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Identifying Effective Intervention Components for Smoking Cessation: A Factorial Screening Experiment

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Abstract

Aims—To identify promising intervention components intended to help smokers to attain and maintain abstinence in their quit smoking attempts.

Design—A fully crossed, 6-factor randomized fractional factorial experiment.

Setting-Eleven primary care clinics in southern Wisconsin, USA.

Participants—637 adult smokers (55% women, 88% White) motivated to quit smoking who visited primary care clinics.

Interventions—Six intervention components designed to prepare smokers to quit, and achieve and maintain abstinence (i.e., for the preparation, cessation, and maintenance phases of smoking

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treatment): 1) preparation nicotine patch vs. none; 2) preparation nicotine gum vs. none; 3) preparation counseling vs. none; 4) intensive cessation in-person counseling vs. minimal; 5) intensive cessation phone counseling vs. minimal; and 6) 16 vs. 8 weeks of combination nicotine replacement therapy (nicotine patch + nicotine gum).

Measurements—7-day self-reported point-prevalence abstinence at 16 weeks.

Findings—Preparation counseling significantly improved week 16 abstinence rates (p<.05), while both forms of preparation nicotine replacement therapy interacted synergistically with intensive cessation in-person counseling (p<.05). Conversely, intensive cessation phone counseling and intensive cessation in-person counseling interacted antagonistically (P<.05)—these components produced higher abstinence rates by themselves than in combination.

Conclusions—Preparation counseling and the combination of intensive cessation in-person counseling with preparation nicotine gum or patch are promising intervention components for smoking and should be evaluated as an integrated treatment package.

Keywords

Smoking cessation; Multiphase Optimization Strategy (MOST); Phase-Based Model of smoking treatment; tobacco dependence; nicotine replacement therapy; chronic care smoking treatment; comparative effectiveness; primary care; factorial experiment

Introduction

The health, economic, and human costs of tobacco use are profound [1], and while there are effective smoking treatments, long-term abstinence rates have increased only modestly over the past two decades [2–6] and remain disappointing (15–35%; [2]). This slow progress may be due, in part, to reliance on randomized controlled trials (RCTs), to the exclusion of other experimental designs. RCTs often compare two multicomponent treatments with one another (skill training, support, relapse prevention counseling+active medication versus the same counseling interventions+placebo medication) and therefore do not reveal the effects of individual intervention components or their interactions with one another. Such information would permit treatment development on a methodologically principled basis [7, 8].

The present research, which is based on the Multiphase Optimization Strategy (MOST) [7–10], uses factorial designs to simultaneously screen multiple intervention components and identify the most promising ones based on main effects and interactions. This is one of four linked articles. One reviews the theory and methods behind this research [11]; the others report factorial experiments of intervention components for the Motivation [12] and Maintenance [13] phases of smoking treatment.

This research experimentally evaluated intervention components designed for three phases of the cessation process: Preparation, Cessation, and Maintenance [14, 15]. These phases, as described in the Phase-Based Model of smoking treatment [11, 14, 15], present distinct challenges and opportunities that can be addressed with different types of intervention components delivered at different times in the cessation process. The *Preparation* phase

prepares smokers for a quit attempt and comprises the \sim 3 weeks prior to the quit day. The goal of the *Cessation* phase is to establish abstinence and comprises the first \sim 2–4 weeks postquit, when withdrawal symptoms tend to peak and most lapses occur [16–19]. The goal of the subsequent *Maintenance* phase, lasting \sim 1–12 months, is to support abstinence and prevent relapse during a time when withdrawal typically diminishes but other risks are present—treatment nonadherence [20, 21], decreased self-efficacy (especially after lapses [22, 23]), and exacerbations of craving [24].

