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Association of amount and duration of NRT use in smokers with cigarette consumption and motivation to stop smoking: A national survey of smokers in England

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HIGHLIGHTS

- Clinical trials demonstrate that NRT for smoking reduction is efficacious.
- At the population level, NRT increases motivation to quit but does not reduce intake.
- It may be that smokers are not using enough NRT or for long enough.
- The current study assessed the extent of dual NRT and cigarette use.
- Findings suggest that effectiveness may partially depend on extent of use.

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ABSTRACT

Introduction: Clinical trials have found that the use of nicotine replacement therapy (NRT) to reduce cigarette consumption results in significant declines in cigarette consumption and increases smokers' propensity to quit. However, observational "real-world" studies have found much smaller effects. This may be because of low levels of NRT use. This study examined the association between amount and duration of NRT use amongst those attempting to reduce their cigarette consumption with motivation to quit and cigarette consumption.
Methods: Data came from 2,158 smokers who took part in the Smoking Toolkit Study. A representative survey of smokers in England aged 16+.
Results: Only 54.4% of patch users and 32.2% of non-transdermal NRT users reported using NRT with a frequency that would be expected to substantially influence cigarette consumption (4+ units per day for acute NRT forms and at least daily for transdermal patches). Those using the patch at or above this threshold smoked 1.3 cigarettes per day fewer than those using it below the threshold ($p = 0.059$), whilst those using non-transdermal NRT at or above this threshold smoked 0.9 cigarettes less per day ($p = 0.022$). In both cases, those using NRT more frequently had greater motivation to quit. Less than 1/5th of participants reported using a combination of NRT products. Use of NRT long-term was associated with lower motivation to quit and higher cigarette consumption.
Conclusion: Smokers attempting to reduce their cigarette intake are underusing NRT and this is associated with cigarette consumption and motivation to quit. These findings may explain why population-based studies have failed to report similar findings to clinical trials.

1. Introduction

The National Institute for Health and Care Excellence (NICE) in the UK recently released guidance on the use of nicotine replacement therapy (NRT) to reduce cigarette intake (NICE, 2013). The focus was predominantly on the use of NRT for *smoking reduction*, i.e. attempting to cut down cigarette consumption without any intention to quit and use during periods of time when they are unable to smoke, i.e. periods of *temporary abstinence*. The UK is currently the only country to have licensed and recommend that smokers use NRT for these purposes and, as a consequence, is at the forefront of the debate on dual NRT and cigarette use.

NICE advocated the use of pharmacology for smoking reduction and/or temporary abstinence on the basis of clinical trials and

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population-based studies demonstrating its efficacy and effectiveness in relation to promoting smoking cessation amongst those who are initially unable or unwilling to stop smoking (Beard, Aveyard, Brown, & West, 2012; Beard, Aveyard, Michie, McNeill, & West, 2013; Beard, Brown, & Robert, 2014; Beard, Fidler, & West, 2011; Beard, McNeill, et al., 2011, 2013; Beard & West, 2012; Moore et al., 2009). However, NICE also acknowledged that any interim reduction in harm was unlikely. Although randomised controlled trials demonstrate that individuals who are unmotivated to stop smoking, and who use NRT concurrently with cigarettes, are more likely to report significant reductions in their cigarette consumption (Moore et al., 2009); similar findings do not translate to the population level. Smokers in the general population using NRT for smoking reduction and/or temporary abstinence smoke more cigarettes than other smokers and report reductions in consumption of only a few cigarettes per day over time (Beard, Aveyard, et al., 2012; Beard, Aveyard, et al., 2013; Beard, Fidler et al., 2011; Beard, McNeill, et al., 2011, 2013; Beard & West, 2012; Beard et al., 2014).

