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Prospective Cohort Study of the Effectiveness of Smoking Cessation Treatments Used in the "Real World"

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Abstract

Objective: To estimate the "real-world" effectiveness of commonly used aids to smoking cessation in England by using longitudinal data.

Patients and Methods: We conducted a prospective cohort study in 1560 adult smokers who participated in an English national household survey in the period from November 2006 to March 2012, responded to a 6-month follow-up survey, and made at least 1 quit attempt between the 2 measurements. The quitting method was classified as follows: (1) prescription medication (nicotine replacement therapy [NRT], bupropion, or varenicline) in combination with specialist behavioral support delivered by a National Health Service Stop Smoking Service; (2) prescription medication with brief advice; (3) NRT bought over the counter; (4) none of these. The primary outcome measure was self-reported abstinence up to the time of the 6-month follow-up survey, adjusted for key potential confounders including cigarette dependence.

Results: Compared with smokers using none of the cessation aids, the adjusted odds of remaining abstinent up to the time of the 6-month follow-up survey were 2.58 (95% CI, 1.48-4.52) times higher in users of prescription medication in combination with specialist behavioral support and 1.55 (95% CI, 1.11-2.16) times higher in users of prescription medication with brief advice. The use of NRT bought over the counter was associated with a *lower* odds of abstinence (odds ratio, 0.68; 95% CI, 0.49-0.94).

Conclusion: Prescription medication offered with specialist behavioral support and that offered with minimal behavioral support are successful methods of stopping cigarette smoking in England.

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The evidence for the efficacy of behavioral support and several medications for smoking cessation is provided by multiple randomized controlled trials.[1-7] It is important to supplement the evidence from these experimental studies with evidence from observational studies in the "real world." In a previous study, we used cross-sectional data from an English population survey to assess the effectiveness of medication for smoking cessation combined with behavioral support in comparison with unaided quitting.[8] A key issue when using nonrandomized observational data is to account for potential confounding by indication; that is, smokers who use one method of quitting may differ from smokers using another method of quitting in terms of prognostic factors. The most important confounder in this regard is cigarette dependence.

In our earlier study,[8] we used a validated measure[9] involving ratings of current urges to smoke assessed at the time of the survey to adjust for potential confounding. In smokers who were abstinent at the time of the survey, these measures were assumed to serve as a valid proxy for urges to smoke at the time of the quit attempt. This assumption holds only when different methods of stopping are not differentially linked to lower or higher levels of urges in abstinent smokers. We indeed found that urges to smoke in smokers vs quitters did not differ as a function of method.[8] Still, smokers who used medication and behavioral support reported higher levels of urges to smoke than did smokers who tried to quit unaided. After adjusting for this confounder, we found that smokers who use a combination of specialist behavioral support and medication in their quit attempts had almost 3 times the odds of success than did those who used neither medication nor behavioral support. We also found that smokers

who bought nicotine replacement therapy (NRT) over the counter with no behavioral support had similar odds of success at stopping as did those who stop without any aid.

It is important to confirm these findings with longitudinal data that are used to measure urges to smoke in current smokers at baseline, before their quit attempt. We conducted a prospective cohort study using data from the Smoking Toolkit Study to achieve this.

PATIENTS AND METHODS

The Smoking Toolkit Study is an ongoing research program designed to provide information about smoking cessation and factors that promote or inhibit it at a population level.[10,11] Each month a new sample of approximately 1800 people 16 years and older completes a face-to-face computer-assisted survey, of whom approximately 450 (25%) are smokers. The general methodology has been described in full elsewhere and has been reported to result in figures for key variables such as smoking prevalence that are nationally representative.[10] The specific methodology used for the present study and described herein was largely based on our previous study and has been described in a different article as well.[8]

Study Population

For the present study, we used aggregated data from respondents to the baseline survey in the period from November 2006 (the start of the survey) to March 2012 (the latest wave of the survey for which 6-month follow-up data were available), who smoked cigarettes (including hand-rolled) or any other combustible tobacco product (eg, pipe or cigar) daily or occasionally at the time of the survey. These respondents were asked whether they were willing to be recontacted. A follow-up questionnaire was sent to consenting respondents 6 months after baseline. Participants were given £5 ($8) remuneration, and 1 reminder letter was sent. Of the 27,219 smokers at baseline, 5757 (21.2%) were followed up 6 months later. The sample followed up differed from those not followed up by being more likely to be female, older, less motivated to stop smoking, and reporting higher strengths of urges to smoke at baseline. The differences were small but statistically significant ($P<.05$).