The intervention components tested in the current experiment were selected to address phase-specific challenges, designed for translation into real-world healthcare settings (with low staff and patient burden, and cost [25–27]), and implemented and tested in primary care clinics. For the Preparation phase, we tested Preparation Nicotine Patch, Preparation Nicotine Gum, and Preparation Counseling. Preparation nicotine replacement therapy (NRT) may prepare smokers for cessation by blunting the pharmacologic effects of smoking, allowing practice of NRT self-administration, reducing smoking, and degrading the smoking-reward contingency [28–30]. Preparation Counseling, which included practice quit attempts, may inculcate relevant skills (coping, medication use [2, 31, 32]), increase self-efficacy [33, 34], provide intratreatment social support [2, 31], reduce cue-smoking contingencies [35–37], and reduce smoking contexts and smoking rate [35, 36, 38–42].

Challenges in the Cessation phase include withdrawal [43, 44], exposure to smoking cues [45–47], and lapse occurrences [16]. In-Person Counseling and Phone Counseling were designed to: 1) promote avoidance of smoking triggers, 2) train coping responses to address withdrawal and lapsing, and 3) provide intratreatment social support to buffer withdrawal distress.

Finally, we tested 16 vs. 8 weeks of postquit combination NRT to address Maintenancephase threats such as withdrawal exacerbation [17, 24] and late lapses [5, 22, 23, 48–50]. Longer-term medication may reduce both lapse-relapse progression [51, 52] and the likelihood or severity of prolonged or recurrent withdrawal (e.g., anhedonia, craving [53]). We used combination NRT as the post-target quit date (TQD) medication for all participants based on its efficacy [2, 54], ability to suppress withdrawal [55–57], cost, and translatability into real-world healthcare settings [2].

In sum, using state-of-the-art theory and methods, this research used a factorial experiment to screen multiple intervention components that were selected to be effective for the Preparation, Cessation, and Maintenance phases of smoking treatment and that had high translation potential. We examined their main and interactive effects to identify effects on initial (2-week), end-of-treatment (16-week), and long-term (6-month) abstinence. The 16-week time point was the primary outcome because of its hypothesized sensitivity, occurring shortly after the delivery of all treatment but before encounters with relapse precipitants unrelated to treatment that could introduce error [14]. Thus, this research yields valuable comparative effectiveness data on multiple intervention components, which should help guide future treatment development (e.g., additional factorial experiments, an RCT that evaluates a multicomponent treatment).

Methods

Procedure

This experiment was conducted from June, 2010 through October, 2013. Participants were recruited from 11 primary care clinics in two health systems in southern Wisconsin. During clinic visits, clinical care staff (i.e., medical assistants) were prompted by electronic health record technology to invite identified smokers to participate in a research program to help them quit smoking [58, 59]. Interested patients were electronically referred by clinic staff and then contacted by research staff to assess their eligibility. The inclusion criteria were:

18 years old; 5 cigarettes/day for the previous 6 months; motivation to quit; ability to read, write, and speak English; no plan to move from the area for at least 12 months; not currently taking bupropion or varenicline; agreement to use only study medication for the duration of the study (e.g., discontinuing on-going NRT use); no medical contraindications to NRT use; and, for women of childbearing potential, agreement to use an approved method of birth control during treatment. Participants interested in quitting were randomly assigned to either this experiment or the cessation experiment described in [13] in this issue. It should be noted that although there were three related experiments (this experiment, [12], and [13]), each used an independent sample.

Eligible patients were invited to return to their primary care clinic to hear more about the study, provide written informed consent, and complete initial assessments. A research database then created intervention and assessment schedules, based on randomly assigned treatment conditions, which guided delivery of interventions by bachelor's level case managers supervised by licensed clinical psychologists.

Experimental Design

This experiment used a balanced fractional factorial design with six factors: 1) Preparation Nicotine Patch vs. None; 2) Preparation Nicotine Gum vs. None; 3) Preparation Counseling vs. None; 4) Intensive Cessation In-Person Counseling vs. Minimal; 5) Intensive Cessation Phone Counseling vs. Minimal; and 6) 16 vs. 8 Weeks of Combination NRT. The fractional nature of the design calls for delivery of half of the experimental component combinations that would have been delivered in a full factorial design (32 versus 64), making the research more logistically manageable. However, this design allows for the estimation of only main effects and two-way interactions (see Supplemental Materials for additional detail [60]).