One possible reason for the discrepancy between clinical trials and the "real world" is that at the population level, smokers are not usually provided with behavioural support or instructions on the use of medicinal nicotine products. This may result in smokers using NRT suboptimally. There is evidence that smokers who are attempting to quit smoking often use too little medication and for too short a period (Shiffman, Hughes, Pillitteri, & Burton, 2003; Shiffman et al., 2002). One reason why smokers' under-dose is that too many of them mistakenly believe that NRT is unsafe—in fact, many believe that NRT is as dangerous as cigarettes (Bansal, Cummings, Hyland, & Giovino, 2004). Similarly, smokers often fail to use combination NRT, which is more effective than the use of only one NRT product (Brose et al., 2011). Although single-form NRT provides effective treatment for tobacco dependence, typically doubling success rates compared with placebo (Stead, Perera, Bullen, Mant, & Lancaster, 2008); a strategy for further improving its efficacy is to combine one medication that allows for passive nicotine delivery (e.g. transdermal nicotine patch), with another medication that permits ad libitum nicotine consumption (e.g. non-transdermal products such as the nicotine gum).

It is important to determine whether dual users similarly underuse NRT and whether this explains the low effectiveness of NRT for smoking reduction and/or temporary abstinence at the population level in relation to reductions in cigarette consumption. Some support for this hypothesis comes from a 2007 study, where high dosages of NRT were found to be associated with larger reductions in cigarette consumption, NNAL and carbon monoxide relative to low doses of NRT amongst continuing smokers (Hatsukami et al., 2007). Moreover, in a recent qualitative study, which assessed smokers' beliefs about and use of NRT for smoking reduction and/or temporary abstinence, we established that smokers use combination NRT sequentially rather than concurrently and that underuse may be due to costs and concerns about overdose (Beard, Vangeli, Michie, & West, 2012). Of course, such qualitative studies cannot provide estimates of the prevalence of the phenomena observed, whilst the findings by Hatsukami et al. (2007) may not apply in the real world outside of a clinical setting.

The current study addressed these issues and extended the findings using data from the Smoking Toolkit Study, a population-based survey of adults aged 16+ in England, by assessing amongst those using NRT for smoking reduction and/or temporary abstinence the association between combination NRT use, length of NRT use and frequency of NRT use, with cigarette consumption and motivation to quit. This is a novel investigation based on the hypothesis that the relationship between extent of NRT use and effectiveness may be moderated by use duration. There is evidence that reductions in consumption amongst those using NRT for smoking reduction subside over time in clinical trials (Haustein, Batra, Landfeldt, & Westin, 2003; Moore et al., 2009); possibly as smokers enter a "maintenance phase" and therefore cease reductions in their cigarette intake, or start to believe that they have failed to cut down and thus increase their cigarette consumption. Similarly, if it is the case that in the "real world" those who are more nicotine dependent use NRT longer, one may expect that those using NRT for extended periods of time will have *higher* cigarette consumption and *lower* odds of a quit attempt due to selection bias.

The findings from this study will help to inform smoking reduction interventions, which is vital given that NICE provides little guidance on how to implement a dual use approach in practice. They will also inform policy makers in countries currently considering whether to licence NRT for smoking reduction and/or temporary abstinence and whether to offer smoking reduction as a tobacco control treatment within health care services. If it is the case that smokers are underusing NRT and that greater effectiveness is observed with better use, then interventions should be aimed at encouraging adherence to pharmacological therapy. Drug adherence interventions to date have had mixed efficacy (e.g. Banning, 2009), partially as they have been based on intuition rather than theoretical knowledge. According to the Necessity-Concerns Framework (Horne & Weinman, 2002), smokers' motivation to start and persist with medication will be influenced by the way in which they judge their personal need for the treatment relative to their concerns about the potential adverse effects. Interventions should, as a consequence, emphasise the pros of NRT use, ensure that smokers hold accurate perceptions about their addiction and understand that use of pharmacological support is the optimal approach to smoking reduction. However, if it is the case that the effectiveness of NRT dissipates over time, such interventions may also constrain pharmacological support to a given time period.

2. Methods

2.1. Design

The study formed part of the Smoking Toolkit Study (http://www.smokinginengland.info), an ongoing population study designed to provide information on smoking and smoking cessation patterns amongst smokers and recent ex-smokers in England. The Smoking Toolkit Study involves monthly household surveys using a random location sampling design, with initial random selection of grouped output areas (containing 300 households), stratified by ACORN (sociodemographic) characteristics (http//www.caci.co.uk/acorn/acornmap.asp) and region. Interviewers then choose which houses within these areas are most likely to fulfil their quotas and conduct face-to-face computer-assisted interviews with one member per household. Further details of which are described elsewhere (Fidler et al., 2011).

