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Effectiveness of Switching Smoking-Cessation Medications Following Relapse

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Abstract

Introduction—Nicotine dependence is a chronic disorder often characterized by multiple failed quit attempts (QAs). Yet, little is known about the sequence of methods used across multiple QAs or how this may impact future ability to abstain from smoking. This prospective cohort study examines the effectiveness of switching smoking-cessation medications (SCMs) across multiple QAs.

Methods—Adult smokers (aged ≥18 years) participating in International Tobacco Control surveys in the United Kingdom, U.S., Canada, and Australia (N=795) who: (1) completed two consecutive surveys between 2006 and 2011; (2) initiated a QA at least 1 month before each survey; and (3) provided data for the primary predictor (SCM use during most recent QA),

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outcome (1-month point prevalence abstinence), and relevant covariates. Analyses were conducted in 2016.

Results—Five SCM user classifications were identified: (1) non-users (43.5%); (2) early users (SCM used for initial, but not subsequent QA; 11.4%); (3) later users (SCM used for subsequent, but not initial QA; 18.4%); (4) repeaters (same SCM used for both QAs; 10.7%); and (5) switchers (different SCM used for each QA; 14.2%). Abstinence rates were lower for non-users (15.9%, OR=0.48, p=0.002), early users (16.6%, OR=0.27, p=0.03), and repeaters (12.4%, OR=0.36, p=0.004) relative to switchers (28.5%).

Conclusions—Findings suggest smokers will be more successful if they use a SCM in QAs and vary the SCM they use across time. That smokers can increase their odds of quitting by switching SCMs is an important message that could be communicated to smokers.

INTRODUCTION

Nicotine dependence is a chronic relapsing disorder often characterized by multiple failed quit attempts (QAs),[1] which calls for a chronic disease management approach.[2] Motivation to quit is an established predictor of making a future QA, but it does not predict sustained abstinence.[3] Thus, even among smokers motivated to quit, most QAs will result in relapse, and most smokers will need to be recycled to another QA. Fortunately, many smokers remain interested in quitting, even after a failed QA. For example, within a sample of smokers who reported making a failed QA, 78% were interested in making another QA within 1 month.[4] Indeed, evidence indicates the vast majority of smokers are frequently thinking about and making efforts to stop smoking.[5]

Although most former and current smokers report making multiple QAs during their lifetime,[6,7] little is known about how methods of quitting vary across attempts, and whether consistency or inconsistency of quit method increases the likelihood of maintaining abstinence over an extended time period. Most QAs are unassisted, that is, without use of any smoking-cessation medications (SCMs) or behavioral treatments, despite strong evidence that both enhance long-term quitting success.[8,9] Observational, prospective cohort studies have characterized frequency of QAs,[7,10] prevalence with which SCMs are used, and the effectiveness of SCMs.[8,11,12] However, little is known about the sequence of quit methods smokers might use across multiple QAs. One study suggests those making a QA in the past year were significantly more likely to try again within 6 months, irrespective of whether they had used a SCM or not, compared with those who had not made a QA in the past year; smokers were also more likely to try the same quit method used on a previous QA within the past 6 months, but this study did not evaluate quit success.[13] On one hand, consistency of quit method might improve quitting success, if only because the smoker is already familiar with the method and presumably knows how to improve upon it (e.g., not make the same mistakes twice). On the other hand, changing the method across QAs might lead to improved quitting by allowing the smoker to try something new with the hope of achieving a different outcome. Complicating this issue is that a smoker might change from using an evidence-based method to one that is not evidence based (e.g., hypnotherapy), or vice versa, and thus evaluation of quitting success may be attributable to the potency of the

quit method used rather than the effect of trying something new. For this reason, analysis in this paper is limited to switching between roughly comparable evidence-based SCMs.

There are few naturalistic evaluations of consistency of SCMs over successive quit attempts, though several RCTs have examined the more general concept of treatment recycling. One study found no benefit of nicotine patch among smokers who initially tried, and failed, and tried again with either patch or nasal spray,[14,15] though another study found success for repeated treatment with patch plus behavioral counseling.[16] Nicotine lozenge improved cessation rates among smokers who had a treatment history with nicotine patch, gum, inhaler, or bupropion.[17] Other studies have shown benefits of retreatment with varenicline[18] and bupropion,[19] the latter being equally efficacious for relapsers who did or did not have a history of nicotine-replacement therapy (NRT) use.[20] Thus, clinical trial evidence is mixed with regard to efficacy of switching versus using the same quit method.

