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Toward Precision Smoking Cessation Treatment II: Proximal Effects of Smoking Cessation Intervention Components on Putative Mechanisms of Action

Megan E. Piper^{1,2}, Jessica W. Cook^{1,2,3}, Tanya R. Schlam^{1,2}, Stevens S. Smith^{1,2}, Daniel M. Bolt⁴, Linda M. Collins⁵, Robin Mermelstein⁶, Michael C. Fiore^{1,2}, and Timothy B. Baker^{1,2}

¹Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health

²University of Wisconsin School of Medicine and Public Health, Department of Medicine, Division of General Internal Medicine

³William S. Middleton Memorial Veterans Hospital

⁴University of Wisconsin, Department of Educational Psychology

⁵The Methodology Center and Department of Human Development and Family Studies, The Pennsylvania State University

⁶University of Illinois at Chicago, Institute for Health Research and Policy

Abstract

Background—Understanding how smoking cessation treatments exert their effects can inform treatment development and use. Factorial designs allow researchers to examine whether multiple intervention components affect hypothesized change mechanisms, and whether the affected mechanisms are related to cessation.

Methods—This is a secondary data analysis of smokers recruited during primary care visits (N=637, 55% women, 87% white) who were motivated to quit. Participants in this fractional factorial experiment were randomized to one level of each of six intervention factors: Prequit Nicotine Patch vs None, Prequit Nicotine Gum vs None, Preparation Counseling vs None, Intensive In-Person Counseling vs Minimal, Intensive Phone Counseling vs Minimal, and 16 vs 8 Weeks of Combination Nicotine Replacement (nicotine patch+nicotine gum). Data on putative

Corresponding author: Megan E. Piper, Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health, 1930 Monroe St., Suite 200, Madison, WI 53711, mep@ctri.wisc.edu.

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mechanisms (e.g., medication use, withdrawal, self-efficacy) and smoking status were gathered using daily assessments and during follow-up assessment calls.

Results—Some intervention components influenced hypothesized mechanisms. Prequit Gum and Patch each reduced prequit smoking and enhanced prequit coping and self-efficacy. In-Person Counseling increased prequit motivation to quit, postquit self-efficacy, and postquit perceived intratreatment support. Withdrawal reduction and reduced prequit smoking produced the strongest effects on cessation. The significant effect of combining Prequit Gum and In-Person Counseling on 26-week abstinence was mediated by increased prequit self-efficacy.

Conclusions—This factorial experiment identified which putative treatment mechanisms were influenced by discrete intervention components and which mechanisms influenced cessation. Such information supports the combined use of prequit nicotine gum and intensive in-person counseling as cessation interventions that operate via increased prequit self-efficacy.

Keywords

Smoking cessation; treatment; mechanisms; factorial design

1. INTRODUCTION

In the United States, cigarette smoking kills almost half a million people each year, making it the leading preventable cause of death and disease (U.S. Department of Health and Human Services, 2014). While evidence-based treatments can more than double a smoker's chances of quitting (Fiore et al., 2008; West et al., 2015), we know relatively little about how these treatments work. A clearer understanding of how treatments work should enhance both treatment development and use.

Mediation analyses have been used to identify mechanisms involved in both pharmacotherapy and counseling effects. Pharmacotherapies appear to enhance long-term abstinence primarily by suppressing withdrawal symptoms, especially craving (e.g., Bolt et al., 2012; Ferguson et al., 2006; Lerman et al., 2002), but other mechanisms may also be implicated (McCarthy et al., 2008; Piper et al., 2008). Research on counseling treatment has fairly consistently supported self-efficacy as a mediator of counseling effects (Graham et al., 2015; Hendricks et al., 2010; McCarthy et al., 2010; Schuck et al., 2014). However, only isolated findings support the roles of other putative mediators: decreased expectations of smoking reward (Schuck et al., 2014), greater avoidance of smoking cues (McCarthy et al., 2010; McCarthy et al., 2008; Schuck et al., 2014), increased perceived partner support (Graham et al., 2015), and reduced guilt and demoralization following repeated lapses (McCarthy et al., 2010). This inconsistency may be due to variation in counseling interventions in these studies (e.g., lengths and types of treatment, control conditions, routes of counseling delivery).

