

Original Contribution

Duration of Nicotine Replacement Therapy Use and Smoking Cessation: A Population-Based Longitudinal Study

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Initially submitted May 30, 2014; accepted for publication September 22, 2014.

In the present study, we examined the association between duration of nicotine replacement therapy (NRT) use and smoking cessation using data from the Ontario Tobacco Survey longitudinal study (3 waves of data collected between July 2005 and December 2009). We used logistic regression with generalized estimating equations to examine the association between NRT use (any use and <4 weeks, 4.0–7.9 weeks, 8.0–11.9 weeks, and \geq 12 weeks of use compared with nonuse) and quitting smoking (\geq 1 month). Using NRT was not associated with quitting when use duration was not taken into account (adjusted odds ratio (OR) = 1.08, 95% confidence interval (CI): 0.86, 1.35). Compared with abstaining from NRT when attempting to quit smoking, using NRT for less than 4 weeks was associated with a lower likelihood of quitting (adjusted OR = 0.51, 95% CI: 0.38, 0.67); however, using NRT for 4 weeks or longer was associated with a higher likelihood of cessation (for 4.0–7.9 weeks of NRT use, adjusted OR = 2.26, 95% CI: 1.58, 3.22; for 8.0–11.9 weeks of NRT use, adjusted OR = 3.84, 95% CI: 2.24, 6.58; and for \geq 12 weeks of NRT use, adjusted OR = 2.80, 95% CI: 1.70, 4.61). Thus, use of NRT for less than 4 weeks was associated with reduced likelihood of cessation, whereas NRT use for longer periods of time was associated with a higher likelihood of cessation.

logistic models; longitudinal studies; nicotine replacement therapy; smoking cessation

Abbreviations: NRT, nicotine replacement therapy; OR, odds ratio.

Nicotine replacement therapy (NRT), including nicotine gum, patches, lozenges, nasal spray, and inhalers, is a first-line medication for smoking cessation (1). In a 2012 review of clinical trials (n = 150), Stead et al. (2) concluded that NRT use increases the rate of quitting by 60%.

NRT was first made available over the counter in numerous countries during the 1990s (3–6). Although many smokers do not use cessation medication when trying to quit smoking, the majority of smokers who do use cessation medication choose over-the-counter NRT products. In a recent real-world study (n = 10,335) using data from respondents to a survey conducted between November 2006 and May 2012 in England, Kotz et al. (7) found that 51% of smokers who attempted to quit smoking in the preceding 12 months did not use cessation medication; however, among those who did use cessation medication, such as bupropion and varenicline), 62% used over-the-counter

NRT products. Findings about the association between NRT use and smoking cessation in general population studies have been inconsistent. Both cross-sectional (6) and cohort (8, 9) studies have found that NRT was not associated with a higher likelihood of smoking cessation. A few other cross-sectional (10, 11) and cohort (12–15) studies have shown that NRT use was associated with a higher likelihood of smoking cessation. Most previous population-based studies only assessed the association between NRT use and smoking cessation by comparing use versus nonuse. However, the impact of duration of NRT use on smoking cessation in the general population has not been fully examined.

To our knowledge, there have been no population-based studies conducted in a representative sample in which the association between duration of NRT use and smoking cessation have been examined. To that end, we sought to study whether duration of NRT use is associated with smoking cessation by using population-based representative longitudinal data.

METHODS

Study design and sample

The longitudinal panel study of the Ontario Tobacco Survey was a regionally stratified, population-based representative telephone survey of adult recent smokers who were 18 years of age or older and had smoked at least 1 cigarette in the past 6 months in Ontario, Canada. Details of the study design of the Ontario Tobacco Survey have been published previously (16). For the present study, we used the longitudinal panel of smokers, in which smokers were recruited and followed-up for 3 additional interviews at 6-month intervals (i.e., waves 1, 2, and 3). Baseline data were collected between July 2005 and June 2008 (response rate: 61%) (17). Eighteen months of follow-up data were collected between January 2007 and December 2009. At baseline, 3,968 current smokers (those who smoked ≥ 100 cigarettes in their lifetime and some in the past 30 days) were recruited. Eligible respondents were current smokers at the beginning of each wave who tried to quit smoking during each 6 months of follow-up. Representativeness of the Ontario Tobacco Survey sample has been confirmed by comparing selected demographic characteristics to census data from Ontario (17).

Among all baseline current smokers, only 400 (10.1%) missed all 3 follow-up interviews. Those lost to follow-up were younger (the mean age was 37.6 years among those lost to follow-up and 44.2 years among those who were included in the analysis) and more likely to be male but less likely to have used NRT than were those who were included in the analysis; however, there was no difference in smoking behaviors (self-perceived addiction, daily smoking status, and number of cigarettes smoked per day) at baseline between the 2 groups. Research ethics approval for this study was obtained from the University of Toronto.

Outcome measures

Quitting smoking (abstinence ≥ 1 month) was measured at each follow-up interview based on answers to the question, "How long ago was it that you last smoked a cigarette?" Those who had smoked their last cigarette at least 1 month prior were classified as quitters.