Several treatment algorithms exist to aid clinicians,[21–24] and public health agencies have related treatment recommendations. The most recent expert treatment algorithm suggests prescription of a new SCM or trial of the same SCM at a higher dose.[21] Unfortunately, the evidence to support a recommendation that patients who quit and relapse should switch or try the same SCM on a subsequent quit attempt is scant. The current study was undertaken to help fill this gap.

In this study, the effectiveness of consistency/variability of SCMs across multiple QAs is examined using data from an international cohort study of adult smokers. Specifically, analyses characterize the prevalence of switching or using the same SCM within approximately 1 year of initial relapse. Relapsers who on a subsequent QA use an SCM (or combination) different from that used during a recent QA are herein referred to as switchers, and those who use the same SCM (or combination) across two QAs are denoted as repeaters. This prospective cohort study tests the hypothesis that switchers will have greater quit success.

METHODS

Study Population

Participants were adult smokers (aged ≥18 years) in the International Tobacco Control Four Country Survey. Nationally representative samples from the United Kingdom (UK), Canada, Australia, and U.S. completed standardized telephone interviews annually since 2002 as part of an ongoing prospective cohort study.[25]

Analyses are restricted to data collected between 2006 and 2011 (Waves 5–8), allowing for equivalent response options for SCMs (i.e., varenicline first available in 2006) and consistency in SCM questions (i.e., assessed differently at other waves). Participants reported the number of QAs made over the past year, duration of most recent QA, and use of SCMs during the most recent QA. Of the 8,245 participants in the Wave 5 assessment (considered baseline herein), those with a QA that started within 1 month of subsequent assessments (n=24) were excluded because the primary outcome was 1-month point prevalence abstinence at follow-ups. Inclusion criteria were:

1. reported QAs on two consecutive waves;
2. and provided valid data for all predictors, smoking status, and control variables.

QAs could have occurred in the time leading up to Waves 6 and 7 (Wave Pair 1, 59%), or Waves 7 and 8 (Wave Pair 2, 41%). The final sample included 1,057 wave pairs that comprised 795 respondents, such that respondents could contribute to a single wave pair (67%) or both (33%).

Measures

At each wave, participants were coded as abstinent when no smoking was indicated within the past month (i.e., ≥1-month point prevalence abstinence).

Smoking-cessation medication use—At each wave, those who made a QA since the last wave were asked which of the following SCMs they used to aid their most recent QA: nicotine gum, nicotine patch, nicotine lozenge, nicotine tab, other NRT, bupropion, varenicline, and other prescription (options were not mutually exclusive). Based on the two consecutive QAs assessed participants could fall into one of these SCM use groups:

1. non-users: no SCM used across both QAs;
2. early users: SCM used for initial, but not subsequent QA;
3. later users: SCM used for subsequent, but not initial QA;
4. repeaters: same SCM (or combination) used for both QAs; or
5. switchers: different SCM (or combination) used for each QA.

When more than one SCM (i.e., combination) was used for both QAs, repeaters were defined as those who used the exact same combination of SCMs across both QAs (e.g., gum and patch), whereas switchers used a different combination for each QA (e.g., gum and patch, then lozenge and patch). Those who used SCMs at both QAs but increased or decreased the number of SCMs used were considered switchers (e.g., gum and patch, then gum).

To replicate analyses conducted in a prior International Tobacco Control Four Country Survey study on the effectiveness of SCMs,[8] the following baseline variables were included: (1) country; (2) sex; (3) ethnicity/racial group (majority or minority, based on racial/ethnic group in the UK, Canada, and U.S., and English language spoken at home in Australia); (4) age group (18–24, 25–39, 40–54, or ≥55 years); (5) level of education (low, moderate, or high; “low” defined as completion of high school or less in Canada, U.S., and Australia, or secondary/vocational or less in the UK, “moderate” as completion of community college/trade/technical school/some university (no degree) in Canada and the U.S., college/university (no degree) in the UK, or technical/trade/some university (no degree) in Australia, and “high” if respondent completed university or postgraduate in all countries); (6) annual household income (low, moderate, high, or unknown; “low” coded if income was <$30,000 in the U.S., Canada, and Australia or <£30,000 in the UK, “moderate” if it was between $30,000 and $59,999 or £30,000 and £44,999, and “high” if it was ≥$60,000 or £45,000; (7) nicotine dependence, as measured by the heaviness of smoking index[26]; and (8) self-

efficacy, as assessed with the item: *If you decided to give up smoking completely in the next 6 months, how sure are you that you would succeed?*, with participants classified as low, moderate, or high ("low" defined as those who responded *not at all sure* or *slightly sure*, "moderate" as those who indicated *moderately sure*, and "high" were those that reported *very sure* or *extremely sure*).