Between July 2010 and December 2013, 79,530 adults were surveyed; of whom, 21.8% ($n = 17{,}284$) reported that they were current smokers. Thirteen percent ($n = 2{,}158$) of smokers were using NRT. These form the sample for this study.

2.2. Measures

Current smokers were asked "Are you currently trying to cut down on how much you smoke but not currently trying to stop?"—(yes; no; don't know). If they answered "yes" they were asked "Which, if any, of the following are you currently using to help you cut down the amount you smoke?—(nicotine patch; nicotine gum; nicotine lozenges/tablets; nicotine inhaler; nicotine nasal spray; I don't know, none of these; other). All smokers were asked "Do you regularly use any of the following in situations when you are not allowed to smoke?—(nicotine patch; nicotine gum; nicotine lozenges/tablets; nicotine inhaler; nicotine nasal spray; I don't know; none of these; other). Those reporting the use of NRT for smoking reduction and/or temporary abstinence were also asked "How many times per day on average do you use a nicotine replacement product?"—(not every day and less than once per week; not every day but at least once a week; once per day; twice per day; 3–4 times per day; 5–6 times per day; 7–11 times per day; more than 12 times per day) and "How long have you used nicotine replacement

products for?"—(less than one week; one to six weeks; more than six weeks up to twelve weeks; more than 12 weeks). Cigarette consumption, motivation to quit and time to first cigarette. Motivation to quit was measured using a dichotomised version of the validated Motivation to Stop Scale (MTSS): participants were divided into those who wanted to quit within the next three months and those who did not (Kotz, Brown, & West, 2013).

2.3. Analysis

For all analyses, R version 2.15.2 was used. We conducted a series of logistic and linear regression analyses with combination NRT use, length of NRT use and frequency of NRT use as independent variables; and baseline cigarette consumption per day and proportion of smokers reporting motivation to quit within the next three months, as dependent variables. Frequency of NRT use was dichotomised according to clinical guidelines into use that would be expected to produce a significant clinical effect (i.e. non-transdermal use of NRT at least 4 times per day and the use of the nicotine patch at least daily) and use that would not be expected to produce a significant clinical effect (i.e. non-transdermal use of NRT less than 3 times per day and non-daily use of the nicotine patch). All analyses were adjusted for age, gender, social grade and time to first cigarette of the day. Associations with cigarette consumption were also adjusted for recent quit attempts. The reason being, that those who attempt to quit and relapse are likely to resume a lower level of smoking (Knoke, Anderson, & Burns, 2006).

To assess the possibility that the association between length of NRT use with cigarette consumption and motivation to quit may not be linear, we also fitted separate segmented regression models, allowing for singular and multiple breakpoints (breakpoints are the values of the independent variable where the slope of the function changes). The "segmented package" was used (Muggeo, 2013). This package adopts an iterative procedure whereby only starting values for the breakpoints are required (Muggeo, 2003). It also implements bootstrap restarting to make the algorithm less sensitive to starting values (Wood, 2001). For reasons of parsimony, only the results of the segmented regression models are reported if they explained more variance than the simple linear and logistic equivalents. STROBE guidelines for the reporting of epidemiological studies were followed throughout (von Elm et al., 2007).