Measures of cessation aids and duration of use

Each cessation aid and its duration of use were measured based on answers to the following questions at each followup: "Over the past 6 months, did you use nicotine patch (gum, lozenges/tablets, or inhalers) to help you quit or stay smokefree?" and "Over the past 6 months, how long did you use the patch (gum or other forms of NRT) to help you quit or stay smoke-free?" The duration of any NRT was calculated as the sum of the durations of use of all NRT forms at any 1 followup. If concurrent use of multiple forms of NRT occurred, the longest duration of the NRT form was used. However, information on whether nonconcurrent use of multiple forms of NRT was consecutive or separate was not available. We categorized the primary independent variables by type (any NRT, nicotine patch, and nicotine gum) and duration (no NRT use and use for <4 weeks, 4.0–7.9 weeks, 8.0–11.9 weeks, and \geq 12 weeks).

Potential confounding variables

A number of variables that influence the use of NRT and smoking cessation were examined. Baseline variables included sociodemographic characteristics (18) (age, sex, educational level, and marital status). Time-varying covariates included self-rated health (19, 20) (1-5 for poor, fair, good, very good, and excellent, respectively), self-perceived addiction (addicted vs. not addicted), tobacco dependence (18, 21, 22) (daily smoking, number of cigarettes smoked per day), use of other tobacco products (23–25) (e.g., snus and cigars), number of lifetime attempts to quit (18, 22, 26), social and environmental factors for quitting (27-29) (other household members who smoke, home smoking restrictions), and use of other cessation aids (2, 30, 31) (bupropion, varenicline, and behavioral support, including group counseling, specialized addiction counseling, telephone or online helpline, and cessation programs). If a variable was found to be associated with both the outcome among nonusers of NRT and the primary independent variable (duration of NRT use) at a level of $P \le 0.2$, the variable was defined as a confounding variable and controlled for in adjusted analyses.

Statistical analyses

We used bivariate analyses to examine the differences in sociodemographic characteristics, smoking-related variables, and other variables by groups of duration of NRT use, using either a χ^2 test (categorical variables) or t test (continuous variables). A dyad format, in which each dyad consisted of 2 consecutive interviews, was used in the data analysis. For each participant, the maximum number of dyads was 3 (i.e., dyad 1, baseline to wave 1; dyad 2, wave 1 to wave 2; and dyad 3, wave 2 to wave 3). To be eligible, a participant had to be a smoker at the time of 1 interview (baseline, wave 1, or wave 2), which was determined based on answers to 3 survey questions: "At the present time, do you smoke cigarettes every day, almost every day, occasionally, or not at all?", "On how many of the past 30 days did you smoke at least 1 cigarette?", and "Have you smoked at least 100 cigarettes in your life?" Participants continued to be eligible if they had attempted to quit during the 6-month follow-up period before the time 2 interview, which was determined based on the answer to the question at the time 2 interview, "Did you try to quit smoking completely during the past 6 months?" Thus, each dyad used information about smoking, cessation aids, and other variables from 2 interviews (baseline to wave 1, wave 1 to wave 2, and wave 2 to wave 3). The primary independent variables (NRT products) and the quitting outcome were measured at the time 2 interview in each dyad. Confounding variables of age, sex, educational level, and marital status were measured at the baseline survey. Time-varying covariates were measured at the time 1 interview of each dyad, except for use of other cessation aids (prescription cessation medication and behavioral support) that were measured at the time 2 interview.

Duration of Use by Cessation Aid	Wave 1 (<i>n</i> = 1,469)			Wave 2 (n = 1,181)			Wave 3 (n = 1,021)		
	No.	%	Mean (SD)	No.	%	Mean (SD)	No.	%	Mean (SD)
Duration of any NRT use, weeks									
None	1,079	73.5		869	73.6		735	72.0	
<4	288	19.6		225	19.1		209	20.5	
4.0–7.9	56	3.8		41	3.5		35	3.4	
8.0–11.9	21	1.4		17	1.4		17	1.7	
≥12	25	1.7		29	2.5		25	2.5	
All groups	1,469	100		1,181	100		1,021	100	
Duration of use, days	8.	0 ^a	22.9 (35.7)	9.	5 ^a	26.0 (40.4)	14	.0 ^a	27.6 (48.4)
Duration of nicotine patch use, weeks									
Non-NRT use	1,079	81.8		869	84.0		735	82.9	
<4	178	13.5		114	11.0		113	12.7	
4.0–7.9	33	2.5		31	3.0		21	2.4	
8.0–11.9	17	1.3		11	1.1		9	1.0	
≥12	12	0.9		10	1.0		9	1.0	
All groups	1,319	100		1,035	100		887	100	
Duration of use, days	9.	5 ^a	21.3 (28.3)	10	.0 ^a	22.5 (28.0)	14	.0 ^a	21.9 (28.4)
Duration of nicotine gum use, weeks									
Non-NRT use	1,079	87.0		869	85.6		735	83.3	
<4	130	10.5		119	11.7		116	13.2	
4.0–7.9	15	1.2		11	1.1		11	1.2	
8–11.9	6	0.5		4	0.4		5	0.6	
≥12	10	0.8		12	1.2		15	1.7	
All groups	1,240	100		1,015	100		882	100	
Duration of use, days	7.	0 ^a	19.5 (37.2)	7.	0 ^a	21.5 (41.9)	7	.0 ^a	24.1 (42.9)

 Table 1.
 Duration of Nicotine Replacement Therapy Use by Type and Study Wave Among Smokers Who Made an

 Attempt to Quit During Follow-up, Ontario, Canada, 2005–2009

Abbreviations: NRT, nicotine replacement therapy; SD, standard deviation.