The slow progress in this research area may be due, in part, to the use of randomized controlled trial (RCT) designs. Such designs typically compare an “active” treatment comprising multiple intervention components (e.g., pharmacotherapy, a website, and counseling) with a control condition comprising a smaller subset of components (e.g.,

pharmacotherapy and a website). This approach has limitations. First, if the active treatment differs from the control treatment (on either the outcome or on a putative mechanism), it is unclear if the effect is due to the main effect of the added component(s) itself, or instead due to the component's interactions with any of the other components. This is a concern since interactions amongst intervention components may be common (Baker et al., 2016). Further, RCTs reveal the effect of a component as it is used with a specific combination of other components; such designs do not reveal whether the observed effects would occur when used with various mixes of other adjuvants. Conversely, factorial designs allow researchers to efficiently explore the mechanisms of multiple, relatively discrete, intervention components. They also permit evaluation of both main and interaction effects, revealing whether mediation differs as function of adjuvant treatment.

Mediation analyses address two key questions regarding how treatments work (Kenny et al., 1998; MacKinnon et al., 2002; McCarthy et al., 2007). First, the *treatment or action model* focuses on whether the treatment affects a mechanism that is hypothesized to produce the desired clinical or public health outcome (see Figure 1). Second, the *conceptual or outcome model* focuses on whether the proposed mechanisms actually influence the desired clinical outcome (e.g., abstinence). Evaluating both models may be informative whether or not significant treatment effects are found (McCarthy et al., 2007). For instance, a failure of the treatment model suggests that the treatment was inadequate; it failed to activate its targeted mechanisms. A failure of the outcome model suggests that the model of change was inadequate; the treatment may have affected the targeted mechanisms, but these did not influence the clinically significant outcomes. The former suggests a need to strengthen the treatment, the latter suggests a need to target different mechanisms.

The analyses reported in the current paper were obtained in a factorial experiment that yielded no significant main effects on abstinence; however, three 2-way interactions were found (Piper et al., 2016). This paper therefore, examined potential mediators for these interaction effects. It also examined the treatment and outcome models for the nonsignificant main effects since it is important to determine if an intervention activates targeted mechanisms and whether the targeted mechanisms influence abstinence (Piper et al., 2016).

The intervention components in this factorial experiment were selected based on evidence that they would be effective for the phase of the smoking treatment in which they were to be used (Baker et al., 2011; Collins et al., 2016; Piper et al., 2016). Three Preparation-phase interventions were designed to prepare smokers for quitting: 3 weeks of prequit nicotine gum (Prequit Gum), 3 weeks of prequit nicotine patch (Prequit Patch), and prequit counseling (Preparation Counseling: 3 sessions designed to help smokers make 2 practice quit attempts, reduce their smoking, and develop coping skills prior to quitting). Prequit Patch and Prequit Gum were intended to: 1) reduce smoking prior to quitting (Hawk et al., 2015; Stead and Lancaster, 2007), 2) increase postquit medication adherence, and 3) reduce withdrawal prequit and postquit. Preparation Counseling was hypothesized to: 1) increase the use of coping skills (Fiore et al., 2008; Shiffman, 1984); 2) increase cessation motivation and self-efficacy (Williams et al., 2006); 3) increase intratreatment social support (Fiore et al., 2008); 4) reduce tobacco dependence via decreased smoking for 2 weeks prior to quitting (Cinciripini et al., 1997; Hughes and Carpenter, 2006); and 5) reduce exposure to

smoking cues through altering life contexts and behaviors (Abrams et al., 1988; Juliano and Brandon, 1998). The two Cessation-phase interventions were designed to help smokers cope with challenges typically encountered early in the postquit period: e.g., negative affect, craving (Baker et al., 2004; McCarthy et al., 2006) and lapses (Kenford et al., 1994). The Cessation-phase In-Person and Phone Counseling both comprised treatment elements identified as effective by the 2008 PHS Guideline: skill training designed to increase avoidance of smoking triggers and execution of coping responses, and intra-treatment support designed to increase perceived intra-treatment social support (Fiore et al., 2008).