Respondents to the 6-month follow-up were asked "Have you made a serious attempt to stop smoking in the past 12 months? By serious attempt I mean you decided that you would try to make sure you never smoked another cigarette? Please include any attempt that you are currently making." Those respondents who answered "Yes" were then asked "How long ago did your quit attempt start?" The response options to this question were as follows: "In the last week"; "More than a week and up to a month"; "More than 1 month and up to 2 months"; "More than 2 months and up to 3 months"; "More than 3 months and up to 6 months"; "More than 6 months and up to a year"; "Can't remember." We included only those respondents who made at least 1 quit attempt about 6 months ago.

Measurement of Effect: Use of Smoking Cessation Treatments

The use of smoking cessation treatments was assessed only for the most recent quit attempt and included the following: (1) NRT on prescription, bupropion, or varenicline in combination with specialist behavioral support (ie, one-to-one or group behavioral support delivered by a National Health Service [NHS] Stop Smoking Service); (2) NRT on prescription, bupropion, or varenicline in combination with brief advice (delivered by the prescribing health care professional); (3) NRT bought over the counter without any behavioral support; (4) none of these. The behavioral support delivered by an NHS Stop Smoking Service generally involves at least 6 sessions with the client (before the quit date, on the quit date itself, and 4 weekly follow-up sessions), with a total potential contact time of at least 1.5 hours.[12]

Measurement of Outcome: Self-Reported Nonsmoking

Our primary outcome was self-reported nonsmoking up to the time of the 6-month follow-up measurement. Respondents were asked "How long did your most recent serious quit attempt last before you went back to smoking?" Those responding "I am still not smoking" were defined as nonsmokers. Previous research has found that self-reported abstinence in surveys of this kind is not subject to the kind of biases observed in clinical trials in which there is social pressure to claim abstinence.[13,14]

Measurement of Potential Confounders

We measured variables potentially associated with the use of smoking cessation treatments

and that may also have an effect on the outcome. These potential confounders were chosen a priori. The most important factor was cigarette dependence for which we used 2 questions assessed at baseline. First, time spent with urges to smoke was assessed by asking "How much of the time have you felt the urge to smoke in the past 24 hours? Not at all (coded 1), a little of the time (2), some of the time (3), a lot of the time (4), almost all of the time (5), all of the time (6)." Second, strength of urges to smoke was assessed by asking "In general, how strong have the urges to smoke been?: slight (1), moderate (2), strong (3), very strong (4), extremely strong (5)." This question was coded "0" for smokers who responded "Not at all" to the previous question. These 2 ratings have been found in this population to be a better measure of dependence (more closely associated with relapse after a quit attempt) than other measures.[9] Demographic characteristics we took into account were age, sex, and social grade (measured on an ordinal scale: AB = managerial and professional occupations; C1 = intermediate occupations; C2 = small employers and own account workers; D = lower supervisory and technical occupations; and E = semiroutine and routine occupations, never workers, and long-term unemployed). With regard to the most recent quit attempt measured at 6-month follow-up, we asked the time since this quit attempt was initiated, the number of quit attempts before this attempt that occurred since baseline, and whether respondents cut down first or stopped abruptly without cutting down.

Data Analyses

Simple associations between potential confounders and use of the smoking cessation treatments were assessed by using analysis of variance for continuous variables and Pearson's χ^2 test for categorical variables. The Games-Howell procedure was used for post hoc multiple comparisons of the continuous variables between pairs of treatment groups.