^a Values are expressed as median.

To account for correlation in each individual (repeated measures in each person), we applied logistic regression by using the generalized estimating equations with exchangeable correlation matrix to estimate the associations of duration of NRT use (any NRT, nicotine patch, and nicotine gum) with smoking cessation (32). Odds ratios and 95% confidence intervals were reported. Analyses were conducted using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina), and all *P* values were 2-sided.

RESULTS

Among those who were current smokers at baseline and attempted to quit during wave 1 (n = 1,469), the majority (74%) did not use any NRT; 20% used NRT for <4 weeks, 4% used NRT for 4.0–7.9 weeks, and only 3% used NRT for ≥ 8 weeks. (Within this section, all percentages corresponding to data in the table have been rounded to the closest digit.) A similar pattern of duration of NRT use was found among persons who were current smokers at the wave 1 interview and made a quit attempt during wave 2 (n = 1,181), and persons who were current smokers at the wave 2 interview and made a quit attempt during wave 3 (n = 1,021). The median duration of NRT use was 8, 9.5, and 14 days during waves 1, 2, and 3, respectively. The use duration patterns for the nicotine patch and gum were similar to that for any NRT use except that the proportion of nonuse was even larger (82%–87%). During the 3 waves, the most commonly used form of NRT was a nicotine patch (57%) and gum (46%), with less frequent use of an inhaler (<10%) or lozenges (<2%) among those who used any NRT during follow-up. (A person might use several forms of NRT during follow-up.) Because of small sample sizes for inhaler and lozenge use, we did not present results for use of these 2 forms of NRT (Table 1).

In waves 1 and 2, the rates of quitting (abstinence ≥ 1 month) were highest among those who used NRT for the recommended duration of 8–12 weeks (47% and 52%), intermediate among those who used NRT for 4.0–7.9 weeks (29% and 29%) or

Table 2. Quitting (Abstinence ≥1 Month) by Duration of Nicotine Replacement Therapy Use in the 3 Study Waves Among Smokers Who Made an Attempt to Quit During Follow-up, Ontario, Canada, 2005–2009

Duration of NRT Use, weeks	Wave 1 (<i>n</i> = 1,469)			ve 2 1,181)	Wave 3 (<i>n</i> = 1,021)		
USE, WEEKS	No.	%	No.	%	No.	%	
None	214	19.8	171	19.7	165	22.5	
<4	22	7.6	20	8.9	18	8.6	
4.0–7.9	16	28.6	12	29.3	14	40.0	
8–11.9	11	52.4	8	47.1	4	25.5	
≥12	8	32.0	6	20.7	9	36.0	

Abbreviation: NRT, nicotine replacement therapy.

≥12 weeks (21% and 32%) and those who did not use NRT (20% and 20%), and lowest among those who used NRT for <4 weeks (8% and 9%). In wave 3, the rate of quitting was highest among those who used NRT for 4.0–7.9 weeks or ≥12 weeks (36% and 40%), intermediate among those who used NRT for 8–11.9 weeks (26%) and those who did not use

NRT (23%), and lowest among those who used NRT for <4 weeks (9%) (Table 2).

Among those who made an attempt to quit during followup (n = 2,221), 68% did not use any NRT in any of the 3 waves, and 32% used NRT in least at 1 wave. Compared with those who did not use any NRT when making an attempt to quit during follow-up, those who did use NRT were older, smoked more cigarettes per day, made more quit attempts, rated their health lower, were more likely to be women and addicted, were more likely to smoke daily and to use prescription medication and behavior support, and were less likely to have smoking restrictions at home (Table 3).

The adjusted logistic regression analysis using generalized estimating equations method showed that using NRT was not associated with quitting when the duration of use was not taken into account (model 1, Table 4). Compared with those who did not use any NRT, persons who used NRT for less than 4 weeks were less likely to quit (adjusted odds ratio (OR) = 0.51, P < 0.0001); those who used NRT for 4 or more weeks had a higher likelihood of cessation (for 4.0–7.9 weeks of NRT use, adjusted OR = 2.26, P < 0.0001; for 8.0–11.9 weeks of NRT use, adjusted OR = 3.84, P < 0.0001; and for ≥ 12 weeks of NRT use, adjusted OR = 2.80, P < 0.0001) (model 2, Table 4). Similarly, compared with persons who

Table 3. Baseline Characteristics of Smokers Who Made an Attempt to Quit During Follow-up by Nicotine

