Nicotine & Tobacco Research, 2017, 916–921
doi:10.1093/ntr/ntx025
Original investigation
Received July 26, 2016; Editorial Decision January 13, 2017; Accepted January 20, 2017

Original investigation

A Mediation Analysis of Motivational, Reduction, and Usual Care Interventions for Smokers Who Are Not Ready to Quit

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Abstract

Introduction: We recently conducted a large randomized controlled trial (RCT) ($N = 560$) that failed to replicate our initial RCT's findings that brief motivational and reduction interventions increased quit attempts (QA) and point-prevalence abstinence (PPA) in smokers not ready to quit. The present study aimed to test why our interventions were ineffective.

Methods: A secondary analysis of a 3-arm RCT tested (1) whether telephone-based motivational or reduction interventions changed the following hypothesized mediators more than usual care: cigarettes per day (CPD), dependence, pros of smoking, cons of smoking, self-efficacy, or intention to quit; (2) whether changes in these hypothesized mediators predicted QAs and PPA at a 6-month follow-up, and (3) whether the interventions affected QAs and PPA via the hypothesized mediators.

Results: In comparison to usual care, the motivational intervention did not significantly influence the hypothesized mediators. The reduction intervention resulted in a significantly greater decrease in CPD and pros of smoking and increase in self-efficacy and intention to quit than usual care. Decreases in CPD and dependence and increases in self-efficacy and intention to quit were associated with increased QAs. The reduction intervention's influence on QAs was mediated by decreases in CPD and increases in self-efficacy and intention to quit. Findings regarding PPA were similar.

Conclusion: Our failure to replicate may be due, in part, to the fact that, compared to usual care, (1) the motivational intervention had no effect on the hypothesized mediators, and (2) the reduction intervention had a statistically significant but clinically insignificant effect on the hypothesized mediators.

Implications: This study demonstrates that mediation analysis may be useful to understand why an intervention is not more effective than usual care. We identified reductions in CPD and dependence and increases in self-efficacy and intention to quit as predictors of quitting. Further research should focus on developing more effective interventions to target these constructs, and cause clinically significant changes among smokers who are not ready to quit.

Introduction

Meta-analyses conclude that motivational interventions increase quit attempts (QAs) and abstinence among smokers who are not ready to quit.[1,2] The United States Public Health Service's (USPHS) Clinical Practice Guideline currently recommends a brief motivational intervention based on motivational interviewing, known as the 5Rs, to facilitate QAs in smokers without plans to quit in the near future.[3] A previous randomized controlled trial (RCT) we conducted found that the 5Rs increased the odds of making a QA fivefold and increased the odds of point-prevalence abstinence (PPA) sixfold.[4]

Meta-analyses have also concluded that nicotine replacement therapy (NRT)-aided interventions to reduce cigarettes per day (CPD) increase QAs and abstinence among smokers who are not ready to quit.[2,4,5] Our previous RCT also found that an NRT-aided reduction intervention increased both the odds of making a QA and of PPA fourfold.[4] However, it is unclear whether the effectiveness of NRT-aided reduction interventions are due to reducing CPD, to NRT use, or both.[6,7]

We recently conducted an RCT[8] to replicate our initial findings[4] of the efficacy of a motivational intervention (ie, 5Rs) and to test whether a reduction intervention without NRT is effective. We made a number of mediation hypotheses: that (1) the motivational intervention would increase quitting by decreasing participants' perceived benefits (ie, "pros") of smoking and increasing perceived detriments (ie, "cons") of smoking; (2) the reduction intervention would increase quitting by decreasing participants' CPD and dependence; and (3) both interventions would increase quitting by increasing participants' self-efficacy and intention to quit. However, neither the motivational nor reduction (without NRT) interventions increased QAs or PPA more than usual care at a 6-month follow-up.[8]

Mediation analysis is one method to determine why interventions in trials are ineffective.[9] Specifically mediation analyses can test whether negative results are due to the intervention not influencing the mediator variables (ie, the pros and cons of smoking, CPD, dependence, self-efficacy or intention to quit) or due to the mediators not influencing the outcomes (eg, QAs or PPA), or both.[10] Thus, one function of mediation analyses is to provide "post-mortem" explanations for why treatments did not have their intended effect. This secondary analysis tests our initial mediation hypotheses to better understand why our interventions failed to increase QAs and PPA in comparison to usual care.[8]

Methods

Overview

The three-arm RCT for this secondary analysis consisted of a motivational, reduction, and usual care condition. The design and main results have been reported fully elsewhere.[8] The aims of the RCT were to test whether brief motivational or reduction interventions increased QAs (primary aim) or PPA (secondary aim) more than usual care among smokers who are not ready to quit. The primary conclusions of the trial were that neither intervention increased QAs or PPA significantly more than usual care at a 6-month follow-up.