The study protocol was approved by the IRBs or research ethics boards of the University of Waterloo, Roswell Park Cancer Institute, Medical University of South Carolina, University of Strathclyde, University of Stirling, The Open University, and The Cancer Council Victoria.

Statistical Analysis

Analyses were conducted in 2016 with SPSS, version 23, and significance indicated by $\alpha<0.05$ (two-tailed). One-way ANOVAs for continuous variables and chi-square analyses for categorical variables were used to explore differences across the five SCM use groups in baseline demographic and smoking-related characteristics. Multi-predictor generalized estimating equations analyses tested demographic and smoking-related characteristics as predictors of SCM use group membership with the following comparisons: repeaters versus all other groups, switchers versus all other groups, and repeaters versus switchers. Generalized estimating equations analyses were used to examine the relationship between SCM use and 1-month point prevalence abstinence. Specifically, repeated longitudinal logistic regression analyses were conducted with specifications for binomial distributions and unstructured within-person correlation matrixes. Analyses allowed participants to contribute to multiple wave pairs, while controlling for correlations between responses. Unadjusted and adjusted analyses showed the same pattern of results, and adjusted results are reported.

RESULTS

Table 1 depicts sample characteristics. Almost half of the sample (45.3%) were non-users, 11.4% were early users, 18.4% were later users, 10.7% were repeaters, and 14.2% were switchers. When comparing repeaters or switchers with other SCM use groups, elevated nicotine dependence was associated with a greater likelihood of being a repeater (OR=1.2, $p=0.02$) and a switcher (OR=1.3, $p<0.001$). Country-level associations were also found, such that relative to U.S. respondents, those in Australia were more likely to be repeaters (OR=2.4, $p=0.005$) and those in the UK were less likely to be switchers (OR=0.5, $p=0.02$). No differences emerged between switchers and repeaters across any baseline characteristics.

As depicted in Table 2, the highest quit rates were observed for switchers. Switchers were the only group significantly different from non-users, being over twice as likely to achieve 1-month point prevalence abstinence. Only repeaters had lower quit rates than non-users, although this was not statistically significant. To allow for comparison of repeaters versus switchers directly, the same analyses were rerun with the switchers as the ref group. Repeaters were less likely to achieve 1-month point prevalence abstinence. The same pattern was true for early users, whereas no significant difference was observed for later users.

To explore if better quit rates for switchers may be accounted for by SCM selection, specific SCMs used by repeaters and switchers were examined (Table 3). Patch only and varenicline only were the most commonly used SCMs for repeaters. Relative to repeaters, switchers had comparable rates of patch-only use at the initial QA and comparable rates of varenicline-only use at the subsequent QA. Switchers also showed a shift away from bupropion only, gum only, and concurrent use of patch and gum. Each of the remaining specific SCMs were used by very few participants so data were collapsed across SCM combinations to determine rates at which any NRT, NRT combo, bupropion, varenicline, and prescription SCM (i.e., bupropion, varenicline, prescription NRT, or other prescription) were used. At the subsequent QA, switchers had lower rates of any NRT use compared with repeaters (–7.0%), but higher rates for NRT combination (+10.0%), bupropion (+4.2%), varenicline (+12.3%), and any prescription SCM (+9.8%). Abstinence outcomes were still significantly better for switchers, relative to repeaters, in generalized estimating equations models that controlled for use of each of the cumulative SCM variables at the subsequent QA (*ps*<0.02).

Overall, there was greater heterogeneity in combinations of SCMs used by switchers. Switchers used 20 different SCM combinations during the initial QA and 33 during the subsequent QA, whereas only 15 were used among repeaters. Repeaters used a single SCM for 89.4% of their QAs, and two SCMs for the remaining 10.6%. Among switchers, initial QAs were aided by a single SCM the majority of the time (78.7%), but two SCMs were used on a considerable portion (20.0%), and a small portion used three or four SCMs (0.7% each). On the subsequent QA, a smaller subset of switchers used a single SCM (68.7%), and higher rates were observed for the use of two (24.7%), three (4.7%), or four (2.0%) SCMs. Thus, switchers showed a trend toward use of more SCMs on any given QA, a pattern that was even more pronounced during the subsequent QA. Switchers still had significantly better abstinence outcomes than repeaters (p=0.002) when number of SCMs used at the subsequent QA was controlled for.