In sum, this research used a factorial experiment to determine whether: 1) distinct, individual Preparation and Cessation-phase intervention components produced hypothesized proximal effects (treatment model); 2) the hypothesized proximal effects influenced long-term abstinence (outcome model); and 3) the significant effects of specific combinations of intervention components on long-term abstinence were mediated by hypothesized proximal effects.

2. METHODS

2.1 Procedure

This is a secondary data analysis of a fractional factorial screening experiment that assessed the efficacies of six smoking cessation intervention components (Piper et al., 2016). Participants (N=637; 55% women, 87% white) were recruited from primary care clinics during regular visits. Eligible patients (18 years old; 5 cigarettes/day for the previous 6 months; motivated to quit; not currently taking bupropion or varenicline; no medical contraindications to nicotine replacement therapy (NRT); and, for women of childbearing potential, agreeing to use an approved method of birth control during treatment) provided written informed consent and completed initial assessments. Participants received interventions at their primary care clinic; a database guided delivery of the interventions by bachelor's level case managers supervised by licensed clinical psychologists.

This study used a balanced fractional factorial design with six factors: 1) Prequit Nicotine Patch vs. None; 2) Prequit Nicotine Gum vs. None; 3) Preparation Counseling vs. None; 4) Intensive In-Person Counseling vs. Minimal; 5) Intensive Phone Counseling vs. Minimal; and 6) 16 vs. 8 Weeks of Combination NRT. Each participant was assigned to one of two levels of each of the six factors. This Resolution VI design reduces the number of conditions needed from 64 to 32 but allows for the estimation of only main effects and two-way interactions (Collins et al., 2016; Piper et al., 2016).

2.2 Intervention Components

2.2.1 Prequit Nicotine Patch—Active condition: 14-mg patches for 3 weeks prior to the target quit day (TQD). Inactive condition: no prequit patches.

2.2.2 Prequit Nicotine Gum—Active condition: 2-mg nicotine gum for 3 weeks prior to the TQD (1 piece/1–2 hours). Inactive condition: no prequit gum. Participants who received both Prequit Patch and Gum were told to use at least 5 pieces/day, unless such use produced adverse effects.

2.2.3 Preparation Counseling—Active condition: three 20-minute counseling sessions prior to the TQD (Weeks –3 and –1 in-person; Week –2 via phone). Counseling focused on smoking reduction, withdrawal coping, environmental restrictions on smoking, intra-treatment social support, autonomous motivation and included two 8-hour practice quit attempts. Inactive condition: no Preparation Counseling.

2.2.4 In-Person Counseling—Intensive condition: three 20-minute face-to-face counseling sessions (Week –1, TQD, and Week 1) focused on intra-treatment social support and skill-building. Minimal condition: one 3-minute in-person session at Week –1.

2.2.5 Phone Counseling—Intensive condition: three 15-minute phone sessions (TQD, Days 2 and 10) that emphasized intra-treatment social support, skill execution, and avoidance of danger situations. Minimal condition: one 10-minute session on the TQD.

2.2.6 Extended Medication—All participants received combination NRT (nicotine patch + nicotine gum) starting on their TQD. Standard duration: 8 weeks of patches and gum. Extended duration: 16 weeks of patches and gum. Participants were advised to use one piece of gum every 1–2 hours until 2 weeks before treatment termination (Fiore et al., 2008), and *at least* 5 pieces/day unless adverse effects occurred.

2.3 Assessments

Participants completed baseline assessments of demographics, smoking history, and tobacco dependence (Fagerström Test of Nicotine Dependence; FTND; Heatherton et al., 1991), and completed daily assessments via automated calls prior to going to bed every other day for 3 weeks prequit, on the target quit day (TQD), and every other day for 2 weeks postquit (19 total). The daily assessments included questions about withdrawal symptoms (items from the Wisconsin Smoking Withdrawal Scale that assessed negative affect, concentration, hunger, and urges to smoke; Welsch et al., 1999), positive and negative affect (items from the Positive and Negative Affect Scale; Watson et al., 1988), stressors, coping techniques, smoking in the past 24 hours, being around other smokers, medication use, confidence in counseling, importance of quitting (motivation), and quitting self-efficacy over the day. Intra-treatment social support was assessed with a modified version of the Important Other Climate Questionnaire-Smoking version (Williams et al., 2006) on the TQD and at Weeks 4 and 8. See Figure 2 for a timeline of interventions and daily assessments. At Weeks 8, 16, and 26 post-quit, participants reported their smoking since last contact and in the last 7 days, using the timeline follow-back method (Robinson et al., 2014). These data were used to establish self-reported 7-day point-prevalence abstinence at 26 weeks post-TQD.