Participants

The trial recruited 560 participants via email invitations to the Nielsen consumer panel of over 350 000 participants (www.ncppanel.com/content/ncp/ncphome.html). Participants in the Nielsen panel are individuals who use the Internet and elected to receive invitations to participate in a variety of online surveys in return for points redeemable for products and services. Our participant flow diagram is displayed in Supplementary Document A. We enrolled adult smokers of ≥ 10 CPD who stated that they were not ready to quit in the next 30 days. Participants were mostly middle-aged (mean 51 years old), female (67%), and white, non-Hispanics (87%). They smoked a mean of 20 CPD at baseline and were moderately dependent (mean Fagerstrom Test for Cigarette Dependence [FTCD][11] = 5.4). One of us (PC) designed a computer-generated block randomization schedule stratified by counselor to assign participants to receive a motivational intervention, a reduction intervention, or usual care.

Interventions

We conducted all interventions by telephone and did not provide any medication. The motivational and reduction conditions received 10–15 minute counseling calls at baseline, week 2, and week 4. The usual care condition consisted of a 5-minute call at baseline.

Usual Care

The usual care condition was based on a prior description of usual care.[12] Counselors asked questions about the participants' smoking, advised participants to quit, and offered treatment information.

Motivational Intervention

Brief motivational counseling was based on the USPHS 5Rs guidelines[3] and was a replication of the motivational intervention in our prior study.[4] The intervention included certain motivational interviewing strategies (eg, develop discrepancy and support self-efficacy) but not others (eg, roll with resistance). The intervention focused on participants' (1) relevant reasons for quitting, (2) risks of smoking of concern to the smoker, (3) rewards of smoking cessation, (4) roadblocks to quitting, and (5) repetition of the topics.[3] Counselors concluded with advice to quit smoking at the last call.

Reduction Intervention

The reduction counseling was an update of the treatment found to be effective in our initial RCT of NRT-aided reduction,[4] except no NRT was used to aid reduction. We did not include NRT in our reduction intervention in order to (1) increase the potential application of our findings for the majority of smokers who do not want to use smoking cessation medications[13,14] and (2) to test whether reducing CPD per se (ie, not NRT pre-treatment) increases QAs and PPA.

Counselors initially recommended that participants reduce 20% of their CPD between each call (ie, over 2 weeks) but ultimately encouraged participants to set their own goals for reduction that they were likely to meet in order to increase self-efficacy. Counselors helped participants choose one of two strategies for reduction: (1) scheduled reduction; that is, smoking on a schedule and increasing time between cigarettes, or (2) hierarchical reduction; that is, eliminating certain cigarettes beginning with those that are the easiest to give up.[15,16] Counselors concluded with advice to quit smoking at the last call.

Assessments

The schedule of assessments is displayed in Supplementary Document B. The hypothesized mediators were assessed at baseline before the first counselor call and after the final call at week 4. We measured CPD as a continuous variable via questions regarding number of

CPD smoked during weekdays and weekends. We measured dependence using the Nicotine Dependence Syndrome Scale (NDSS)[17] because the scale has good reliability and predictive validity[18] and is not influenced by changes in CPD. The overall NDSS (NDSS-T) score is calculated with weighted parameters for 14 of the 19 NDSS items and produces z-scores.[17] We also conducted analyses using raw NDSS scores (ie, the mean of all 19 NDSS items.)[19] Findings from analyses using raw NDSS scores are reported in Supplementary Document C and are similar to the findings from analyses that used NDSS-T scores, reported below. We used Velicer's "Pros vs Cons" scales[20] to measure decisional balance.[21] It appears to have good construct, discriminant, convergent and predictive validity.[22] Self-efficacy to quit was measured with Velicer's Self-Efficacy Scale, which also appears to have good predictive validity.[4,23] Intention to quit was measured with a 10-point Intention-to-Quit ladder,[24] which prospectively predicts quit attempts.[4,24] Our primary outcome was whether or not participants reported a QA that lasted ≥24-hours between baseline and the 6-month follow-up. Our secondary outcome was self-reported 7-day PPA at the 6-month follow-up.