DISCUSSION

This study examined variability in SCMs used across two QAs, and its impact on cessation outcomes. Smokers were more likely to succeed in quitting when they used a different SCM after a failed attempt than smokers who tried to quit again using the same SCM. Findings parallel prior population-based studies that show most smokers make QAs in the absence of any SCM. However, the current data show a considerable subset of smokers report use of evidence-based SCMs after a failed QA, and this is beneficial for quitting success. No differences were found between repeaters and switchers on baseline demographic and smoking-related variables, although both groups were more nicotine dependent than smokers who used SCMs on only one QA (early/later users) or not at all (non-users). Overall, results suggest smokers could be advised try a new SCM (or combination thereof) upon making a new QA.

Findings raise the question of why switching SCMs may improve cessation outcomes. Type and number of SCMs were explored as potential explanations. Repeaters primarily used only one SCM, whereas switchers were shifting toward the use of more than one SCM on a given QA. For example, rates of any use of varenicline (i.e., with or without additional SCM) were

higher for switchers than repeaters at the subsequent QA. Switchers also were more likely to use any prescription SCM at the subsequent QA, which provides the advantage of interaction with a health professional who may provide counseling. Despite differences in the number or type of SCMs used at the subsequent QA, controlling for these variables statistically did not suppress the effects of switching on quit success. Thus, results suggest improved cessation cannot be attributed to progression to a superior SCM (e.g., varenicline) or number of SCMs used, although it would be prudent to attempt replication as SCM availability/use patterns change over time. The act of switching appeared to be driving better quit success, regardless of the SCMs smokers were switching to/from. Future studies could test this systematically through sequential, multiple assignment, randomized trial designs,[27] with relapsers (i.e., treatment non-responders) assigned to the same or alternative SCM regime. Potential mechanisms could also be explored to delineate whether effects are due to reducing the difficulty of quitting (e.g., nicotine withdrawal, stress/negative affect) or enhancing treatment engagement (e.g., less treatment fatigue).

Limitations

First, only variability in the use of SCMs was examined. The degree to which these findings apply to behavioral treatments, or combined use of pharmacologic and behavioral strategies, is unknown. Second, quit success was based on self-reported abstinence without biochemical verification. Although this approach conforms to recommendations put forward by the Society for Research on Nicotine and Tobacco,[28,29] there are numerous definitions of quit success and methods to validate smoking status. Third, characterization of SCMs used on QAs was based on the most recent QA prior to each assessment wave. Additional QAs may have occurred between waves, and may or may not have involved SCMs, but the current analyses are unable to account for potential QAs/SCMs. Finally, SCM use for each QA was examined, but not the dose or duration of each, which is an important limitation as proper dosing of SCMs is likely to be an important correlate of smoking abstinence.[30,31] Adherence regimens vary across SCMs, which may influence perceptions of treatment burden/fatigue, noncompliance, and ultimately relapse.[32] Noncompliance is commonly observed,[31] so perhaps switchers had better outcomes because they moved to SCMs to which they could better adhere. Even with these limitations, this study provides the first real evidence to support a recommendation to encourage smokers who fail on one SCM (or combination) to switch to a different SCM (or combination) on a subsequent QA.

CONCLUSIONS

Future research should replicate findings, and expand upon the current study with greater precision by including more frequent assessments and examining variability in the use of both pharmacologic and behavioral treatments across QAs. Future studies should also examine a wide range of potential explanations for the observed effects to contribute toward a precision medicine approach. In addition to adherence issues noted above, some medications may be more effective for certain types of smokers. For example, pharmacogenomic studies suggest NRT may be better suited for smokers with genotypes associated with nicotine metabolism[33] or reduced aversive responses to nicotine.[34] Those without these genotypes may not find NRT effective, or may experience side effects that

limit adherence. There is a need for future work to explore interactions between genetic and psychosocial predictors of switching, as well as potential order effects (e.g., SCMs trials).