2.4 Analytic Plan

General linear regression models (IBM Corporation, 2013) with the 6 main effects and 15 2-way interactions using effect coding (levels are coded –1 and +1 (Baker et al., 2016) were used to analyze each of the following hypothesized mechanisms: 1) prequit smoking rate; 2) postquit medication use; 3) withdrawal prequit and 2 weeks postquit; 4) use of coping skills; 5) exposure to smoking temptation and cues; 6) motivation; 7) self-efficacy; and 8) intra-treatment social support. The first 7 putative mechanisms were analyzed using the mean

prequit and postquit daily assessment values as the outcomes. Intra-treatment social support was analyzed as the mean of the three assessments (TQD, Weeks 4 and 8). To examine the impact of smoking on withdrawal measures during the first 2 weeks postquit mean number of postquit cigarettes smoked per day (CPD) were included as a covariate for all daily assessment analyses.

Tests of treatment effects on putative mechanisms (i.e., the treatment model) included all main effects and two-way interactions so that the influence of all factors could be controlled in statistical tests. Two-way interactions were evaluated only if there were significant main effects for one or more of the contributing factors. Significant interaction effects were graphed with 95% confidence intervals for interpretation. It should be noted that non-overlapping 95% confidence intervals represent a very conservative test (i.e., $p < .006$); 95% confidence intervals that overlap by up to 25% are still statistically significant (Cumming and Finch, 2005). Results are presented using a standard $p < .05$ alpha for each effect as well as using a more stringent Benjamini-Hochberg p-value (for the 21 effects in each hypothesis test) to control the false discovery rate. Unless otherwise noted, effects reported were significant with the Benjamini-Hochberg correction.

Tests of the ability of the putative mechanisms to predict 26-week self-reported abstinence (outcome model) were conducted using logistic regression and evaluated using overall $\alpha = .05$ and the Benjamini-Hochberg p-value for the 21 putative mechanisms tested. Finally, exploratory mediation analyses were conducted using the SPSS Process macro (Hayes, 2013) for pairs of components whose 2-way interactions significantly predicted both a putative mediator (treatment model) and abstinence at 26-weeks post-quit (the three 2-way interactions that predicted significant effects on 26-week abstinence were: Prequit Patch x In-Person Counseling, Prequit Gum x In-Person Counseling, and In-Person Counseling x Phone Counseling).

3. RESULTS

Participants ($N=637$; 55% women; 87% white, 8% African-American; 4% Hispanic) averaged 45.8 ($SD=12.0$) years of age and smoked 17.7 ($SD=8.2$) cigarettes/day. Participants completed a mean of 11.3 ($SD=6.3$) out of 19 daily assessment calls; more than half of participants completed at least 12 calls. The mean cigarettes/day during the first 2 weeks postquit was 2.2 ($SD=4.0$; range of 0–34.3); 43% reported 0 cigarettes/day during the first 2 weeks postquit. Table 1 reports the descriptive statistics for each putative mechanism.

3.1 Treatment Models

Table 2 and Figure 3 present the significant effects of interventions on putative mechanisms.

3.1.1 Prequit smoking—We hypothesized that Prequit Gum, Prequit Patch, and Preparation Counseling would each reduce prequit smoking. Regression results showed that prequit smoking was reduced by Prequit Patch (Patch=8.37 vs No Patch=10.43 cigarettes/day) and Prequit Gum (Gum=8.76 vs No Gum=10.08 cigs/day); but not by Preparation Counseling. There was a significant Prequit Gum x Preparation Counseling interaction (not

significant with the Benjamini-Hochberg correction), with Prequit Gum and Preparation Counseling together producing relatively large prequit smoking reduction (see Figure 4a).