For our primary analysis, we used a multiple logistic regression model in which we regressed the outcome measure (self-reported nonsmoking at 6-month follow-up compared with smoking) on the effect measure (use of each of the 3 smoking cessation treatments compared with no use of such treatments), adjusted for the above-mentioned confounders and year of the survey.

In addition to the model from this primary analysis ("fully adjusted model"), we constructed a simple model including only the effect measure ("unadjusted model") and a model that included the effect measure, year of the survey, and all confounders except for the 2 measures of tobacco dependence ("partially adjusted model") to show the extent of confounding effects of tobacco dependence.

In a sensitivity analysis, we excluded respondents who had used telephone counseling for smoking cessation during their most recent quit attempt; very few smokers in England use this form of treatment, and so it is not possible to assess its association with abstinence. In the primary analysis, these smokers were conservatively counted in the "no-treatment" group unless they had also used medication, whereas in the sensitivity analysis, they were excluded from the analysis.

All analyses were performed with complete cases. Respondents with missing data on 1 or more of the confounding variables were excluded (0.3% of the eligible sample).

RESULTS

The study population consisted of 1560 respondents with complete baseline and 6-month follow-up data who made at least 1 quit attempt between the 2 time points. Demographic and smoking-related characteristics are summarized in Table 1. The percentage of usage of smoking cessation treatments during the last quit attempt was 4.8% (n=75) for prescription medication combined with specialist behavioral support, 20.8% (n=324) for prescription medication combined with brief advice, 29.9% (n=467) for NRT bought over the counter, and 44.5% (n=694) for using none of these treatments. A total of 399 respondents (25.6%) had used some form of prescription medication during their most recent quit attempt; most of them had used NRT on prescription (56.9%, n=227), followed by varenicline (35.1%, n=140) and bupropion (6.0%, n=24). The remaining 2.0% (n=8) of respondents had used some combination of these medications.

A total of 1201 respondents (77.0%) smoked, and 359 (23.0%) reported not smoking at the 6-month follow-up. The unadjusted abstinence rates were 38.7% (n=29) for users of medication on prescription combined with specialist behavioral support, 27.8% (n=90) for

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users of prescription medication combined with brief advice, 15.4% (n=72) for users of NRT bought over the counter, and 24.2% (n=168) for those using none of these treatments.

The use of treatments was associated with age, time since last quit attempt started, number of quit attempts before the most recent one, the 2 measures of dependence (time spent with and strength of urges to smoke), and social grade (Table 2). The post hoc comparisons established that users of medication (on prescription or over the counter) reported higher levels of dependence than did respondents who had tried to quit unaided.

Table 3 reveals that the fully adjusted odds of nonsmoking in users of prescription medication in combination with specialist behavioral support were 2.58 times higher (95% CI, 1.48-4.52) than in the no-treatment group. The odds were 1.67 times higher (95% CI, 0.94-2.98) than in the group that used prescription medication combined with brief advice, but this difference was not statistically significant (figures not shown in the table). In the latter group, the odds were 1.55 times higher (95% CI, 1.11-2.16) than in the no-treatment group. The use of NRT bought over the counter was associated with *lower* odds of abstinence (odds ratio, 0.68; 95% CI, 0.49-0.94). In the partially adjusted model, the odds ratios for the 2 groups that used prescription medication were slightly lower than in the fully adjusted model, whereas the odds ratio for the group that used NRT bought over the counter was slightly more extreme.

A total of 24 respondents (1.5%) reported having used telephone counseling during their most recent quit attempt. Excluding these respondents from the primary analysis changed the odds ratios of the fully adjusted model only minimally.

