagelkerke R^2	.02		.07*	–

Note. Beta = standardized regression coefficient; *B* = unstandardized regression coefficient; FTND = Fagerström Test for Nicotine Dependence; SE = standard error of unstandardized coefficient.
* $p < .05$.

DISCUSSION

Participants in a smoking cessation trial in primary care were highly adherent to NRT. Prescribing higher doses of NRT was associated with higher consumption. The use of nicotine inhalators was associated with higher levels of adherence relative to other oral NRT products, which were similar to one another. Finally, each milligram per day of nicotine consumed was associated with a 5% increase in the odds of subsequent abstinence having controlled for reverse causation.

The levels of adherence seen in this study were high, but it is difficult to determine whether these levels are comparable with those that have been observed previously because of different methods of measuring and reporting adherence. Previous examples (Alterman, Gariti, Cook, & Cnaan, 1999; Joseph et al., 1996; Lam, et al., 2005; Okuyemi, Zheng, Guo, & Ahluwalia, 2010; Stein, Anderson, & Niaura, 2006; Wiggers et al., 2006), respectively, report NRT adherence levels of 56%–73%, 94.5%, 16%, 55%, 36.6%, and 37%, but these are the percentages of study participants who met particular and varying criteria for being considered adherent and at a range of timepoints.

These data show that prescribing higher doses does lead to higher consumption, but also that the dose of nicotine consumed depends on the form in which it is prescribed. Although prescribing additional dose as patches leads to larger increases in dose consumed, most additional oral NRT prescribed was also consumed, even though this required almost hourly dosing by participants. Randomized trials provide evidence that higher doses of NRT are associated with a modest increase in abstinence (Stead, et al., 2008). Taken together, these data support prescribing higher doses where clinically appropriate.

There were effects on adherence and consumption of the preferred oral NRT delivery method chosen to supplement a patch. The inhalator (the product most often chosen) was associated with highest adherence and consumption. This finding merits further investigation; Hajek et al. (1999) found that gum was better adhered to than inhalator or nasal spray as a means of oral NRT delivery. It is possible that the apparent benefit of inhalator use observed in our study is spurious. An inhalator cartridge contains sufficient nicotine for a very large number of uses, but all that was required to claim 100% adherence was to change this four times a day (in the high-dose [12 mg] condition). It is possible that those reporting using lozenges or gum, for example, would in fact extract more available nicotine than would people reporting using the requisite number of inhalator cartridges. It is also unclear whether the practice of allowing patients to choose their preferred form of NRT is beneficial in itself (Fagerstrom, Tejding, Westin, & Lunell, 1997; McClure & Swan, 2006). In this study, participants were allowed to choose their oral NRT product. It could be counterproductive to assign participants to a product shown to be associated with highest use, as the act of choosing a preferred product (even if supposedly a suboptimal choice) may improve adherence.

Our data support the conclusion that higher consumption is associated with improved abstinence outcomes. We excluded reverse causation by examining the relationship between consumption and subsequent abstinence only in those who were initially abstinent. These results are consistent with other studies that address this issue (Shiffman, 2007, 2008). Although excluding reverse causation in this way supports causality, it probably underestimates the strength of the association between consumption and abstinence. The true variable that relates to abstinence is consumption from quit day until the precise point where a person abandons their quit attempt, which is difficult to determine in large studies such as this. Consumption during the first week probably relates only moderately to consumption over this period, weakening the strength of association observed.

The key strengths of this study are that it addresses adherence and consumption within a substantial sample in a primary care setting, using good-quality outcome measurement. It addresses some notable limitations apparent within the existing literature on the use of NRT. First, we used a robust measure of adherence and consumption. There are often limitations with the methods of measuring adherence, raising questions about validity and reliability. For example, adherence has often been measured using retrospective self-report which may also be collected infrequently (Alterman, et al., 1999; Cooper et al., 2004; Okuyemi, et al., 2010; Stein, et al., 2006). Second, many previous studies have assessed adherence among particular subgroups of the population (Fish et al., 2009; Stein, et al., 2006; Wiggers, et al., 2006). We provide data on a population quitting smoking in primary care, where most cessation treatment is provided. Third, we used a sensitive measure of adherence. Previous studies report adherence in several ways which make understanding and comparing data across studies difficult. Adherence is often presented as it relates to an entire study population, rather than for those people who are continuing a quit attempt. Including those people who abandon a quit attempt and are therefore not prescribed further NRT has some value, but in our view it is not the most informative approach because NRT is not indicated when a person has ceased trying to quit smoking. In addition, the measures that are used vary widely. For example, studies that report adherence in dichotomous terms, that is, as adherent or not, may use definitions ranging from continuous use without gaps for a defined period (Wiggers, et al., 2006), to a set percentage of adherence (Okuyemi, et al., 2010), or use a median split in levels of adherence to define what is high or low (Shiffman, 2007, 2008). Given that level of use predicts cessation, and there is not clear guidance as to what should be regarded as an adequate or effective level, we think that it is most appropriate to report adherence as a continuous outcome: in this case as a percentage of the prescribed amount used over the specified treatment period and also to report mean daily consumption in milligrams. The system of describing adherence we used seems generally applicable across many contexts, and we recommend it as a standard for future studies.

The study design also has limitations. The participants in this study chose to participate in a clinical trial of smoking cessation and so may not be representative of users of smoking cessation services in primary care. The behavioral support program was typical of those provided within the NHS Stop Smoking Service in England, but we paid unusual attention to adherence, explaining the rationale explicitly and measuring it carefully every week, which may have increased adherence. The generalizability of our findings could therefore be questioned. However, qualitative interviews showed that the

fact that participants were in a trial impinged little on their consciousness and their motivation for joining the trial was the same as that of smokers joining cessation programs generally (Wright, manuscript in preparation). It is both appropriate and likely that smoking cessation clinics provide an explicit rationale for NRT use and check on adherence regularly, and these data support this. They suggest that patients should be informed as to why treatment is helpful and their use of it monitored carefully, and that such practices are likely to lead to higher abstinence.

In conclusion, most patients in a primary care–based behavioral support program take most of their prescribed NRT when the rationale for taking it is explained and adherence is monitored. Prescribing higher doses leads to higher consumption. Consuming more seems causally associated with higher abstinence. By identifying factors that are both associated with increasing NRT use and importantly which are likely to be readily influenced by clinicians, there are clear implications for research into ways of increasing NRT use still further.

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DECLARATION OF INTERESTS

PA has done consultancy and research on smoking cessation for pharmaceutical companies. All other authors declare no interests.

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