3. Results

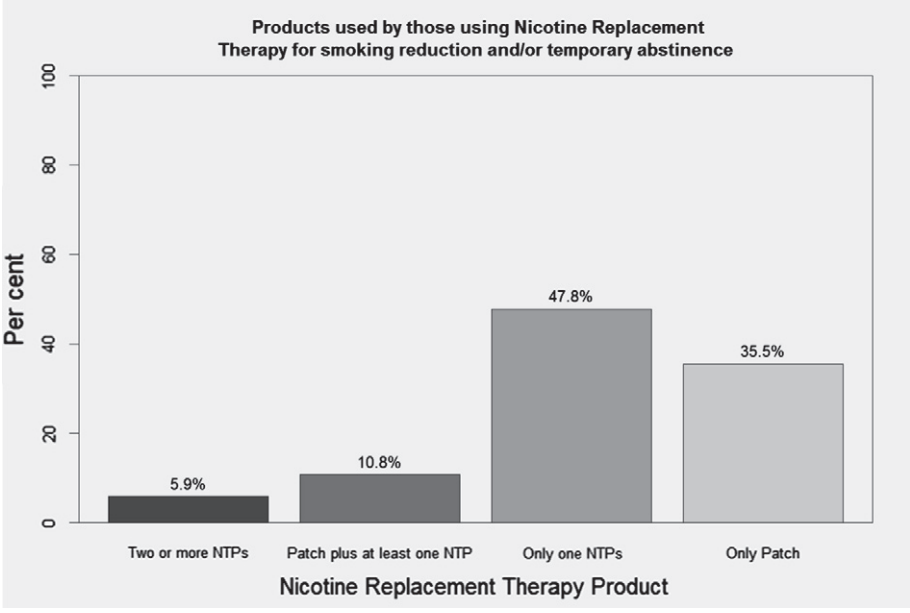
Forty-eight percent ($n = 1{,}029$) of smokers using NRT were male, with a mean [standard deviation (SD)] age of 43.0 (15.56) years. The percentages of participants in each social grade were as follows: AB (12.0%, $n = 259$), C1 (22.0%, $n = 475$), C2 (21.8%, $n = 470$), D (18.1%, $n = 391$) and E (26.1%, $n = 563$). The mean (SD) daily cigarette consumption was 12.8 (8.56), with 22.1% ($n = 476$) reporting smoking a cigarette within 5 minutes of wakening, 35.0% ($n = 754$) between 6 and 30 minutes after wakening, 19.2% ($n = 413$) within 31–60 minutes of wakening and 23.7% ($n = 509$) more than an hour after wakening.

3.1. Combination NRT

Eighty-three percent ($n = 1{,}798$) of those using NRT for smoking reduction and/or temporary abstinence used only one NRT product, whilst 16.7% ($n = 360$) used a combination of NRT products. The most frequent combination being the patch plus one or more non-transdermal product (see Fig. 1). After adjusting for socio-demographic characteristics and time to first cigarette of the day, those using a combination of NRT products had a higher odds of reporting a previous quit attempt compared to those using only one product [72.2% ($n = 257$) versus 66.1% ($n = 1174$)]. There was no association with motivation to quit. Forty-four percent ($n = 783$) and 42.2% ($n = 152$) of those using only one product and those using more than one product reported that they were motivated to quit smoking within the next three months, respectively. Those using more than one product had a higher cigarette consumption than those using only the patch or only one non-transdermal product (M = 14.2 [SD ± 10.30] versus M = 12.5 [SD ± 8.14]).