 Replacement Therapy Use, Ontario, Canada, 2005–2009
 2009

Characteristic) NRT Use 7 = 1,501)	Any NRT Use (<i>n</i> = 720)		<i>P</i> Value ^a
		Mean (SD)	%	Mean (SD)	
Age, years		42.2 (15.2)		44.3 (13.7)	0.0012
Female sex	53.5		59.0		0.014
Educational level					
High school or less	45.4		47.6		0.33
Some or complete postsecondary schooling	54.6		52.4		
Marital status					
Never married	25.5		18.2		0.86
Married/common law	53.3		56.3		
Widowed/separated/divorced	21.2		24.9		
Self-rated health ^b		3.4 (1.0)		3.2 (1.0)	<0.0001
Self-perceived addiction to smoking	82.7		98.2		<0.0001
Daily smoking	66.5		85.4		<0.0001
No. of cigarettes smoked per day		10.7 (10.2)		15.5 (10.1)	<0.0001
No. of lifetime attempts to quit		3.0 (7.2)		4.3 (7.2)	0.0001
Use of other tobacco products (e.g., snuff or cigars)	2.2		1.5		0.29
Other household member(s) who smoke	14.0		15.0		0.53
Home smoking restrictions	59.4		44.9		<0.0001
Use of bupropion or varenicline to quit	18.9		37.9		<0.0001
Use of behavioral support to quit ^c	10.5		17.8		<0.0001

Abbreviations: NRT, nicotine replacement therapy; SD, standard deviation.

^a All *P* values are 2-sided.

^b Rated on a scale of 1 to 5 (poor, fair, good, very good, and excellent).

^c Behavioral support included group counseling, specialized addiction counseling, Ontario Quitline, smokers helpline online, and cessation programs.

Table 4.Logistic Regression Analysis Using Generalized Estimating Equations for the Association BetweenDuration of Nicotine Replacement Therapy Use and Smoking Cessation^a Among Those Who Made an Attempt to QuitDuring Follow-up, Ontario, Canada, 2005–2009

Model ^b and Cessation Aid		Crude Analys	is	Adjusted Analysis			
Use at Follow-up	OR	95% CI	P Value ^c	OR	95% Cl	<i>P</i> Value ^c	
Model 1 ^d							
Any NRT use	1.25	1.02, 1.54	0.033	1.08	0.86, 1.35	0.49	
Model 2 ^d							
NRT use <4 weeks	0.44	0.34, 0.58	<0.0001	0.51	0.38, 0.67	<0.0001	
NRT use 4.0–7.9 weeks	1.98	1.42, 2.77	<0.0001	2.26	1.58, 3.22	<0.0001	
NRT use 8.0–11.9 weeks	3.02	1.84, 4.97	<0.0001	3.84	2.24, 6.58	<0.0001	
NRT use ≥12 weeks	2.53	1.59, 4.05	<0.0001	2.80	1.70, 4.61	<0.0001	
Model 3 ^e							
Patch use <4 weeks	0.52	0.37, 0.73	0.0002	0.64	0.45, 0.93	0.018	
Patch use 4.0–7.9 weeks	2.12	1.37, 3.29	0.0008	2.49	1.58, 3.95	<0.0001	
Patch use 8.0–11.9 weeks	4.67	2.33, 9.36	<0.0001	5.91	2.85, 12.23	<0.0001	
Patch use \geq 12 weeks	2.24	1.17, 4.31	0.016	2.80	1.44, 5.45	0.0024	
Model 4 ^f							
Gum use <4 weeks	0.47	0.34, 0.64	<0.0001	0.42	0.36, 0.73	0.0002	
Gum use 4.0–7.9 weeks	1.43	0.87, 2.34	0.15	1.60	0.94, 2.72	0.084	
Gum use 8.0-11.9 weeks	2.33	1.04, 5.25	0.041	2.61	1.03, 6.59	0.043	
Gum use ≥12 weeks	2.53	1.23, 5.21	0.012	2.68	1.22, 5.88	0.014	

Abbreviations: CI, confidence interval; NRT, nicotine replacement therapy; OR, odds ratio.

^a Abstinence for 1 month or longer.

^b The reference group for all models was no NRT use.

^c All *P* values are 2-sided.

^d Adjusted for age, self-perceived health, self-perceived addiction, daily smoking, number of cigarettes smoked per day, number of lifetime attempts to quit, and smoking restrictions at home.

^e Adjusted for age, marital status, self-perceived health, self-perceived addiction, daily smoking, number of cigarettes smoked per day, number of lifetime attempts to quit, and smoking restrictions at home.