Analyses

We conducted all analyses with SPSS (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) We first compared the effect of motivational versus usual care and reduction versus usual care interventions on change in the hypothesized mediators. We determined a priori not to compare the motivational to the reduction intervention. Change in the hypothesized mediators were calculated by subtracting values at week 4 from baseline values. We controlled for baseline values of the hypothesized mediators and conducted linear regression analyses of the effect of treatment on the hypothesized mediators.

Next we used logistic regression analyses to test whether the hypothesized mediators predicted if participants made a 24-hour QA or were abstinent (7-day PPA) at a 6-month follow-up. We controlled for treatment as well as baseline values of the hypothesized mediators in each logistic regression analysis.

Finally, we conducted mediation analyses to test whether, in comparison to usual care, the effects of the interventions on QAs and PPA occurred via the hypothesized mediators. Despite prior recommendations,[25] mediation analysis in the absence of a significant main effect can still provide useful information.[10] For example, mediation analysis has been used to identify influential variables in smoking cessation counseling that failed to produce significant main effects.[9] We examined mediation only when the hypothesized mediators were both influenced by intervention and predicted QAs or PPA. We controlled for baseline values of the mediator construct in each mediation analysis. We used PROCESS to conduct mediation analyses.[10] PROCESS is a statistical macro that uses an ordinary least squares-based path analytical framework to test indirect effects. Bias-corrected bootstrap analyses (10 000 resamples) were used to estimate the 95% confidence intervals (CI) for the indirect effects.[10]

Of the 560 total participants, 171 (31%) were missing data on whether or not they made a QA during the 6-month study and 207 (37%) were missing data on whether or not they were abstinent at the end of the 6-month study. One hundred and sixty-six (30%) were missing data for the hypothesized mediator constructs. The amount of missing data did not differ between treatment conditions and usual care nor were baseline characteristics associated with missing data. In our analyses we assumed that missing outcome data indicated no QA or continued smoking. We imputed missing data for the hypothesized mediators using multiple imputation.[26] Thus we did not exclude data from any participants. We conducted sensitivity analyses where we (1) used multiple imputation for outcome data, (2) excluded missing outcome data, (3) assumed that missing mediator construct data indicated no change, and (4) excluded missing mediator construct data. In all cases there were no substantial differences in findings with those reported below.

Results

Descriptive statistics regarding the hypothesized mediators are displayed in Table 1. At the 6-month follow up, 34% in the usual care condition, 38% in the motivational condition, and 31% in the reduction condition had made a QA. In comparison to usual care, neither motivational nor reduction interventions significantly influenced making a QA (motivational vs. usual care OR = 1.19, 95% CI = 0.78–1.82; reduction vs. usual care OR = 0.89, 95% CI = 0.57–1.36) at the 6-month follow-up. Five percent in the usual care condition, 11% in the motivational condition, and 8% in the reduction condition were abstinent. The motivational intervention had a marginally significant influence on PPA (OR = 2.17, 95% CI = 0.99–4.77) but the reduction intervention had no effect (OR = 1.57, 95% CI = 0.69–3.59).[8]

Interventions' Effect on Hypothesized Mediators

In comparison to usual care, the motivational intervention did not affect any of the hypothesized mediators. The reduction intervention decreased CPD and the pros of smoking as well as increased

Table 1. Mean (*SE*) Values for Hypothesized Mediators

	Usual care (*n* = 189)		Motivational (*n* = 185)		Reduction (*n* = 186)	
	Baseline	Week 4	Baseline	Week 4	Baseline	Week 4
CPD	20.0 (0.60)	17.0 (0.82)	20.0 (0.63)	16.8 (0.64)	20.0 (0.61)	15.1 (0.69)
Dependence (NDSS-T scores) scale: –2.6 (least) to 2.3 (most)[a]	–0.3 (0.07)	–0.5 (0.08)	–0.3 (0.07)	–0.4 (0.08)	–0.2 (0.08)	–0.6 (0.04)
Pros of smoking scale: 1 (least) to 5 (most)	3.4 (0.04)	3.2 (0.05)	3.4 (0.04)	3.2 (0.05)	3.4 (0.04)	3.1 (0.05)
Cons of smoking scale: 1 (least) to 5 (most)	3.8 (0.04)	3.9 (0.05)	3.7 (0.04)	3.9 (0.05)	3.7 (0.04)	3.9 (0.05)
Self-efficacy scale: 0 (least) to 5 (most)	2.4 (0.08)	2.3 (0.09)	2.4 (0.08)	2.4 (0.09)	2.3 (0.07)	2.7 (0.08)
Intention to quit scale: 0 = very definitely no; 10 = very definitely yes	3.0 (0.16)	3.9 (0.21)	3.1 (0.19)	4.4 (0.22)	2.9 (0.18)	4.6 (0.22)