Participants were randomized to treatment conditions via a database that used stratified permuted block randomization; we stratified by gender and clinic with a fixed block size of 32 based on the 32 unique treatment conditions (in random order within each block). Staff were blinded to randomization until eligibility was confirmed; participants were blinded until consent was provided.

Experimental Factors

The intervention components were designed to be consistent with the 2008 US Public Health Service Clinical Practice Guideline recommendations [2], address phase-specific cessation

challenges and opportunities, and be feasible for real-world healthcare. See Supplemental Materials for counseling protocol summaries and fidelity assessments.

Preparation-Phase Intervention Components

<u>Preparation Nicotine Patch:</u> Participants assigned to the active level (i.e., the active condition) received 14-mg patches for the 3 weeks prior to the TQD while the other half did not receive prequit patches.

<u>Preparation Nicotine Gum:</u> Participants in the active condition received 2-mg nicotine gum for the 3 weeks prior to the TQD (9/day, 1 piece/1–2 hours); the other half did not receive gum. Participants who received both Preparation Patch and Gum were told to use at least 5 pieces/day of gum, unless such use produced adverse effects.

Preparation Counseling: Participants in the active condition received 20-minute counseling sessions 1 (in-person), 2 (phone) and 3 (in-person) weeks prior to the TQD. The counseling focused on smoking reduction, withdrawal coping, environmental restrictions on smoking, intra-treatment social support, and autonomous motivation. Participants were also asked to engage in two 8-hour practice quit attempts. The other half of participants did not receive this counseling.

Cessation-Phase Intervention Components

Cessation In-Person Counseling: Participants in the intensive condition received three 20minute face-to-face counseling sessions: one week pre-TQD (Week –1), TQD, and Week 1. The counseling emphasized intra-treatment social support and skill-building [2]. Participants assigned to the minimal level received one 3-minute in-person session at Week –1 [2].

Cessation Phone Counseling: Participants in the intensive condition received three 15minute phone sessions (TQD, Days 2 and 10). These calls emphasized intra-treatment social support, skill execution, and avoidance of danger situations [61–64]. Participants assigned to the minimal condition received one 10-minute session on the TQD that provided support and addressed motivation to quit, strategies for coping with craving, and medication use. Thus, all participants received some TQD phone counseling.

Cessation and Maintenance-Phase Intervention Component

Extended Medication: All participants received Cessation- and Maintenance-phase combination NRT (nicotine patch + nicotine gum) starting on their TQD. Half were assigned to receive 8 weeks of patches (>9 cigarettes/day=4 weeks of 21-mg, 2 weeks of 14-mg, and 2 weeks of 7-mg nicotine patches; 5–9 cigarettes/day=4 weeks of 14-mg and 4 weeks of 7-mg nicotine patches) and 8 weeks of nicotine gum (smoke within 30 minutes of waking=4-mg; smoke more than 30 minutes after waking=2-mg). The other half received 16 weeks of patches (>9 cigarettes/day=21-mg for 12 weeks, 14-mg for 2 weeks, and 7-mg for 2 weeks; 5–9 cigarettes/day=14-mg for 12 weeks and 7-mg for 4 weeks) and 16 weeks of gum. Participants were advised to use one piece of gum every 1–2 hours until 2 weeks before treatment termination [2], and *at least* 5 pieces/day unless such use produced adverse

effects. Participants were instructed to decrease gum use over the final 2 weeks of medication treatment.

Combinations of Intervention Components: The intervention components were designed to be distinct but also complementary (e.g., when a participant received phone and in-person counseling, the case manager would integrate information across the two types of contacts). Even the timing was complementary, i.e., contacts were shifted slightly to prevent conflicts. Thus, intervention components were independent, but integrated when offered together, as would occur in real-world use.