TABLE 1. Sample Characteristics (N=1560)[a]

Nonsmoker at follow-up	23.0 (359)
Age at baseline	46.5±15.7
Female sex	55.8 (871)
Social grade	
AB	11.0 (171)
C1	20.9 (326)
C2	22.0 (343)
D	17.5 (273)
E	28.7 (447)
Time spent with urges to smoke at baseline[b]	3.2±1.2
Strength of urges to smoke at baseline[c]	2.2±1.0
Time since last quit attempt started at follow-up	
≤1 wk	10.5 (164)
2-4 wk	21.1 (329)
5-8 wk	21.0 (327)
9-12 wk	19.8 (309)
13-26 wk	27.6 (431)
Number of quit attempts before the most recent one and up to 6 mo at follow-up	
0	69.2 (1079)
1	22.5 (351)
2	8.3 (130)
Stopped abruptly during last quit attempt at follow-up (vs cut down first)	47.9 (747)
Use of smoking cessation treatments during last quit attempt at follow-up	
Medication on prescription combined with specialist behavioral support[d]	4.8 (75)
Medication on prescription combined with brief advice[d]	20.8 (324)
NRT bought over the counter	29.9 (467)
None of the above	44.5 (694)

[a]Values are expressed as mean ± SD or as No. (percentage).
[b]Time spent with urges to smoke: 1 (not at all) to 6 (all the time).
[c]Strength of urges to smoke: 0 (no urges) to 5 (extremely strong urges).
[d]Medication on prescription included nicotine replacement therapy (NRT), varenicline, or bupropion.

DISCUSSION

This prospective cohort study found that the use of prescription medication in combination with specialist behavioral support provided by an NHS Stop Smoking Service was associated with the highest success of attempts to quit smoking. The use of prescription medication with limited behavioral support by the prescribing health care professional was also associated with higher success than was unaided quitting, whereas the use of NRT bought over the counter was associated with *lower* success.

Comparison With Findings From Randomized Controlled Trials

Our estimated effectiveness of adding specialist behavioral support provided by an NHS Stop Smoking Service to prescription medication (adjusted odds ratio, 1.67) is similar to that from a meta-analysis performed for the US guidelines.[15] Also, our estimated effectiveness of prescription medication combined with limited behavioral support by the prescribing health care professional compared with unaided quitting (adjusted odds ratio, 1.55) is similar to that from meta-analyses of randomized placebo-controlled trials.[4-6] However, our adjusted odds ratio of 0.68 in users of NRT bought over the counter compared with that in those who used

TABLE 2. Associations Between Characteristics of the Sample and Use of Smoking Cessation Treatments[a]

Variable	Medication on prescription combined with specialist behavioral support[b] (n=75)	Medication on prescription combined with brief advice[b] (n=324)	NRT bought over the counter (n=467)	None of the others (n=694)	*P*
Age at baseline	52.0±13.0[1]	48.6±13.8[2]	46.6±15.4[1]	44.9±16.8[1,2]	<.001
Female sex	50.0 (31)	56.4 (167)	57.1 (306)	54.1 (398)	.22
Social grade					
AB	16.1 (10)	8.1 (24)	11.0 (59)	11.7 (86)	.007
C1	14.5 (9)	22.6 (67)	20.0 (107)	20.8 (153)	
C2	30.6 (19)	16.9 (50)	22.2 (119)	23.1 (170)	
D	4.8 (3)	20.9 (62)	15.7 (84)	18.2 (134)	
E	33.9 (21)	31.4 (93)	31.2 (167)	26.1 (192)	
Time spent with urges to smoke at baseline[c]	3.7±1.2[3]	3.5±1.2[4]	3.3±1.2[5]	2.9±1.1[3,4,5]	<.001
Strength of urges to smoke at baseline[d]	2.5±1.0[6]	2.4±1.1[7]	2.3±1.0[8]	2.0±1.0[6,7,8]	<.001
Time since quit attempt started at follow-up					<.001
≤1 wk	4.8 (3)	8.8 (26)	9.1 (49)	12.8 (94)	
2-4 wk	25.8 (16)	11.5 (34)	23.3 (125)	22.4 (165)	
5-8 wk	16.1 (10)	20.9 (62)	22.0 (118)	20.3 (149)	
9-12 wk	24.2 (15)	26.0 (77)	17.7 (95)	18.1 (133)	
13-26 wk	29.0 (18)	32.8 (97)	27.8 (149)	26.4 (194)	
Number of quit attempts before the most recent one and up to 6 mo at follow-up					.002
0	75.8 (47)	77.4 (229)	67.2 (360)	67.6 (497)	
1	14.5 (9)	17.2 (51)	23.9 (128)	23.1 (170)	
2	9.7 (6)	5.4 (16)	9.0 (48)	9.3 (68)	
Stopped abruptly during last quit attempt at follow-up (vs cut down first)	48.4 (30)	44.9 (133)	45.7 (245)	50.1 (368)	.14