3.1.2 Postquit medication use—We hypothesized that each intervention component would increase medication adherence. However, only Prequit Gum increased postquit gum use (Prequit Gum=4.31 vs No Prequit Gum=3.47 postquit pieces of gum/day); there were no 2-way interactions with Prequit Gum with regard to medication use. Results were similar when we adjusted for postquit smoking. There were no main effects on postquit patch use.

3.1.3 Prequit and short-term postquit withdrawal—All three Preparation intervention components were hypothesized to reduce prequit withdrawal symptoms (i.e., craving, negative affect) and all components except Extended Medication were hypothesized to reduce withdrawal early in the postquit period. There were no significant main effects on prequit or postquit withdrawal.

3.1.4 Prequit and postquit use of coping skills—Daily assessments asked participants to recall the most stressful event of the day and report whether they used any of the following techniques to cope with smoking urges or stress: thoughts and behaviors (combined due to their high intercorrelation, $r=.80$), talking, nicotine gum, or nothing. Use of thoughts/behaviors and gum were the most common coping responses prequit and postquit. It was hypothesized that the counseling interventions would increase coping.

3.1.4.1 Prequit coping: Preparation Counseling was not related to execution of any prequit coping responses. Prequit Patch increased reports of talking to cope (not significant with the Benjamini-Hochberg correction) and using thoughts/behaviors to cope (see Table 2). Prequit Gum increased coping using thoughts/behaviors (not significant with the Benjamini-Hochberg correction), talking, and gum, and was inversely related to doing nothing to cope.

3.1.4.2 Postquit coping: Prequit Gum increased talking to cope and contributed to a Prequit Gum x In-Person Counseling interaction for talking to cope (not significant with the Benjamini-Hochberg correction). Participants who received both Prequit Gum and Intensive In-Person Counseling were more likely to report talking to others to cope postquit (see Figure 4b). These effects were similar after adjusting for postquit smoking.

3.1.5 Exposure to smoking temptation and cues—There were no significant main effects or interaction effects to support the hypothesis that Preparation or Cessation phase interventions would decrease the amount of time participants spent with other smokers or spent in places where smoking was permitted.

3.1.6 Motivation—Preparation and Cessation phase interventions were hypothesized to increase motivation to quit. In-Person Counseling increased prequit motivation (not significant using the Benjamini-Hochberg cut-off); one In-Person Counseling session occurred one week prior to the target quit day and thus had the potential to affect prequit motivation. There was also a significant Preparation Counseling x In-Person Counseling interaction effect on prequit motivation. In-Person Counseling improved motivation in the

prequit period, and this was especially true if the participant also received Preparation Counseling (see Figure 4c). There were no significant main effects on postquit motivation.

3.1.7 Self-efficacy—We hypothesized that all intervention components would increase self-efficacy. Prequit Patch and Prequit Gum each increased prequit self-efficacy. There was also a Prequit Gum x In-Person Counseling interaction (not significant with the Benjamini-Hochberg correction). Participants who received both Prequit Gum and Intensive In-Person Counseling had especially high prequit self-efficacy (Figure 4d). In-Person Counseling increased postquit self-efficacy. However, this effect was no longer significant after adjusting for postquit smoking.

3.1.8 Intra-treatment social support—All counseling intervention components were hypothesized to increase perceived intra-treatment social support (assessed at the TQD and at Weeks 4 and 8). The regression analyses revealed main effects of Preparation Counseling and In-Person Counseling but not Phone Counseling.

3.2 Outcome Models

Of the 21 putative mechanisms examined, 10 were related to point-prevalent abstinence at 26 weeks post-quit (see Table 3). Participants were less likely to be abstinent if they reported being around other smokers frequently postquit (not significant with the Benjamini-Hochberg correction), or if they reported higher: numbers of cigarettes per day in the 3 weeks before quitting, prequit craving, postquit craving, prequit negative affect, or postquit negative affect. Conversely, participants were more likely to be abstinent if they reported higher levels of: using thoughts and behaviors to cope with stress and urges either prequit or postquit, prequit self-efficacy, or intra-treatment social support (none of these findings was significant with the Benjamini-Hochberg correction). None of the following was significantly related to 26-week abstinence: postquit gum or patch use; talking to cope, using nicotine gum, doing nothing to cope with stress and urges prequit or postquit; being in places where there was smoking postquit; prequit or postquit motivation; and postquit self-efficacy.