^f Adjusted for age, educational level, self-perceived health, self-perceived addiction, daily smoking, number of cigarettes smoked per day, number of lifetime attempts to quit, and smoking restrictions at home.

did not use any NRT, those who used a nicotine patch for less than 4 weeks were less likely to quit (adjusted OR = 0.64, P < 0.05); those who used a nicotine patch for 4 or more weeks had an higher likelihood of cessation (for 4.0-7.9 weeks of nicotine patch use, adjusted OR = 2.49, P < 0.0001;for 8.0-11.9 weeks of nicotine patch use, adjusted OR = 5.91, P < 0.0001; and for >12 weeks of nicotine patch use, adjusted OR = 2.80, P < 0.01) (model 3, Table 4). Compared with those who did not use any NRT, persons who used nicotine gum for less than 4 weeks were less likely to guit (adjusted OR = 0.42, P < 0.001; gum use for 4.0–7.9 weeks was not significantly associated with quitting, and gum use for 8.0-11.9 weeks (adjusted OR = 2.61, P < 0.05) and ≥ 12 weeks (adjusted OR = 2.68, P < 0.05) had similar associations with quitting (model 4, Table 4). Almost all crude odds ratios were smaller than the adjusted odd ratios, indicating that NRT users were more tobacco-dependent than were persons who did not use NRT (adjusted odds ratios were only slightly higher than crude odds ratios when the model did not control for tobacco-dependence variables, including daily smoking status, number of cigarettes per day smoked, and self-perceived addiction; data not shown).

Compared with persons who did not use any NRT during follow-up, those who used NRT for less than 4 weeks rated their health lower, smoked more cigarettes per day, were more likely to perceive themselves as addicted to tobacco, smoke daily, and use prescription medication and behavioral support to quit and were less likely to have smoking restrictions at home. Compared with those who used NRT for 4 or more weeks, persons who used NRT less than 4 weeks smoked more cigarettes per day and made fewer attempts to quit; however, there was no difference with regard to other baseline characteristics (data not shown).

DISCUSSION

In the present study, we found that the majority of smokers $(\geq 72\%)$ in the general population did not use any NRT when making an attempt to quit smoking. When using NRT to quit, the majority (86%) used it for less than the recommended duration of 8–12 weeks. NRT users smoked more cigarettes per day and had tried to quit more often in the past compared with persons who did not use NRT. There was no overall association between NRT use and quitting when duration of use was not taken

into account. When duration of NRT use was considered, we found that persons who used NRT for less than 4 weeks were less likely to quit (adjusted OR = 0.51, P < 0.0001), whereas those who used NRT for longer (\geq 4 weeks) were more likely to quit. This finding helps to explain the null findings of some previous studies that did not include such detailed data on duration of use.

Findings of the suboptimal prevalence and duration of NRT use in the present study are consistent with those from other studies (5, 10, 33–36). For example, only 20%–23% of recent quitters reported having used NRT in their attempts to quit in a study in Massachusetts (34), and in other studies in the United States (33, 35), 20%–32% of smokers who attempted to quit used medication. The median duration of NRT use was 14 days among smokers who attempted to quit in a study from California (10). These population-based studies help us understand what cessation methods smokers use and how they use cessation medication when making an attempt to quit in the general population. They might also explain why NRT has not been consistently associated with a higher likelihood of cessation in the general population (i.e., inadequate and underuse of NRT).

In the present study, we found that smokers who chose to use NRT were those who would be expected to have worse outcomes; that is, these smokers were more dependent or had trouble quitting in the past. Almost all crude odds ratios were smaller than the adjusted odds ratios, indicating that NRT users were more addicted to smoking than were persons who did not use, because when we did not control for tobaccodependence variables (daily smoking status, number of cigarettes per day smoked, and self-perceived addiction), the odds ratios after adjustment for other variables were only slightly larger than the crude odds ratios (data not shown). This finding is similar to those from other nonrandomized studies (35, 37, 38), which suggests that a lack of or a negative association between NRT and smoking cessation reported in population studies might be due to inadequate control of confounding.

We also found that persons who used NRT (patch or gum) for less than 4 weeks had a lower odds of quitting compared with those who did not use NRT. Those who used NRT for less than 4 weeks were more addicted to tobacco compared with those who did not use NRT and those who used NRT for 4 or more weeks. Although we controlled for several factors related to addiction, residual confounding might still exist. These smokers might also have comorbid conditions (e.g., mental health or alcohol problems), as shown in other studies (15, 39, 40). Unfortunately, information on comorbid conditions was not collected in the Ontario Tobacco Survey.

To our knowledge, this is the first population-based longitudinal study using a representative sample of smokers in which the association between duration of NRT use and smoking cessation (≥ 1 month) was examined. There appeared to be a threshold association (4.0–7.9 weeks of NRT use resulted in double the odds of quitting) and a ceiling association (using NRT for the recommended duration of 8–12 weeks resulted in almost quadruple the odds of quitting) with quitting for 1 month or longer. Using NRT for 12 or more weeks was associated with 2.8 times higher odds of quitting, which was lower than that for using NRT for 8.0–11.9 weeks. These associations were mainly from using a nicotine patch; using a nicotine patch for the recommended duration was associated with even higher odds (5.9 times higher) of quitting. With regard to the duration of nicotine gum use, the threshold seemed to be the recommended duration (8–12 weeks) and beyond. A ceiling association could not be determined for nicotine gum use because the odds of quitting after using gum for 12 or more weeks were very similar to that for using gum between 8.0–11.9 weeks, and the sample size of persons who used gum for 16 or more weeks was too small.