[a]Values are expressed as mean ± SD or as No. (percentage).
[b]Medication on prescription included nicotine replacement therapy (NRT), varenicline, or bupropion.
[c]Time spent with urges to smoke: 1 (not at all) to 6 (all the time).
[d]Strength of urges to smoke: 0 (no urges) to 5 (extremely strong urges).
Superscript numbers 1-8 indicate statistically significant ($P<.05$) differences between groups with the same letter according to the post hoc analyses.

neither medication nor behavioral support (indicating a *reduced* likelihood of quitting in users of NRT bought over the counter) conflicts with a meta-analysis that reported a pooled odds ratio of 2.5 for active NRT bought over the counter vs placebo.[16] This discrepancy seems unlikely to relate to the difference in study designs or unmeasured confounding because our prospective cohort design yielded similar results as experimental designs with regard to the use of prescription medication and behavioral support, as noted above. Therefore, the most likely explanation for the low success rate of NRT bought over the counter in our study is

TABLE 3. Unadjusted and Adjusted Odds of Self-Reported Nonsmoking at 6-mo Follow-Up Stratified by the Method of Quitting

Smoking cessation treatment	Odds ratio (95% CI)		
	Unadjusted model	Partially adjusted model[a]	Fully adjusted model[b]
Medication on prescription combined with specialist behavioral support (n=62)[c]	1.98 (1.20-3.24)	2.27 (1.32-3.92)	2.58 (1.48-4.52)
Medication on prescription combined with brief advice (n=296)[c]	1.20 (0.89-1.62)	1.38 (1.00-1.91)	1.55 (1.11-2.16)
NRT bought over the counter (n=536)	0.57 (0.42-0.78)	0.62 (0.45-0.85)	0.68 (0.49-0.94)
None of the above (reference) (n=735)	1	1	1

[a]Partially adjusted model was adjusted for age, sex, social grade, time since last quit attempt started, number of quit attempts before the one in question, stopping abruptly vs cutting down, and year of the survey.
[b]Fully adjusted model was adjusted for the variables from the partially adjusted model and for time spent with urges to smoke and strength of urges to smoke.
[c]Medication on prescription included nicotine replacement therapy (NRT), varenicline, or bupropion.

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inappropriate usage and low adherence in the real world.[17,18] Experimental studies cannot mimic the usual environment in which over-the-counter medication is used because trial participants are instructed on how to use the medication, and their adherence to this medication is monitored and promoted during the trial. For example, the authors from the largest placebo controlled trial of NRT bought over the counter, which contributed to the above-mentioned meta-analysis, acknowledged that "complete reproducibility of the over-the-counter setting was impossible."[19] In that trial, participants were asked to set a quit date within 7 days; they were given instructions on how to use the medication, the first use was under supervision, adverse events were monitored, and adherence was maintained during several site visits.[19] This is a different situation from the real-world setting of our study in which smokers use the medication in an uncontrolled yet more realistic fashion.

Comparison With Findings From Observational Studies

One of the aims of this prospective cohort study was to confirm the findings from our earlier cross-sectional study on the real-world effectiveness of smoking cessation treatments.[8] The findings from the present study regarding prescription medication largely confirm those from our earlier study, even though the 2 effect estimates for prescription medication with or without specialist behavioral support were closer to 1 in this study, suggesting that residual confounding played a greater role in our previous study. Although NRT bought over the counter was equally associated with the success of quitting than not using treatment in our earlier study (adjusted odds ratio, 0.96; 95% CI, 0.81-1.13),[8] NRT bought over the counter was associated with a significant *reduction* in success in our present study (adjusted odds ratio, 0.68; 95% CI, 0.49-0.94).