3.3 Mediation Analysis

One potential mediator was significantly related to both treatment (Prequit Gum x In-Person Counseling combination) and cessation outcome: prequit self-efficacy. We conducted a formal mediation analysis with treatment coded as receiving both Prequit Gum and Intensive In-Person Counseling (coded as 1) vs. the other 3 combinations (neither Prequit Gum nor Intensive In-Person Counseling, or receiving one but not the other; coded as 0). Unlike the effect coding used in the omnibus tests of effect of treatment on putative mediators, this coding allowed us to examine the treatment combination that appeared to be exerting the strongest effect on the mediator (see Figure 4d). Figure 5 depicts the full exploratory mediation model. The direct effect of treatment on 26-week abstinence was statistically significant ($b=.41$, $p=.03$); however, once the indirect effect of prequit self-efficacy was included in the model, the direct EFFECT WAS NO LONGER SIGNIFICANT ($B=.29$, $P=.15$), SUGGESTING MEDIATION.

4. DISCUSSION

This factorial experiment revealed that some intervention components significantly affected multiple, targeted mechanisms through both main and interaction effects. For instance, Prequit Gum reduced prequit smoking, enhanced prequit and postquit coping and prequit self-efficacy, and increased postquit nicotine gum use by <1 piece per day. In-Person Counseling increased prequit motivation to quit, postquit self-efficacy, and postquit perceived intra-treatment support. In addition, Prequit Gum and Cessation-phase In-Person Counseling interacted synergistically to increase prequit self-efficacy and postquit coping. In-Person Counseling also interacted synergistically with Preparation Counseling to improve prequit motivation. Prequit Patch performed less well than Prequit Gum. Like Prequit Gum, Prequit Patch increased prequit coping and prequit self-efficacy and reduced prequit smoking. However, unlike Prequit Gum, Prequit Patch did not contribute to interactions nor did it produce main effects on postquit coping or postquit medication use.

Many of the putative mechanisms were associated with long-term abstinence, including craving, negative affect, and amount of time spent around smokers after the quit day, consistent with prior research (Baker et al., 2004; Cofta-Woerpel et al., 2011; Piper et al., 2011; Toll, et al., 2007). However, these specific mechanisms were not influenced by the interventions manipulated in this experiment. This may be because all smokers received at least 8 weeks of combination NRT which has been shown to suppress withdrawal (Bolt et al., 2012). Interestingly, receiving prequit medication did reduce the number of cigarettes smoked in the prequit period, which was related to higher abstinence rates; however, there were no direct effects of prequit medication on cessation outcome. Prior research has found that prequit smoking reduction does not necessarily facilitate cessation (Lindson-Hawley et al., 2016; Lindson and Aveyard, 2011). Therefore, it is important to explore this mechanism more thoroughly, especially in light of the increased use of non-combustible tobacco products in smoking reduction as a pathway towards complete cessation (Malas et al., 2016).

The combination of Prequit Gum and Intensive In-Person Counseling produced especially high abstinence rates at 26 weeks and this effect was mediated by higher prequit self-efficacy ratings. It may be that the support provided by more intense counseling, and the prequit practice with prn medication, increases smokers' confidence in their ability to quit. The mediation analysis suggests that this confidence translates into long-term cessation success. It may be that prequit self-efficacy is especially meaningful in this research (cf. Baker and Cannon, 1988; Gwaltney et al., 2009) because level of prequit intervention was experimentally manipulated and was intended to prepare smokers for the upcoming quit attempt. Further, prequit self-efficacy may permit stronger inferences than does postquit self-efficacy since the latter likely is influenced by the success of the quit attempt (in part, reflecting success vs. causing it). This result is intriguing but should be viewed with some caution as it represents one of many effects tested; it certainly might be fortuitous.