Findings from this study suggest a subset of smokers remain highly engaged in quitting despite a history of relapse, and are willing to use SCMs to aid future QAs. The finding that smokers can increase their odds of abstinence by varying their use of SCMs provides evidence to suggest smokers could be advised to try new quit methods.

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Table 1

Sample Characteristics by Smoking Cessation Medication (SCM) Use Across Two Quit Attempts (QAs)

			SCM users during 1 QA		SCM users during both QAs		Significance tests			
Covariate	**Overall**	**Non-users**	**Early users (prior QA)**	**Later users (current QA)**	**Repeaters (same SCM)**	**Switchers (different SCM)**	**Omnibus**	**Repeaters vs. all others**	**Switchers vs. all others**	**Repeaters vs. switchers**
Total QA pairs (N=1,057)		45.3% (n=479)	11.4% (n=120)	18.4% (n=195)	10.7% (n=113)	14.2% (n=150)				
Country							**χ^2=35.8 *****	**χ^2=9.8 ***	**χ^2=8.9 ***	χ^2=4.5
United Kingdom	27.4 %	54.1%	11.0%	17.2%	9.0%	8.6%				
Canada	23.1 %	47.5%	11.9%	15.2%	12.3%	13.1%				
Australia	18.7 %	34.3%	10.1%	20.7%	16.2%	18.7%				
U.S.	30.7 %	42.5%	12.0%	20.6%	7.7%	17.2%				
Sex							**χ^2=11.5 ***	χ^2=0.6	χ^2=2.1	χ^2=0.1
Female	61.3 %	41.2%	12.0%	20.1%	11.4%	15.3%				
Male	38.7 %	51.8%	10.3%	15.9%	9.5%	12.5%				
Age group (years)							χ^2=13.3	χ^2=0.7	χ^2=3.7	χ^2=1.1
18-24	5.9%	56.5%	9.7%	11.3%	9.7%	12.9%				
25-39	22.5 %	45.0%	11.8%	13.9%	11.3%	18.1%				
40-54	41.2 %	44.1%	12.6%	20.2%	10.3%	12.6%				
55+	30.5 %	45.0%	9.6%	20.8%	10.9%	13.7%				
Majority / Minority status							**χ^2=13.2 ****	χ^2=3.8	χ^2=1.4	χ^2=0.5
Majority	88.5 %	43.6%	11.9%	18.3%	11.4%	14.8%				
Minority	11.5 %	58.2%	7.4%	19.7%	4.9%	9.8%				
Education							**χ^2=16.0 ***	χ^2=3.8	χ^2=1.8	χ^2=0.2
Low	49.4 %	43.1%	12.6%	22.2%	8.8%	13.2%				
Moderate	32.8 %	47.3%	11.0%	15.3%	12.1%	14.4%				
High	17.8 %	47.9%	8.5%	13.8%	13.3%	16.5%				
Income							χ^2=10.0	χ^2=2.5	χ^2=2.4	χ^2=3.1
Low	33.3 %	44.3%	11.1%	20.5%	10.2%	13.9%				
Moderate	32.5 %	46.2%	11.0%	18.0%	9.3%	15.4%				

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Covariate	Overall	Non-users	SCM users during 1 QA: Early users (prior QA)	SCM users during 1 QA: Later users (current QA)	SCM users during both QAs: Repeaters (same SCM)	SCM users during both QAs: Switchers (different SCM)	Significance tests: Omnibus	Significance tests: Repeaters vs. all others	Significance tests: Switchers vs. all others	Significance tests: Repeaters vs. switchers
High	28.7 %	43.2%	12.9%	17.8%	11.9%	14.2%				
Unknown	5.5%	56.9%	6.9%	12.1%	15.5%	8.6%				
Self-efficacy							**χ^2=26.48 *****	χ^2=0.3	χ^2=4.1	χ^2=2.1
Low	48.4 %	42.4%	10.5%	18.9%	11.1%	17.0%				
Moderate	33.4 %	46.5%	11.9%	18.1%	10.2%	13.3%				
High	18.2 %	51.0%	12.5%	17.7%	10.4%	8.3%				
Nicotine dependence (0-6), M(SE)	2.5 (1.5)	2.1 (1.5)	2.7 (1.4)	2.9 (1.5)	2.8 (1.4)	3.1 (1.3)	**F^2=18.8 *****	**χ^2=5.8 ***	**χ^2=22.0 *****	χ^2=1.5

Note: Boldface indicates statistical significance;

* $p<0.05$;

** $p<0.01$

*** $p<0.001$

795 respondents contributed to 1,057 QAs.