Our finding of a positive association between the use of prescription medication and the success of attempts to quit smoking is largely consistent with previous prospective cohort studies.[20-25] For example, a study using data from 12,156 treatment episodes routinely recorded by 31 NHS Stop Smoking Services in England found that specialist behavioral support combined with dual NRT (but not single NRT), varenicline, or bupropion was associated with a higher rate of success of quit attempts than was behavioral support without medication.[20] A study in 7436 smokers taking part in the International Tobacco Control Four Country Study reported higher success rates in smokers trying to quit who used NRT, varenicline, or bupropion than in smokers trying to quit without medication, although the effect estimates were much higher than in our study.[21] Another international study in more than 1089 smokers from 5 different countries reported a higher success rate in smokers who used NRT than in smokers who did not use NRT, again with higher effect estimates than in our study.[22]

Study Limitations

This study has several limitations. First, the response to our 6-month follow-up was only 21% and the response also differed slightly by demographic and smoking characteristics. A higher response would have resulted in increased statistical power, but our sample was large enough to statistically detect the differences in success rates between the treatment groups. We have no reason to assume that the somewhat differential nonresponse biased our estimates for the relative effectiveness of the treatments, but it may have reduced the generalizability of our findings to a small extent. Second, nonrandomized studies are generally vulnerable to confounding. We reduced this risk further than did many previous studies by adjusting for tobacco dependence—measured before a quit attempt was initiated—and several other potential confounders. However, residual confounding may have occurred because not all factors associated with self-selection of treatment, such as comorbidity[26] or psychological distress,[27] were measured in our survey. Third, our self-reported outcome measure of abstinence from smoking was not biochemically validated. In observational studies such as ours, however, it is unlikely that misreporting of abstinence is associated with the type of treatment respondents used during the last quit attempt they recall.[13,14] Fourth, we did not have data on actual use of, and adherence to, the medication and the behavioral support. We have no reason to assume that the report of various treatments was dependent on the respondents' smoking status at the 6-month follow-up measurement. If bias occurred, this would have led to an underestimation of the effectiveness of prescription medication and specialist behavioral support

because unaided quit attempts that fail are more likely to be forgotten.[28] An improved real-world design that would reduce the risk of confounding and the reliance on recall data may involve baseline characteristics to be collected first and then recent treatment assessed at a second time point before assessing smoking status at the final follow-up. Finally, our sample size was too small for comparing the differential effectiveness of different prescription medications.

Strengths

As far as we are aware, our study is the first prospective cohort study comparing prescription medication when offered with specialist behavioral support with prescription medication offered without such support. A major strength of our study is the use of a representative sample of the English population that was sufficiently large to detect an effect of specialist behavioral support despite its low prevalence. We used aggregated data from monthly surveys over a period of more than 5 years and therefore minimized potential bias from the rate of quit attempts depending on the time of the year.

CONCLUSION

The use of prescription medication with specialist behavioral support delivered by an NHS Stop Smoking Service or with minimal behavioral support is associated with improved outcomes compared with unaided quitting. Thus, more smokers should be guided into these forms of treatment because currently only 1 of 4 smokers attempting to quit use them. The most frequently used form of treatment, NRT bought over the counter, appears to be associated with *reduced* success rates. More research is urgently needed on the effectiveness of NRT bought over the counter in the real world.

Abbreviations and Acronyms: **NHS** = National Health Service; **NRT** = nicotine replacement therapy

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Potential Competing Interests: Pfizer, Johnson & Johnson, and GlaxoSmithKline are manufacturers of smoking cessation products who had no involvement in the design of the study, collection, analysis or interpretation of the data, the writing of the report, or the decision to submit the paper for publication. Dr West has undertaken research and consultancy and received travel funds from companies that develop and manufactures smoking cessation medications. He has a share of a patent for a novel nicotine delivery device. He is a trustee of the stop-smoking charity, QUIT, and a co-director of the National Centre for Smoking Cessation and Training. Dr Kotz has received an unrestricted research grant from Pfizer for a smoking cessation trial. Dr Brown has received an unrestricted research grant from Pfizer.

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