Assessments

All participants had 3 study visits (Weeks -3, -1, and 4); those assigned to Intensive In-Person Cessation Counseling also had two counseling-only visits (TQD and Week 1). Participants completed baseline assessments of vital signs, exhaled carbon monoxide using the Bedfont Smokerlyzer (Bedfont Scientific, Rochester, England), demographics, smoking history, and tobacco dependence (Fagerström Test of Nicotine Dependence; FTND [65]). At subsequent study contacts (visits at Week -1 and 4 and calls at Weeks 8, 16, and 26) participants were asked about medication adverse events and about their smoking since last contact and in the last 7 days, using the validated timeline follow-back method [66]. These data were used to establish self-reported 7-day point-prevalence abstinence at 2, 16, and 26 weeks post-TQD. Medication adherence was assessed during automated calls that occurred every other evening from Week -3 to Week 2.

Outcome Measures

The primary outcome was self-reported 7-day point-prevalence abstinence (PPA) at 16 weeks, with secondary outcomes at 2 and 26 weeks, assessed by staff who were not involved in treatment, but were not blind to treatment assignment¹. These time points were selected to index sensitively the effects of intervention components that were delivered at different treatment phases [14]. The 16-week outcome was deemed to be an early, sensitive index of treatment effects, occurring shortly after treatment completion. The 2-week outcome reflects the effects of the Preparation and Cessation-phase components on early cessation, and Week 26 reflects Maintenance-phase effects, permitting comparison with other treatment research.

Analytic Plan

Initial analyses characterized the study population and examined treatment engagement and safety. We examined the likelihood of participant dropout in relation to treatment components to inform missingness analyses. Logistic regression (SPSS [67]) modeled the 6 main effects and 15 2-way interactions using effect coding (levels are coded –1 and +1 [11]), to analyze self-reported PPA at each time point. Analyses were conducted with and without adjusting for a predetermined set of demographic and tobacco dependence covariates: gender, race (White vs. non-White), age, education (up to high school/GED vs. at least some college), the Heaviness of Smoking Index [68], baseline exhaled carbon monoxide, and healthcare system (A vs. B). Reported results reflect intent-to-treat analyses

¹Based upon reviewer recommendations the designation of outcomes was altered from what was listed in trial registration materials.

assuming that missing=smoking. These analyses were supplemented with multiple imputation (MI)/sensitivity analyses (see Supplemental Materials [69]). The results of the missing=smoking and MI/sensitivity analyses were similar, therefore, we present only the results of the former.

Results

Participants

Of the smokers who were interested in quitting, 1349 were referred to this experiment, and 637 consented (see Figure 1 for the CONSORT diagram and Supplemental Materials for sample size justification). Table 1 describes the demographic and tobacco dependence characteristics of the sample. The 11 clinics recruited 23–89 participants each.

Treatment Engagement

On average, participants in the Preparation Counseling condition attended 2.50 (*SD*=.74) out of 3 counseling sessions and 69% reported making a practice quit attempt. Participants in the Intensive Cessation In-Person Counseling condition completed 2.13 (*SD*=1.13) out of 3 sessions, significantly more than those in the Intensive Cessation Phone Counseling condition (M=1.74 out of 3 sessions, *SD*=1.19, p<.01). Participants in the Preparation Patch condition used an average of 6.24 patches/week (*SD*=3.97) and those in the Preparation Gum condition used an average of 3.19 pieces of gum/day (*SD*=2.37). Participants in the 16 vs. 8 week medication duration conditions did not differ in postquit patches used/week (M=4.59, *SD*=2.87 vs. M=4.98, SD=2.77) or postquit pieces of gum/day (M=4.02, SD=3.31 vs. M=3.81, SD=3.34).