Although some intervention components yielded relatively promising effects on putative mediators, many of these did not produce significant mediation. Indeed, some central, hypothesized mediational effects were not found. Thus, the skill training that was part of both Intensive In-Person and Phone Counseling produced neither coping skill increases, nor

avoidance of smoking contexts, that led to higher long-term abstinence rates. Similarly, the use of prequit NRT did not lead to reduced withdrawal severity, (craving or negative affect) or reduced smoking, that mediated long-term outcomes. In fact, the only significant mediational model involved a nonspecific mediator (self-efficacy) that does not support any particular theoretical model of treatment. Thus, the current results join prior findings (McCarthy et al., 2010) in raising questions about the effectiveness of some of our commonly used interventions and the theoretical models upon which they are based. They suggest the need for using more intense interventions, different types of intervention, or at the least, finding optimal combinations of interventions.

Limitations of this work include the conduct of multiple statistical analyses, which likely increased Type 1 error. We controlled for false discovery rate using the Benjamini-Hochberg procedure, but these results require replication. Also, changes in the intervention components or research setting would likely affect the pattern of findings. For instance, changing the base pharmacotherapy (e.g., to NRT monotherapy), might affect the pattern of main and interactive effects. Finally, further research is needed to examine whether treatment adherence, or other variables, might moderate the treatment or outcome models.

In sum, the tested Preparation and Cessation phase intervention components decreased prequit smoking rates (Prequit Patch and Gum), increased postquit use of nicotine gum (Prequit Gum), increased active postquit coping (Prequit Gum especially when combined with In-Person Counseling), increased intra-treatment social support (Preparation and In-Person Counseling), and increased prequit motivation to quit (In-Person Counseling especially when combined with Preparation Counseling). However, in many cases, putative mechanisms did not link treatment to long-term outcomes in a significant manner (i.e., they did not produce significant mediation). Nevertheless, these findings might guide the development and selection of intervention components allowing for the selection of interventions that yield complementary effects on mechanisms. In addition, these findings may enhance our understanding of reasons that smoking treatments do or do not work. This research also underscores the importance of conducting factorial experiments, which permit the examination of both the main and interactive effects of relatively discrete interventions.

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Highlights

- This factorial design study examined the effects of five different intervention components and component combinations on hypothesized mechanisms, the effects of the hypothesized mechanisms on long-term cessation success, and mediation.
- Use of prequit nicotine gum or prequit nicotine patch reduced prequit smoking and enhanced prequit smoking and self-efficacy; prequit gum also increase postquit gum use.
- The combination of prequit gum and in-person counseling produced enhanced long-term cessation rates via an increase in prequit self-efficacy.

Figure 1.
The mediation model.

Figure 2.
Timing of phases, interventions, and ecological momentary assessments.

Figure 3.

Summary of the significant main and interaction effects of Preparation and Cessation phase intervention components on putative mechanisms. The straight lines indicate that the effects were significant after controlling for postquit smoking; the dashed lines indicate an effect that was no longer significant after controlling for postquit smoking. See Figure 4 for the nature of the interaction effects.

Figure 4.

The graphic depiction of the significant interaction effects on putative mechanisms.

- The Preparation Counseling x Prequit Gum interaction predicting prequit cigarettes smoked per day. This figure depicts the mean number of cigarettes smoked per day for each treatment group and the 95% confidence intervals.
- The In-Person Cessation Counseling x Prequit Gum interaction predicting postquit talking with others to cope. This figure depicts the mean postquit reports of talking with others to cope with stress and urges for each treatment group and the 95% confidence intervals.
- The Preparation Counseling x In-Person Counseling interaction predicting prequit motivation. This figure depicts the mean prequit motivation scores and the 95% confidence intervals.
- The Prequit Gum x In-Person Counseling interaction predicting prequit self-efficacy. This figure depicts the mean prequit self-efficacy scores and the 95% confidence intervals.

Figure 5.

Mean prequit self-efficacy mediates the effect of receiving both Prequit Gum and Intensive In-Person Counseling, relative to receiving either one without the other or neither of these interventions, on 26-week self-reported abstinence. A = the path between treatment and the mediator; B = the path from the mediator to the outcome; C = the direct effect of treatment on outcome, without taking into account the indirect effect; C' = the direct effect of treatment on outcome when the indirect effect is included in the model.