The findings of the present study uniquely support the recommendation to use NRT for 8–12 weeks in the clinical practice guideline by the US Public Health Service, which reflects efficacious clinical treatments for tobacco dependence (41). Our findings are consistent with those from a large clinical trial (n = 2,861) and a medium-sized trial (n = 568) included in the 2012 Cochrane review on NRT for smoking cessation (2) in which investigators found no difference in cessation rates when comparing nicotine patch use for 28 weeks with use for 12 weeks in the large trial and use for 24 weeks with use for 8 weeks in the medium-sized trial. These suggest the ceiling association of 8–12 weeks of NRT or nicotine patch use on smoking cessation.

Strengths and limitations

The strengths of the present study included the populationbased longitudinal study design, a relatively large representative sample of smokers, use of generalized estimating equations methods for analysis (42), the relatively short time period from one wave to the next (6 months), and the ability to control for many covariates, especially time-varying covariates. Using a representative sample allowed the study findings to be generalizable to the general population and provided specific evidence of the effectiveness of NRT because real-life situations were reflected.

A potential source of bias was the reliance upon selfreported cessation status. Because of the social undesirability of smoking, some participants might have misreported their smoking status (smokers who identified as quitters). However, an expert scientific review on biochemical verification has found that there is little reason to expect differential misrepresentation rates between biochemical validation and selfreported smoking status in most smoking cessation studies (43) because the levels of misrepresentation are generally low (0%– 8.8%) (44–47). A recent study using representative data for the Canadian population showed no significant difference between national estimates of smoking prevalence based on self-report and those based on urinary cotinine concentration (smoking prevalence based on urinary cotinine concentration) (48).

In the present study, there might have been some measurement error for NRT use and quitting outcomes when smokers were asked to recall NRT use and smoking behaviors in the previous 6 months at each follow-up interview. In a recent population-based study, Borland et al. (21) reported better recall of attempts to quit among smokers who use cessation medication than among self-quitters. If this difference in recall was present in our study, it would have had the effect of biasing the assessed associations between use of cessation medication and cessation outcomes toward the null. Thus, if this recall bias could be corrected, the observed association would be even stronger. It was not clear if nonconcurrent use of multiple forms of NRT was consecutive or separate, which might be a limitation. However, findings of any NRT use and nicotine patch use were very similar, bearing in mind that NRT might consist of multiple forms of medication but a nicotine patch is just one form of NRT.

Loss to follow-up had the potential to threaten the validity of the present findings. However, smokers with partial data (e.g., persons who were current smokers at wave 1, attempted to quit at wave 2, and lost to follow-up at wave 3) were included in the analysis. The proportion of complete loss to follow-up was small (10%), and loss to follow-up was not associated with smoking behaviors. Therefore, the findings of the present study were likely not affected by loss to follow-up.

It is possible that duration of NRT use itself might be a proxy for smoking abstinence. This means that if a smoker used NRT for more than 4 weeks, the smoker likely would not have been smoking for those 4 weeks (reverse association). If smokers stopped using NRT early because they felt, for example, that it was "too expensive" or "not safe" as opposed to "not working," the findings of the present study would be strengthened. Unfortunately, information on reasons for stopping use of NRT was not collected in the Ontario Tobacco Survey. If the reverse association were true, the association between duration of NRT use and quitting would increase with higher duration of NRT use. However, among those who used NRT for 4 weeks or longer, the rate of quitting was higher among smokers who used NRT 8.0-11.9 weeks (42%) than among those using NRT for 4.0-7.9 weeks (30%) or for >12 weeks (28%). Furthermore, among smokers who used NRT for 4 weeks or longer, the majority (67%) did not quit smoking for at least 1 month, indicating that duration of NRT use is not perfectly associated with duration of abstinence. Nevertheless, the present study cannot prove the causal relationship between duration of NRT use and smoking cessation. Future research is needed to confirm whether the association between duration of NRT use and smoking cessation is causal.

Another limitation was the lack of information on NRT dosage in the current study, which might explain the lower odds ratios for nicotine gum use. Prior research has shown that lower dosing of nicotine gum is common (49). Future studies might consider including dosage information to better understand the role of dosage. Information on comorbid conditions (depression and mental health) should be collected in future studies to more fully control for possible confounders.

Conclusion

Our study finds that using NRT for at least 4 weeks, especially using the patch for the recommended duration (8–12 weeks), is associated with a higher likelihood of quitting in the general population. However, the majority of smokers in the general population does not use NRT or uses it much less than the recommended duration when making an attempt to quit. Smokers should be encouraged to use NRT for the recommended duration to achieve better quitting outcomes.

ACKNOWLEDGMENTS

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We thank the Ontario Tobacco Research Unit, Dalla Lana School of Public Health, University of Toronto, Ontario, Canada for allowing us to use the Ontario Tobacco Survey data. The Ontario Tobacco Survey is an initiative of the Ontario Tobacco Research Unit, which is supported by the Ontario Ministry of Health and Long Term Care.