CPD = Cigarettes per day; NDSS = Nicotine dependence syndrome scale.

[a]The NDSS-T yields z-scores.[17] See Supplementary Document C for NDSS raw scores.

self-efficacy and intention to quit, but did not affect NDSS-T scores or the cons of smoking more than usual care (Table 2).

Hypothesized Mediators' Effect on Outcome

Quit Attempts

Four of the six hypothesized mediators predicted QAs (Table 3). A reduction of 1 CPD was associated with a 19% increase in the odds of making a QA. A one unit decrease in the NDSS-T scores was associated with a 62% increase in the odds of making a QA. A one unit increase in self-efficacy was associated with a 54% increase in the odds of making a QA. A one unit increase in intention to quit was associated with a 35% increase in the odds of making a QA. Change in the pros and cons of smoking had no significant effect on QAs.

Abstinence

Four of the six hypothesized mediators predicted PPA (Table 3). A reduction of 1 CPD was associated with a 12% increase in the odds of PPA. A one unit decrease in the NDSS-T scores was associated with a 54% increase in the odds of PPA. A one unit decrease in the pros of smoking was associated with a 116% increase in the odds of PPA. A one unit increase in intention to quit was associated with a 35% increase in the odds of PPA. Change in self-efficacy and the cons of smoking had no significant effect on PPA.

Overall, though changes in five of the six hypothesized mediators had large effects on QAs or PPA (Table 3), the absolute changes in the hypothesized mediators (Table 1) as well as the differences in changes between the active and comparison conditions (Table 2) were not large enough to achieve a total effect of the interventions on QAs or PPA.

Mediation: Indirect Effects of Interventions on Outcomes

We tested mediation (Table 4) only in the instances in which the hypothesized mediators were both influenced by treatment (Table 2) and predicted QAs or PPA (Table 3). All of these were tests of the reduction intervention effects.

Quit Attempts

Change in CPD, self-efficacy, and intention to quit independently mediated reduction intervention's effect on QAs. In comparison to usual care, the reduction intervention resulted in a greater decrease in CPD and increase in self-efficacy and intention to quit, each of which increased the odds of making a QA. A summary of the a priori hypothesized mediators is illustrated in Supplementary Document D.

Despite the mediation described above, the proportion of participants that made a QA was non-significantly greater in the usual care condition (34%) than the reduction condition (31%). This apparent discrepancy occurred because, although the reduction intervention decreased CPD and increased self-efficacy and intention to quit more than the usual care condition (Table 2), changes in these mediators among usual care participants were more strongly associated with QAs than changes in these mediators among participants who received the reduction intervention. A full description of this finding is described in Supplementary Document E.

Abstinence

Change in CPD, and intention to quit independently mediated the reduction intervention's effect on PPA. In comparison to usual care, the reduction intervention resulted in a greater decrease in CPD and

Table 2. Interventions as Predictors of Change in Hypothesized Mediators

Outcomes[a]	Motivational vs. Usual care interventions:	Reduction vs. Usual care interventions:
(hypothesized mediators)	Beta (95% CI)	Beta (95% CI)
Decrease in CPD	0.28 (−1.10 to 1.65)	1.96 (0.81 to 3.12)
Decrease in dependence (NDSS-T scores[b])	−0.15 (−0.35 to 0.05)	0.09 (−0.08 to 0.26)
Decrease in pros of smoking	0.05 (−0.07 to 0.17)	0.12 (0.02 to 0.22)
Increase in cons of smoking	0.09 (−0.01 to 0.20)	0.05 (−0.05 to 0.14)
Increase in self-efficacy	0.09 (−0.10 to 0.29)	0.40 (0.22 to 0.59)
Increase in intention to quit	0.46 (−0.08 to 1.00)	0.79 (0.22 to 1.35)

CI = Confidence interval; CPD = Cigarettes per day; NDSS = Nicotine Dependence Syndrome Scale; OR = Odds ratio. All analyses controlled for baseline values of the outcome.