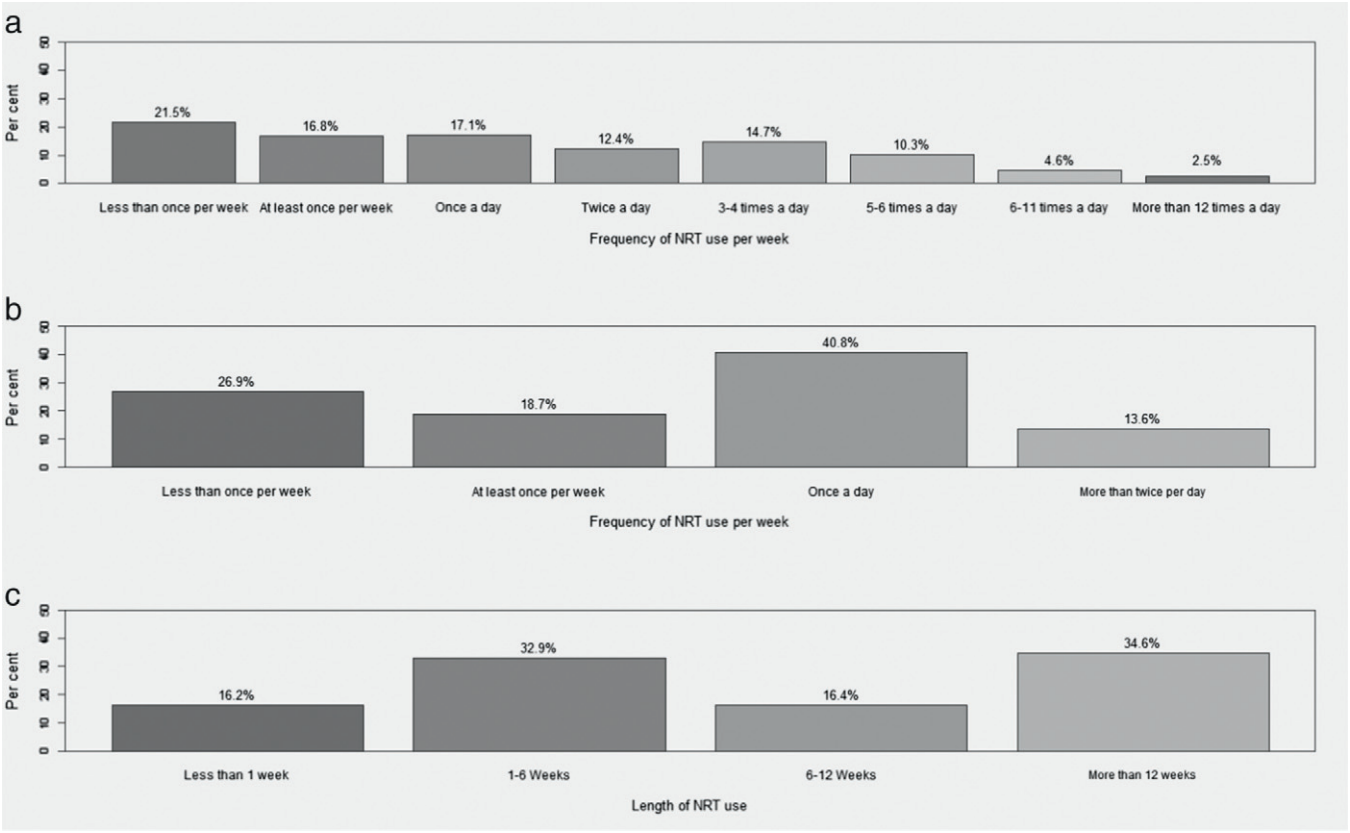
3.2. Amount of NRT used

Fig. 2a and b show the average times per day smokers used NRT. Table 1 shows average cigarette consumption and motivation to quit as a function of frequency of NRT use.



Note: NTP=Non-Transdermal Product e.g. nicotine gum, lozenges, nasal spray and inhalator

Fig. 1.



Note: For (a) and (b) missing data: n=239; total sample 1919 out of a possible 2158; For (c) missing data: n=140; total sample 2018 out of a possible 2158

Fig. 2. (a) Frequency of NRT use per week amongst those using at least one non-transdermal NRT product; (b) frequency of NRT use per week amongst those using only the nicotine patch; and (c) length of NRT use amongst those using any product.

Amongst those using the nicotine patch, 54.4% ($n = 375$) used it at least daily. Of these, 59.5% ($n = 223$) reported that they were motivated to quit smoking within the next 3 months; whilst only 31.8% ($n = 100$) of those using the nicotine patch less than daily reported similar motivation. This difference was significant (see Table 2). Those using the patch daily had a lower cigarette consumption, albeit not quite significant, compared to those using it less regularly [13.7 (SD ± 8.56) versus 12.4 (SD ± 8.61)].

Table 1
Motivation to quit and cigarette consumption as a function of the frequency and length of dual NRT use.

	Cigarette consumption per day M (SD)	Motivation to quit within the next three months %(n)
Frequency of non-transdermal NRT %(n)		
Less than 3 times per day	12.8 (9.33)	35.3 (294)
At least 4 times per day	11.9 (7.31)	53.3 (211)
Frequency of the nicotine patch %(n)		
Non-daily	13.7 (8.56)	31.8 (100)
Daily	12.4 (8.61)	54.4 (375)
Length of NRT use		
Less than 1 week ($n = 326$)	13.1 (10.11)	52.8 (172)
1–6 weeks ($n = 664$)	12.2 (8.38)	55.3 (367)
6–12 weeks ($n = 330$)	12.0 (7.40)	43.9 (145)
More than 12 weeks ($n = 698$)	13.5 (8.52)	40.7 (192)

Note: NRT = nicotine replacement therapy; M = mean; SD = standard deviation.