S.J.B. has had no relationship with the tobacco industry and has not worked an employee or consultant for any pharmaceutical firm. She has been an investigator for the Smoking Treatment for Ontario Patients (STOP) Study, which received nicotine replacement therapy at a discount from Johnson & Johnson, maker of nicotine replacement products. P.S. is the principal investigator for the STOP Study. Currently, he serves as a consultant to Pfizer Canada, the maker of varenicline, and he has received honoraria for his work; he has also received peer-reviewed grant funding sponsored by Pfizer International Corporation. He has received funding for consultation and speaker fees for training in motivational interviewing from Abvie, the manufacturers of treatments for inflammatory bowel disease. He has been a member on an arm's length data and safety monitoring board for Nicovax. B.Z. and J.E.C have no financial disclosures.

Conflict of interest: none declared.

REFERENCES

- 1. Corelli RL, Hudmon KS. Medications for smoking cessation. *West J Med.* 2002;176(2):131–135.
- 2. Stead LF, Perera R, Bullen C, et al. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev.* 2012;11:CD000146.
- Shiffman S, Gitchell J, Pinney JM, et al. Public health benefit of over-the-counter nicotine medications. *Tob Control*. 1997;6(4): 306–310.
- 4. Balmford J, Borland R, Hammond D, et al. Adherence to and reasons for premature discontinuation from stop-smoking medications: data from the ITC Four-Country Survey. *Nicotine Tob Res.* 2011;13(2):94–102.
- Paul CL, Walsh RA, Girgis A. Nicotine replacement therapy products over the counter: real-life use in the Australian community. *Aust N Z J Public Health*. 2003;27(5):491–495.
- Buck D, Morgan A. Smoking and quitting with the aid of nicotine replacement therapies in the English adult population. Results from the Health Education Monitoring Survey 1995. *Eur J Public Health*. 2001;11(2):211–217.
- Kotz D, Brown J, West R. 'Real-world' effectiveness of smoking cessation treatments: a population study. *Addiction*. 2014;109(3):491–499.
- Alberg AJ, Patnaik JL, May JW, et al. Nicotine replacement therapy use among a cohort of smokers. *J Addict Dis.* 2005; 24(1):101–113.
- Ferguson J, Bauld L, Chesterman J, et al. The English smoking treatment services: one-year outcomes. *Addiction*. 2005; 100(suppl 2):59–69.

- Pierce JP, Gilpin EA. Impact of over-the-counter sales on effectiveness of pharmaceutical aids for smoking cessation. *JAMA*. 2002;288(10):1260–1264.
- Zhu S, Melcer T, Sun J, et al. Smoking cessation with and without assistance: a population-based analysis. *Am J Prev Med.* 2000;18(4):305–311.
- Swartz SH, Cowan TM, Klayman JE, et al. Use and effectiveness of tobacco telephone counseling and nicotine therapy in Maine. *Am J Prev Med.* 2005;29(4):288–294.
- Miller N, Frieden TR, Liu SY, et al. Effectiveness of a large-scale distribution programme of free nicotine patches: a prospective evaluation. *Lancet*. 2005;365(9474):1849–1854.
- West R, Zhou X. Is nicotine replacement therapy for smoking cessation effective in the "real world"? Findings from a prospective multinational cohort study. *Thorax*. 2007;62(11): 998–1002.
- Kasza KA, Hyland AJ, Borland R, et al. Effectiveness of stop-smoking medications: findings from the International Tobacco Control (ITC) Four Country Survey. *Addiction*. 2013; 108(1):193–202.
- Diemert LM, Bondy SJ, Victor JC, et al. Efficient screening of current smoking status in recruitment of smokers for populationbased research. *Nicotine Tob Res.* 2008;10(11):1663–1667.
- 17. Diemert L, Victor JC, Chaiton M, et al. *Ontario Tobacco Survey Technical Report 1: Baseline Data*. Toronto, ON, Canada: Ontario Tobacco Research Unit; 2010.
- Fong GT, Cummings KM, Borland R, et al. The conceptual framework of the International Tobacco Control (ITC) Policy Evaluation Project. *Tob Control*. 2006;15(suppl 3):iii3–iii11.
- Gilpin E, Pierce JP, Goodman J, et al. Reasons smokers give for stopping smoking: do they relate to success in stopping? *Tob Control*. 1992;1(4):256–263.
- Centers for Disease Control (CDC). Smokers' beliefs about the health benefits of smoking cessation—20 U.S. communities, 1989. MMWR Morb Mortal Wkly Rep. 1990;39(38):653–656.
- Borland R, Partos TR, Cummings KM. Systematic biases in cross-sectional community studies may underestimate the effectiveness of stop-smoking medications. *Nicotine Tob Res.* 2012;14(12):1483–1487.
- Hyland A, Borland R, Li Q, et al. Individual-level predictors of cessation behaviours among participants in the International Tobacco Control (ITC) Four Country Survey. *Tob Control*. 2006;15(suppl 3):iii83–iii94.
- 23. Fagerstrom K, Rutqvist LE, Hughes JR. Snus as a smoking cessation aid: a randomized placebo-controlled trial. *Nicotine Tob Res.* 2012;14(3):306–312.
- Melikian AA, Hoffmann D. Smokeless tobacco: a gateway to smoking or a way away from smoking. *Biomarkers*. 2009; 14(suppl 1):85–89.
- Hyland A, Li Q, Bauer JE, et al. Predictors of cessation in a cohort of current and former smokers followed over 13 years. *Nicotine Tob Res.* 2004;6(suppl 3):S363–S369.
- Marques-Vidal P, Melich-Cerveira J, Paccaud F, et al. Prevalence and factors associated with difficulty and intention to quit smoking in Switzerland. *BMC Public Health.* 2011;11:227.
- Siahpush M, Borland R, Scollo M. Factors associated with smoking cessation in a national sample of Australians. *Nicotine Tob Res.* 2003;5(4):597–602.
- Lee CW, Kahende J. Factors associated with successful smoking cessation in the United States, 2000. Am J Public Health. 2007;97(8):1503–1509.
- Lennox AS, Taylor RJ. Factors associated with outcome in unaided smoking cessation, and a comparison of those who have never tried to stop with those who have. *Br J Gen Pract*. 1994;44(383):245–250.