Table 1

Descriptive statistics for the putative mechanisms

	Mean	Standard Deviation	Range
Prequit number of cigarettes smoked per day	9.37	5.82	0–42
Postquit number of pieces of nicotine gum used per day	3.91	3.32	0–21
Postquit proportion of days of nicotine patch use	0.82	0.31	0–1
Prequit negative affect score	3.90	1.71	1–9
Postquit negative affect score	4.12	2.06	1–9
Prequit craving score	4.96	1.75	1–9
Postquit craving score	5.05	2.09	1–9
Prequit proportion of days reported use of skills to cope with stress or urges:			
Distracting or helpful thoughts or behaviors	0.61	0.32	0–1
Talk to someone	0.38	0.34	0–1
Use nicotine gum	0.42	0.42	0–1
Did nothing	0.36	0.34	0–1
Postquit proportion of days reported use of skills to cope with stress or urges:			
Distracting or helpful thoughts or behaviors	0.67	0.38	0–1
Talk to someone	0.46	0.39	0–1
Use nicotine gum	0.72	0.38	0–1
Did nothing	0.27	0.36	0–1
Postquit around smokers score	2.02	0.93	0–4
Postquit time spent in places where you could smoke score	3.21	0.85	0–4
Prequit motivation score	7.61	1.78	1–9
Postquit motivation score	8.06	1.74	1–9
Prequit self-efficacy score	6.76	1.90	1–9
Postquit self-efficacy score	7.56	1.86	1–9
Intra-treatment social support score	6.00	1.38	1–7

Table 2

Statistically significant effects of interventions on putative mechanisms

Putative Mechanisms	Intervention	B	p-value
Prequit number of cigarettes smoked per day *	Prequit Patch	-1.06	<.001
	Prequit Gum	-.69	.004
	Prequit Gum x Prequit Counsel	-.54	.025 [†]
Postquit number of pieces of gum used per day	Prequit Gum	.40	.01
Prequit percentage of days reported use of skills to cope with stress or urges:			
Distracting or helpful thoughts or behaviors *	Prequit Patch	.04	.003
	Prequit Gum	.03	.03 [†]
Talk to someone	Prequit Patch	.03	.02 [†]
	Prequit Gum	.04	.003
Use nicotine gum	Prequit Gum	.32	<.001
Did nothing	Prequit Gum	-.06	<.001
Postquit percentage of days reported use of skills to cope with stress or urges:			
Talk to someone	Prequit Gum	.05	.01
	Prequit Gum x In-Person Counseling	.04	.04 [†]
Prequit motivation score	In-Person Counseling	.15	.04 [†]
	Preparation Counseling x In-Person Counseling	.18	.02
Prequit self-efficacy score *	Prequit Patch	.33	<.001
	Prequit Gum	.24	.003
	Prequit Gum x In-Person Counseling	.16	.04 [†]
Postquit self-efficacy score	In-Person Counseling	.20	.02 ^{††}
Intra-treatment social support score *	Preparation Counseling	.23	<.001
	In-Person Counseling	.11	.01

Note.

* Significantly related to 26-week abstinence.

[†] Not significant with the Benjamini-Hochberg correction.^{††} Not significant after adjusting for postquit smoking (B=.16, p=.07).

Table 3

Statistically significant outcome model logistic regression results predicting 26-week abstinence

Putative Mechanisms	B	OR	95% CI	p-value
Prequit number of cigarettes smoked per day [*]	-.07	.93	.90-.97	<.001
Prequit negative affect score	-.22	.81	.71-.91	.001
Postquit negative affect score	-.16	.85	.76-.95	.005
Prequit craving score	-.16	.86	.77-.95	.005
Postquit craving score	-.18	.83	.76-.92	<.001
Prequit percentage of days reported use of distracting or helpful thoughts or behaviors to cope with stress or urges [*]	.63	1.87	1.05-3.35	.04 [†]
Postquit percentage of days reported use of distracting or helpful thoughts or behaviors to cope with stress or urges [*]	.68	1.98	1.17-3.36	.01 [†]
Postquit around smokers score	-.25	.78	.63-.98	.03 [†]
Prequit self-efficacy score [*]	.12	1.13	1.02-1.25	.02 [†]
Intra-treatment social support score [*]	.19	1.21	1.003-1.45	.047 [†]

Note.

^{*} Significantly related to intervention effects.[†] Not significant with the Benjamini-Hochberg correction.