Amongst those using the non-transdermal NCPs, 32.2% ($n = 396$) used them at least 4 times per day. These individuals had over twice the odds of reporting that they were motivated to quit smoking than those using non-transdermal NCPs less than 4 times per day [53.3% ($n = 211$) versus 35.3% ($n = 294$)]. Cigarette consumption was also significantly lower amongst those using NRT more than 4 times per day [11.9 (SD ± 7.31) versus 12.8 (SD ± 9.33); see Table 2].

3.3. Length of NRT use

Fig. 2c shows the length of time smokers had used NRT for. Only 34.6% reported having used NRT for more than 3 months. Table 1 shows the percentage of participants reporting motivation to quit within the next three months and average cigarette consumption as a function of length of NRT use. Use of NRT longer than 6 weeks and 12 weeks was associated, respectively, with reduced motivation to quit and increased cigarette consumption (see Table 1).

4. Discussion

Those using a combination of NRT products had higher cigarette consumption and similar motivation to quit compared with those using only one NRT product. Frequency of NRT use was negatively associated with cigarette consumption and positively associated with motivation to stop. Use of NRT longer than 6 weeks was associated with reduced motivation to quit, whilst NRT use longer than 12 weeks was associated with increased cigarette consumption.

Table 2
Regression analysis of the association between combination NRT, amount of NRT used and length of use with motivation to quit and cigarette consumption.

	Motivation to quit			Cigarette consumption		
	OR	95% CI	*p*	*β*	95% CI	*P*
Combination NRT	0.96	0.76 to 1.21	0.716	1.34	0.46 to 2.22	0.003
Amount of NRT used (patch)						
Non-daily	1			1		
Daily	3.18	2.30 to 4.40	<0.001	−1.13	−2.30 to 0.04	0.059
Amount of NRT used (non-transdermal)						
Less than 3 times per day	1			1		
Four or more times per day	2.09	1.63 to 2.67	<0.001	−0.86	−2.089 to −0.17	0.022
Length of NRT use ϕ						
Up to 6 weeks	0.11	0.85 to 1.45	0.296			
More than 6 weeks	0.49	0.37 to 0.64	<0.001			
Up to 12 weeks				−0.73	−0.76 to 0.31	0.156
More than 12 weeks				1.28	0.26 to −2.31	0.020

Note: NRT = nicotine replacement therapy. All analyses were adjusted for age, gender, social grade and time to first cigarette of the day. Associations with cigarette consumption were also adjusted for previous attempts to quit smoking; ϕ segmented regression identified a break point in the association between length of NRT use and cigarette consumption at 12 weeks and motivation to quit at 6 weeks.

This is the first study, to our knowledge, that has assessed combination NRT use amongst dual cigarette and NRT users not attempting to quit. Less than 17% of participants reported using multiple NRT products whilst concurrently smoking. This is much lower than the previously reported prevalence of combined NRT use amongst those attempting to quit (e.g. Johnson, Anderson, & Lockhart, 2014). This likely reflects the cost of NRT and lack of professional support. Smokers using NRT for smoking reduction generally purchase NRT over the counter (Hammond et al., 2008), whereas those smokers attempting to quit often obtain NRT on prescription from general practitioners at a reduced cost or for free.

Previous clinical trials have demonstrated that combination NRT is more effective than the use of only one product amongst those attempting to quit. Combination NRT has been to shown to increase smoking abstinence rates, lead to higher salivary cotinine concentrations and lower withdrawal scores (Stead et al., 2008). The failure to find a benefit of combined NRT use in the current study may be due to the cross-sectional nature of the data precluding any change in cigarette consumption or motivation to quit. Those opting for multiple products may have a priori been more nicotine dependent and less enthused about stopping, and thus any increase in motivation and/or decrease in consumption, unless excessive, would not be detected.

An alternative explanation is that smokers using a combination of NRT products for smoking reduction do so sequentially rather than concurrently (Beard, Vangeli, et al., 2012). Sequential use is unlikely to prevent compensatory smoking since smokers cannot adequately replace all the nicotine lost from their cigarettes. For this to be abated, complete nicotine substitution through the concurrent use of multiple forms of NRT is likely to be necessary. A final explanation, which is supported by the other findings in this paper, is that smokers were not using an adequate amount of either NRT to produce a clinical benefit, possibly due to the lack of behavioural support at the population level.