Table 2

1-month Point Prevalence Abstinence as a Function of Smoking Cessation Medication Use Across Quit Attempts

		Adjusted (*N*=795; Wave Pairs=1,057)							
		Model 1: Non-users as referent				Model 2: Switchers as referent			
SCM use	**% Quit**	**OR**	**95% CI**		***p*-value**	**OR**	**95% CI**		***p*-value**
			Lower	**Upper**			**Lower**	**Upper**	
Non-users	15.9%	ref	-	-	-	**0.48**	**0.30**	**0.76**	**0.002**
Early users (prior QA)	16.6%	1.05	0.61	1.80	0.86	**0.50**	**0.27**	**0.92**	**0.03**
Later users (current QA)	20.0%	1.32	0.86	2.03	0.21	0.63	0.37	1.06	0.08
Repeaters	12.4%	0.75	0.40	1.40	0.36	**0.36**	**0.18**	**0.72**	**0.004**
Switchers	**28.5 %**	**2.10**	**1.31**	**3.36**	**0.002**	ref	-	-	-

Note: Boldface indicates statistical significance (*$p<0.05$). Adjusted models included: country, sex, age, majority/minority status, education, income, self-efficacy, and heaviness of smoking index.

SCM, smoking cessation medication; QA, quit attempt

Table 3

Frequencies of Smoking Cessation Medications (SCMs) Used by Repeaters and Switchers

SCM use	Overall first QA (N=263)	Overall second QA (N=263)	Repeaters (N=113)	Switchers first QA (N=150)	Switchers second QA (N=150)	Repeaters vs switchers second QA
Specific SCM(s) used						
Patch	36.1%	25.9%	38.9%	34.0%	16.0%	−22.9%
Varenicline	23.2%	31.6%	30.1%	18.0%	32.7%	2.6%
Bupropion	8.4%	4.2%	5.3%	10.7%	3.3%	−2.0%
Gum	8.4%	6.1%	8.0%	8.7%	4.7%	−3.3%
Patch and gum	6.8%	3.0%	3.5%	9.3%	2.7%	−0.8%
Lozenge	3.8%	4.2%	4.4%	3.3%	4.0%	−0.4%
Other prescription	1.5%	3.0%	0.9%	2.0%	4.7%	3.8%
Gum and lozenge	1.5%	1.1%	0.0%	2.7%	2.0%	2.0%
Patch and lozenge	1.5%	0.8%	0.9%	2.0%	0.7%	−0.2%
Other NRT	1.1%	1.9%	0.9%	1.3%	2.7%	1.8%
Gum and Varenicline	1.1%	1.1%	0.9%	1.3%	1.3%	0.4%
Patch and Bupropion	1.1%	1.5%	1.8%	0.7%	1.3%	−0.5%
Patch and other NRT	1.1%	3.8%	0.9%	1.3%	6.0%	5.1%
Patch and tab	1.1%	1.5%	1.8%	0.7%	1.3%	−0.5%
Gum and other NRT	0.4%	1.1%	0.9%	0.0%	1.3%	0.4%
Cumulative SCM(s) used						
Any NRT	66.5%	59.7%	63.7%	68.7%	56.7%	−7.0%
Any NRT combo	13.3%	13.7%	8.0%	17.3%	18.0%	10.0%
Any Bupropion	9.9%	9.5%	7.1%	12.0%	11.3%	4.2%
Any Varenicline	25.1%	38.0%	31.0%	20.7%	43.3%	12.3%
Any prescription	49.4%	63.1%	57.5%	46.7%	67.3%	9.8%

Note: 19 additional SCMs were used by <1% of the sample during either the first or second QA (tab, patch, and other prescription, patch and Varenicline, Varenicline and other prescription, patch and gum and other NRT, patch and gum and Bupropion and other prescription, Bupropion and other, prescription, gum and Bupropion, lozenge and Varenicline, other NRT and other prescription, other NRT and Varenicline, tab and Varenicline, other NRT and Varenicline and other prescription, patch and Bupropion and Varenicline, patch and gum and lozenge, patch and other NRT and Bupropion, patch and other NRT and Varenicline, patch and Bupropion and Varenicline and other prescription, patch and gum and Bupropion amd Varenicline

QA, quit attempt; NRT, nicotine replacement therapy