Safety

Reports of adverse events were low (e.g., 10% of those who received Preparation Patch or Gum reported vivid dreams, skin rash occurred in 8% of participants while on combination NRT post-quit) and there were no serious adverse events related to study participation or study medications.

Missing Data

Rates of missing PPA data went from 15.1% at Week 2 to 23.7% at Week 16 to 30.0% at Week 26. Missingness was significantly more likely amongst participants receiving no Preparation Patch versus those receiving Preparation Patch (28.6% vs. 19.1%; Week 16) and those receiving 16 weeks of combination NRT versus 8 weeks (33.9% vs. 26.4%; Week 26).

Cessation Outcome

Table 2 presents the self-reported 7-day PPA rates for each main effect at 2, 16, and 26 weeks postquit. Table 3 presents the logistic regression results for the 2-, 16-, and 26-week outcomes. The patterns of statistical significance were consistent between the adjusted and unadjusted models. The only significant main effect on the Week 16 primary outcome was that participants who received Preparation Counseling had higher abstinence rates.

There were five significant 2-way interactions at Week 16: Preparation Patch x Cessation Phone Counseling, Preparation Patch x Cessation In-Person Counseling, Preparation Gum x Cessation In-Person Counseling, Cessation In-Person Counseling x Cessation Phone Counseling, and Preparation Counseling x Cessation Phone Counseling. The three interactions involving Preparation NRT and Cessation-phase counseling interventions were synergistic; i.e., the combination of Preparation NRT and Cessation counseling yielded better 16-week abstinence rates than would be expected based upon summing the main effects (Figures 2a–c). As Figure 2c shows, participants who received Preparation Gum and Intensive Cessation In-Person Counseling had a higher 16-week PPA rate (42.8%), than did participants who received only one of these components (31.1% or 29.1%) or neither (36%). Similar patterns were found at Week 26; differences tended to be less pronounced at Week 2 (Figure 2c).

The Cessation In-Person Counseling x Cessation Phone Counseling interaction was antagonistic—participants receiving either of those interventions without the other had higher abstinence rates at Weeks 16 and 26 than did participants receiving both (Figure 2d). The Week 16 Preparation Counseling x Phone Counseling interaction was also antagonistic (Figure 2e). The Preparation Patch x Preparation Counseling interaction was significant only at Week 2. Participants receiving either of those components, without the other, actually had lower abstinence rates than those receiving both components or neither (Figure 2f).

Discussion

The goal of this screening experiment was to identify Preparation, Cessation, and Maintenance-phase intervention components that yield patterns of promising effects on smoking abstinence when used in a primary care setting. In keeping with MOST, after these components are identified, they would then undergo further research evaluation such as an RCT that would determine their effects when they are used together as an integrated treatment (see [11] for more detail about subsequent experiments). This research also provides important comparative effectiveness data that suggest that Preparation-phase treatment can indeed enhance abstinence rates (cf. [30]) and that combining in-person and phone counseling might constitute ineffective duplication. Finally, the results provide insight into how intervention components work together (i.e., interact).

The only significant main effect was that Preparation Counseling improved abstinence rates at Week 16. However, interaction effects revealed meaningful differences in component effectiveness depending on the levels of other components. In particular, the effects of Cessation-phase counseling were enhanced by the use of Precessation NRT (Figures 2a–c). That this pattern appeared with regard to both the patch and gum, and manifested at two time points, suggests the robustness of this relation. Thus, while prior data have yielded a mixed picture of the effectiveness of Preparation pharmacotherapy [28–30], the current results suggest that NRT pretreatment can be helpful, but its benefit depends on the nature of the cessation counseling that is provided, with intensive Cessation-phase counseling providing more benefit than minimal counseling.

Conversely, some intervention components appeared to undermine each other's effects. For instance, there was evidence that the two intensive levels of counseling used together produced lower abstinence rates than when either was used without the other (i.e., at Weeks 16 and 26, Intensive Cessation In-Person and Intensive Cessation Phone Counseling produced lower abstinence rates when used together than when used by themselves: Figure 2d). This may be due to redundancy in treatment mechanism or to participant burden—the content of the two counseling types were similar and were designed to last 15 (phone) to 20 (in-person) minutes.