[a]Change is from baseline to week 4.

[b]The NDSS-T yields z-scores therefore the displayed betas are standardized. See Supplementary Document C for NDSS raw scores.

Table 3. Change in the Hypothesized Mediators as Predictors of Quit Attempts and Abstinence

Predictors[a]	Quit attempts that lasted ≥ 24 h:	7-day point prevalence abstinence:
(hypothesized mediators)	OR (95% CI)	OR (95% CI)
Decrease in CPD	1.19 (1.12 to 1.27)	1.12 (1.04 to 1.20)
Decrease in dependence (NDSS-T scores[b])	1.62 (1.26 to 2.09)	1.54 (1.06 to 2.26)
Decrease in pros of smoking	1.48 (0.99 to 2.22)	2.16 (1.08 to 4.33)
Increase in cons of smoking	1.39 (0.86 to 2.26)	1.18 (0.56 to 2.48)
Increase in self-efficacy	1.54 (1.13 to 2.09)	1.29 (0.86 to 1.93)
Increase in intention to quit	1.35 (1.23 to 1.48)	1.35 (1.18 to 1.55)

CI = Confidence interval; NDSS = Nicotine Dependence Syndrome Scale; OR = Odds ratio. All analyses control for condition and baseline values of the predictor.

[a]Change is from baseline to week 4.

[b]The NDSS-T yields z-scores. See Supplementary Document C for NDSS raw scores.

Table 4. Indirect Effects of Condition on Outcome Via Mediators That Were Both Predicted by Condition and Predictors of Outcome

Intervention	Mediator	Outcome	Indirect effect: Beta (95% CI)
Reduction vs. Usual care	Decrease in CPD	QA	0.33 (0.14 to 0.61)
Reduction vs. Usual care	Decrease in CPD	PPA	0.32 (0.10 to 0.70)
Reduction vs. Usual care	Decrease in pros of smoking	PPA	0.06 (–0.01 to 0.17)
Reduction vs. Usual care	Increase in self-efficacy	QA	0.17 (0.06 to 0.33)
Reduction vs. Usual care	Increase in intention to quit	QA	0.26 (0.09 to 0.47)
Reduction vs. Usual care	Increase in intention to quit	PPA	0.24 (0.06 to 0.54)

CI = Confidence interval estimated with bias-corrected bootstrap analysis (10 000 resamples); CPD = Cigarettes per day; NDSS = Nicotine dependence syndrome scale; PPA = 7-day point-prevalence abstinence; QA = Quit attempt lasting ≥ 24 h.

increase in intention to quit, each of which increased the odds of PPA at 6 months. Change in the pros of smoking did not mediate the reduction intervention's effect on PPA in comparison to usual care.

Discussion

Motivational Intervention

The motivational intervention's lack of a significant effect on quitting appears to be due, in part, to its failure to influence the hypothesized mediators. Though five of the six hypothesized mediators predicted QAs or PPA, the motivational intervention did not affect any of these constructs in comparison to usual care. However, in our initial trial, the motivational intervention also did not significantly affect the hypothesized mediators (ie, CPD, self-efficacy, and intention to quit) during treatment but still significantly increased QAs (51% vs. 16%) and PPA (23% vs. 4%) compared to no treatment at 6 months.[4] Another explanation for the lack of a significant effect in our recent trial[8] could be that our use of an active (usual care) instead of no treatment comparison condition resulted in an elevated incidence of QAs and PPA that was similar to the motivational intervention.

Reduction Intervention

The reduction intervention reduced CPD and increased self-efficacy and intention to quit more than usual care and these mediators influenced QAs or PPA. Despite this, the reduction intervention did not have a total effect on QAs or PPA.[8] This could be because (1) participants interpreted that reducing CPD, and not quitting, was the goal of the intervention or (2) the intervention had an effect on the mediators that, in comparison to usual care, was not large enough to achieve a total effect (ie, clinically insignificant).