Of interest, is that the majority of smokers failed to use non-transdermal nicotine products as frequently as recommended (e.g. nicotine gum can be used up to 15 times per day) and only half of the smokers reported having used NRT for longer than 6 weeks. This is consistent with previous population-based studies looking at adherence to nicotine-containing products (Shiffman et al., 2003), but is in contrast to the clinical trials that reported high adherence to the NRT regimen (Moore et al., 2009). Poor adherence may be a consequence of cost, inaccurate beliefs about the safety of NRT or lack of knowledge regarding the product's use.

The fact that those who used NRT frequently enough for a clinical benefit to have been expected had significantly lower cigarette consumption than those using NRT infrequently, suggests that the poor adherence may at least partially explain why, at the population level, those using NRT for smoking reduction do not report significantly large declines in their cigarette consumption (Beard et al., 2014). However, declines were still not in the region of those reported in the clinical trials (i.e. over 50%). Although the true extent of reduction may be precluded by the cross-sectional nature of the study, it is possible that the behavioural support offered by these trials also had a significant impact on outcomes. This assertion is supported by the previous finding that even over a 6-month period, reductions in cigarette consumption at the population level ranged from 1 to 2 cigarettes per day (Beard, McNeill, et al., 2013).

Length of NRT use also appears to be an important factor. Up to three months of use, there appears to be a decline, albeit not significant, in cigarette consumption. Following this point, there is an increase in cigarette intake per day. This might reflect the fact that those who use NRT for longer are more nicotine dependent, although dependency was adjusted for in the analysis. Moreover, this finding of a non-linear relationship between length of NRT use and cigarette consumption is consistent with previous studies (Haustein et al., 2003; Moore et al., 2009). It may be that over time, smokers enter a "maintenance phase" and therefore cease reductions in their cigarette intake and/or start to believe that they have failed in their attempts to cut down, with decreasing self-efficacy resulting in them abandoning attempts to reduce their intake.

Finally, although caution should be taken when interpreting the positive association between extent of use and motivation to quit, this finding suggests that the "effectiveness" of NRT for smoking reduction and/or temporary abstinence at the population level may be increased by encouraging smokers to use NRT products more regularly. At the same time, the finding that motivation to quit is lower following 6 weeks of NRT use suggests that caution may be warranted regarding the long-term use of nicotine-containing products during smoking reduction. This is in contrast to previous research on the long-term use of NRT for complete substitution of cigarettes. It is largely accepted that long-term NRT use amongst smokers who have quit smoking could be beneficial (e.g. Agboola, McNeill, Coleman, & Bee, 2010). The premise is that complete substitution with NRT could prevent relapse and that the risks would be limited only to maintaining nicotine addiction without the adverse consequences of continued tobacco consumption. A similar benefit may not be expected amongst those partially substituting their cigarettes for NRT as smokers are likely to enter a maintenance phase when they become complacent with their smoking habit. Reductions in cigarette consumption amongst dual users of NRT cigarettes were found to subside over time in previous clinical trials (Haustein et al., 2003; Moore et al., 2009). Similarly, if it is the case that in the "real world" those who are more nicotine dependent

use NRT for longer, one may expect that those using NRT for extended periods of time will have *higher* cigarette consumption and *lower* odds of a quit attempt due to selection bias.

In conclusion, these findings suggest that the association between the use of NRT for smoking reduction and attempts to quit smoking and cigarette consumption may at least be partially dependent on extent of NRT use. Although this is the first study to our knowledge that has assessed extent of NRT use amongst those using NRT for smoking reduction and/or temporary abstinence, it does suffer from several limitations. First, care must be taken when making conclusions about the effectiveness of NRT for smoking reduction and/or temporary abstinence on the basis of this data alone. The cross-sectional analyses mean that directional relationships cannot be determined. For example, it might be the case that greater NRT use increases smokers' motivation to quit, or that smokers who are more motivated to quit opt to use more NRT. Secondly, although reduced cigarette consumption is indicative of a reduction in harm, future studies would benefit from the inclusion of biological measures of toxin intake.

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Contributions

All authors contributed to the manuscript. EB, CB and RW designed the study and wrote the first draft. JB and AM revised the manuscript.

Conflicts of interest

EB and JB have received unrestricted funding from Pfizer. RW undertakes research and consultancy for pharmaceutical companies. He also has a share of a patent for a nicotine delivery device.

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