Three types of intervention components yielded promising effects—Preparation NRT, Preparation Counseling, and Intensive Cessation In-Person counseling—based on patterns of effects observed across the three time points. Preparation Counseling produced a significant main effect at 16 weeks, and a significant synergistic interaction with Preparation Patch at 2 weeks (Table 3). Preparation NRT (either Patch or Gum) and Intensive Cessation In-Person Counseling interacted synergistically at both 16- and 26-weeks. Cessation In-Person Counseling appears more promising than Cessation Phone Counseling because it produced a somewhat stronger main effect at 2 weeks (although not significant: Table 3), and it uniquely participated in the synergistic interactions with Preparation NRT at Weeks 16 and 26. The data do not permit a clear-cut decision as to whether Preparation Patch or Gum would be superior. They produced similar synergistic interactions with Cessation In-Person Counseling at both 16- and 26-weeks, and the two could not be distinguished based on their main effects (Tables 2 & 3).

However, the evidence supporting these three components is not wholly compelling. The main effect for Preparation Counseling occurred at only one time point, and the promise of the other components is supported by interaction effects, which show that a component can be effective, but its effects are conditional on the presence of another component [70]. Another concern with interactions is that the cause of the interaction is unknown—does it occur because of antagonistic effects on change mechanisms, or because of some other factor such as perceived burden? These interactions involve factors that have been experimentally manipulated in a controlled fashion, which increases the likelihood of replicability. However, future research is required to identify the extent to which such interactions replicate, especially when they are not stipulated *a priori*.

The number of interaction effects, and the fact that they reflect both synergistic and antagonistic effects amongst components, illustrates the importance of evaluating intervention components with factorial designs before combining components into treatment packages [8]. One cannot confidently extrapolate the joint actions of intervention components based upon their individual effects or on their effects as elements of unvaried combinations of components as occurs in standard RCTs [7, 9, 10]. This highlights a potential value of factorial designs (as per MOST [8]), which uniquely permit the modeling of interaction effects.

The Phase-Based Model emphasizes the importance of examining component effectiveness over time. In fact, Preparation NRT and Cessation-phase counseling interactions were present at the 16 and 26 weeks but not at 2 weeks. This suggests that some treatment effects

take time to appear—they may "incubate". Thus, there may be no simple relation between temporal propinquity and sensitivity to treatment effects [14]; more research is needed to characterize the main and interactive effects of intervention components over time and to elucidate the mechanisms that account for observed patterns.

Additional research is also needed to confirm which intervention components are most effective at the three treatment phases targeted in this research and to assess the effects of components on other outcome criteria, both general (e.g., cost) and phase-relevant (e.g., does Preparation-phase intervention reduce prequit smoking? [14]) criteria. In addition, our use of a fractional factorial design precluded the estimation of higher-order interactions; such interactions are assumed to be negligible relative to main effects and two-factor interactions but we were unable to test this empirically. Further, this research examined intervention components that function primarily during the Preparation and Cessation phases; it is possible that a longer duration of medication use would produce stronger Maintenance-phase effects [13, 71]. Finally, consistent with this experiment's goal of hypothesis generation, it was not powered for simple effects tests; therefore, interactions were interpreted via an appraisal of consistent patterns of effects [11].