Although the reduction intervention had a greater effect on the mediators than usual care, changes in the mediators in the usual care condition had a greater impact on quitting than changes in the reduction condition. This could have occurred because, even though the reduction intervention ended with advice to quit, participants interpreted the reduction intervention as permission for a goal other than quitting (ie, reducing CPD). Thus, even though participants in the reduction condition had increased self-efficacy, they may not have applied this to a cessation goal. Further, increases in intention to quit may have been more strongly related to QAs in usual care because quitting was the only goal that was proposed in that intervention. Thus changes in CPD, self-efficacy, and intention to quit could be more strongly related to quitting in the usual care than reduction conditions due to differences in the perceived goals of the interventions. Unfortunately, we have no data on how participants perceived the goals of the reduction and usual care interventions.

The reduction intervention in our recent trial did not include NRT and, although statistically significant, had relatively small effects on the mediators in comparison to usual care. In contrast, the reduction intervention in our initial trial included NRT to aid reduction and compared this to no treatment rather than usual care.[4] Differences between reduction and no treatment conditions in that trial were greater for QAs (43% vs. 16%), PPA (18% vs. 4%), reductions in CPD (30% vs. 9%) and increases in self-efficacy (20% vs. 5%) and intentions to quit (77% vs. 12%) than differences between reduction and usual care conditions in our recent trial.[8] Reduction in CPD and increases in self-efficacy and intentions to quit also predicted quitting in our initial trial.[4] Thus, another possible explanation is that counseling without NRT and the use of a usual care comparison condition in our recent trial[8] resulted in changes in CPD, self-efficacy, and intention to quit in the reduction condition that were not large enough to substantially affect QAs or PPA more than the usual care condition.

Hypothesized Mediators' Effect on QAs and Abstinence

Our findings that the hypothesized mediators' directly influenced quitting are important. In previous trials it was unclear whether the effectiveness of reduction interventions[2] was due to reducing CPD, to NRT use, or both.[6,7] Our findings suggest that, though participants self-selected the amount they reduced, reducing CPD per se was associated with increased QAs and PPA. Further, this study replicates prior findings that decreased dependence and pros of smoking and increased self-efficacy and intention to quit are associated with increased QAs or PPA.[4,18,27–29]

Assets and Limitations

One asset of this study was that it was a longitudinal trial that utilized a large national sample of smokers. We successfully recruited participants who had no intention to quit smoking in the next month. Further, we examined mediators to understand better our failure to replicate previous findings and identify constructs that predict quitting among smokers who are not ready to quit.

There were multiple differences between our initial and recent tests of motivational and reduction interventions (eg, use of NRT and comparison condition); thus our ability to determine why we failed to replicate is limited. We limited our analyses to six hypothesized mediators, but other factors could explain our failure to replicate (eg, differences in participants' perception of the interventions' goal and suppression of withdrawal symptoms, etc.) Further, our initial trial randomized treatment but not the hypothesized mediators. Thus, we cannot ensure that the mediators are free of systematic relationships to unobserved variables.[30] Greater than 10 years separate our initial and recent trials of motivational and reduction interventions; thus, differences in findings could also be due to changes in the characteristics of smokers or tobacco regulation. Finally, as is common for studies with minimal contact,[31] we had a substantial amount of missing data.

Conclusion

We found changes in CPD, dependence, pros of smoking, self-efficacy, and intention to quit were strong predictors of making a QA or PPA. However, our motivational and reduction interventions did not have large effects on these constructs in comparison to usual care. Future research should focus on developing stronger interventions to produce clinically meaningful change in these constructs as well as test other constructs that may contribute to increasing quitting in smokers who are not ready to quit.

Supplementary Material

Supplementary data are available at *Nicotine & Tobacco Research* online.

Funding

This work was supported by research grant NCI CA163176 from the National Cancer Institute (JH) and training grant T32 DA007242 from the National Institute on Drug Abuse (EK).

Declaration of Interests

EMK, PWC, and LJS have nothing to disclose. JRH has received consulting and speaking fees from several companies that develop or market pharmacological and behavioral treatments for smoking cessation or harm reduction and from several non-profit organizations that promote tobacco control. He also consults (without payment) for Swedish Match.

Acknowledgments

We thank Tonya Ferraro, Amy Huckins-Noss, Jennifer Kerns, Erin Kretzer, and Janine Zimnie for their assistance. Clinical Trial Registration: www.clinicaltrials.gov NCT01866722.

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