- Prochazka AV, Caverly TJ. ACP Journal Club. Review: varenicline is better than bupropion but not nicotine patch for smoking abstinence in adults. *Ann Intern Med.* 2012;157(6): JC3–JC7.
- West R. Behavioural support programmes for smoking cessation: needs and opportunities. *Eur J Public Health*. 2000; 10(suppl 3):25–29.
- 32. Hanley JA, Negassa A, Edwardes MD, et al. Statistical analysis of correlated data using generalized estimating equations: an orientation. *Am J Epidemiol*. 2003;157(4):364–375.
- Shiffman S, Brockwell SE, Pillitteri JL, et al. Use of smoking-cessation treatments in the United States. *Am J Prev Med.* 2008;34(2):102–111.
- Alpert HR, Connolly GN, Biener L. A prospective cohort study challenging the effectiveness of population-based medical intervention for smoking cessation. *Tob Control.* 2013;22(1): 32–37.
- Cokkinides VE, Ward E, Jemal A, et al. Under-use of smoking-cessation treatments: results from the National Health Interview Survey, 2000. *Am J Prev Med.* 2005;28(1):119–122.
- Burns EK, Levinson AH. Discontinuation of nicotine replacement therapy among smoking-cessation attempters. *Am J Prev Med.* 2008;34(3):212–215.
- Bansal MA, Cummings KM, Hyland A, et al. Stop-smoking medications: who uses them, who misuses them, and who is misinformed about them? *Nicotine Tob Res.* 2004;6(suppl 3): S303–S310.
- Shiffman S, Brockwell SE, Pillitteri JL, et al. Individual differences in adoption of treatment for smoking cessation: demographic and smoking history characteristics. *Drug Alcohol Depend*. 2008;93(1-2):121–131.
- Pasco JA, Williams LJ, Jacka FN, et al. Tobacco smoking as a risk factor for major depressive disorder: population-based study. *Br J Psychiatry*. 2008;193(4):322–326.
- 40. Falk DE, Yi HY, Hiller-Sturmhöfel S. An epidemiologic analysis of co-occurring alcohol and tobacco use and disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Alcohol Res Health*. 2006;29(3):162–171.
- Fiore MC. Treating tobacco use and dependence: an introduction to the US Public Health Service Clinical Practice Guideline. *Respir Care*. 2000;45(10):1196–1199.
- Ghisletta P, Spini D. An introduction to generalized estimating equations and an application to assess selectivity effects in a longitudinal study on very old individuals. *J Educ Behav Stat.* 2004;29(4):421–437.
- SRNT Subcommittee on Biochemical Verification. Biochemical verification of tobacco use and cessation. *Nicotine Tob Res.* 2002;4(2):149–159.
- Velicer WF, Prochaska JO, Rossi JS, et al. Assessing outcome in smoking cessation studies. *Psychol Bull*. 1992;111(1):23–41.
- Glasgow RE, Mullooly JP, Vogt TM, et al. Biochemical validation of smoking status: pros, cons, and data from four low-intensity intervention trials. *Addict Behav.* 1993;18(5):511–527.
- Patrick DL, Cheadle A, Thompson DC, et al. The validity of self-reported smoking: a review and meta-analysis. *Am J Public Health*. 1994;84(7):1086–1093.
- Community Intervention Trial for Smoking Cessation (COMMIT): I. cohort results from a four-year community intervention. *Am J Public Health*. 1995;85(2):183–192.
- Wong SL, Shields M, Leatherdale S, et al. Assessment of validity of self-reported smoking status. *Health Rep.* 2012; 23(1):47–53.
- Cummings KM, Hyland A. Impact of nicotine replacement therapy on smoking behavior. *Annu Rev Public Health*. 2005; 26:583–599.