Conclusion

Using innovative, efficient strategies to investigate approaches for treating smokers recruited in primary care, this research identified three intervention components that demonstrated promising effects on abstinence: Preparation NRT, Preparation Counseling, and Intensive Cessation In-Person Counseling. Intensive Cessation Phone Counseling and Extended Medication (16 vs. 8 weeks of combination NRT) demonstrated less evidence of effectiveness. The multiple statistical interactions amongst the different intervention components support the use of factorial experiments to screen intervention components for their main and interactive effects, prior to assembling multi-component treatments. The promising intervention components identified in this research should undergo further evaluation, including an RCT that would determine their effects when they are used together as an integrated treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. CONSORT Diagram



2a. Preparation Patch x Cessation Phone Counseling - Significant at Weeks 2 and 16















2e. Preparation Counseling x Cessation Phone Counseling – Significant at Week 16







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Demographic and smoking history characteristics

	Total Samnle	Prepai	ration	Prepa	ration	Prepar	ration elino	In-Pe Couns	erson selin o	Pho	one selino	Medic	ation
	4	On	Off	On	Off	On	off	On	off	On	off	On	Off
Women (%)	54.6	54.3	55.0	55.3	53.9	54.6	54.7	55.4	53.9	53.8	55.5	56.3	53.2
Age (mean, SD)	45.8 (12.0)	45.3 (11.9)	46.2 (12.2)	45.2 (11.8)	46.3 (12.3)	46.2 (12.2)	45.3 (11.9)	45.8 (12.2)	45.7 (11.9)	45.1 (12.0)	46.4 (12.0)	45.1 (12.2)	46.4 (11.6)
High School diploma or GED only (%)	31.4	32.0	30.7	31.4	31.5	34.5	28.4	30.1	32.7	32.5	30.4	30.6	32.2
At least some college (%)	58.7	57.2	60.2	57.6	59.7	55.7	61.5	58.7	58.2	58.1	59.1	60.1	57.3
White (%)	87.8	87.8	87.8	87.8	87.7	88.5	87.0	87.8	87.7	89.5	86.0	87.0	88.4
African-American (%)	7.8	0.6	6.5	8.6	7.0	6.7	8.9	8.4	7.2	7.0	8.6	9.3	6.4
Hispanic (%)	3.9	4.5	3.1	3.1	4.7	4.2	3.5	4.2	3.5	4.5	3.2	5.1	2.8
Health System A (%)	57.3	55.5	59.4	6.63	54.5	56.8	57.8	61.1	53.6	59.1	55.5	6.09	54.1
Cigs/day (mean, SD)	17.7 (8.2)	17.5 (8.4)	17.9 (7.9)	18.1 (8.0)	17.2 (8.4)	17.8 (8.4)	17.5 (8.1)	17.9 (8.2)	17.4 (8.2)	18.1 (8.4)	17.3 (7.9)	17.8 (7.8)	17.6 (8.5)
Baseline carbon monoxide (mean, SD)	20.3 (11.4)	20.3 (11.7)	20.4 (11.0)	20.6 (10.7)	20.0 (12.1)	20.6 (11.3)	20.0 (11.4)	20.3 (11.6)	20.4 (11.1)	20.2 (11.4)	20.4 (11.3)	19.6 (10.8)	21.0 (11.9)
FTND (mean, SD)	4.8 (2.2)	4.8 (2.1)	4.8 (2.3)	4.9 (2.2)	4.7 (2.1)	4.9 (2.2)	4.7 (2.1)	4.9 (2.1)	4.7 (2.1)	4.9 (2.2)	4.8 (2.1)	4.8 (2.2)	4.8 (2.1)
Heaviness of Smoking Index (mean, SD)	3.1 (1.4)	3.1 (1.4)	3.1 (1.4)	3.2 (1.4)	3.0 (1.4)	3.1 (1.5)	3.0 (1.4)	3.2 (1.4)	3.0 (1.5)	3.2 (1.4)	3.0 (1.4)	3.1 (1.4)	3.1 (1.4)

Note. On = Factor was present or at the intensive level or longest duration (e.g., intensive counseling, 16 weeks of medication). Off = Factor was not present or was at the minimal level or shortest duration (e.g., minimal counseling, 8 weeks of medication). The study was conducted in two healthcare systems (A and B). FTND = Fagestrom Test of Nicotine Dependence.

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Factor	LCEIL AUSUIL	ent at 2 Weeks	Percent Abstine	ent at 16 Weeks	Percent Abstine	ent at 26 Weeks
	On	Off	On	Off	On	IJО
Preparation Patch	44.1	43.2	36.5	32.5	29.8	26.0
Preparation Gum	43.4	44.0	36.3	32.6	29.8	25.8
Preparation Counseling	44.5	42.8	38.2	30.9	30.3	25.6
Cessation In-Person Counseling	47.5	39.9	36.3	32.8	27.7	28.2
Cessation Phone Counseling	43.1	44.2	35.6	33.4	30.3	25.6
Medication Duration	44.1	43.2	36.2	33.0	28.5	27.3

Note. On = Factor was present or at the intensive level or longest duration (e.g., intensive counseling, 16 weeks of medication). Off = Factor was not present or was at the minimal level or shortest duration (e.g., minimal counseling, 8 weeks of medication).

Table 3

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		2 Weeks F	ost-TQ	_		16 Weeks	Post-T(Q.		26 Weeks F	ost-TQ	
	Unae	djusted	Adju	ısted ^{**}	Una	ljusted	Adjı	ısted ^{**}	Unad	ljusted	Adju	ısted ^{**}
Variable	q	p-value	q	p-value	q	p-value	q	p-value	q	p-value	q	p-value
Intercept	26	.001	.43	.45	70	<.001	69	.25	-1.04	<.001	34	.59
Preparation Patch	.01	.87	.04	.66	.08	.34	.11	.22	60.	.34	.11	.24
Preparation Gum	01	.95	00	96.	.11	.21	.12	.19	.12	.20	.12	.23
Preparation Counseling	.03	69.	.04	.60	.18	.04	.19	.03	.11	.23	.11	.23
Cessation In-Person Counseling	.14	.10	.15	.07	.05	.54	.06	.48	04	.68	03	.80
Cessation Phone Counseling	03	.72	03	.75	.05	.59	.06	.54	.12	.21	.12	.20
Medication Duration	.02	.78	.01	.91	.08	.39	.07	.46	02	.80	03	.73
Preparation Patch x Preparation Gum	.05	.56	.05	.54	.04	.68	.04	.65	.06	.54	.06	.53
Preparation Patch x Preparation Counseling	.16	.050	.18	.04	.15	.10	.17	.07	.18	.07	.19	.06
Preparation Patch x Cessation In-Person Counseling	.14	60 [.]	.15	80.	.19	.03	.20	.03	.22	.02	.22	.02
Preparation Patch x Cessation Phone Counseling	.20	.01	.23	.01	.18	.047	.20	.03	.13	.18	.15	.14
Preparation Patch x Medication Duration	06	.50	07	.43	.00	.97	00	96.	01	.95	02	.84
Preparation Gum x Preparation Counseling	.10	.22	.05	.59	06	.52	11	.22	05	.61	09	.35
Preparation Gum x Cessation In-Person Counseling	.11	.18	.12	.15	.20	.02	.21	.02	.22	.02	.22	.02
Preparation Gum x Cessation Phone Counseling	07	.37	08	.37	01	.96	.01	.93	06	.51	06	.52
Preparation Gum x Medication Duration	00	66.	00	.97	.01	.89	00	96.	04	.67	05	.60
Preparation Counseling x Cessation In-Person Counseling	04	.59	03	.68	10	.26	10	.26	17	80.	16	60.
Preparation Counseling x Cessation Phone Counseling	01	.95	.00	1.00	18	.04	19	.04	14	.15	14	.14
Preparation Counseling x Medication Duration	.05	.58	.06	.48	.06	.52	.06	.48	11	.29	11	.27
Cessation In-Person Counseling x Cessation Phone Counseling	05	.56	06	.47	28	.002	28	.002	23	.02	23	.02
Cessation In-Person Counseling x Medication Duration	06	.46	04	.65	13	.15	10	.27	08	.40	05	.61
Cessation Phone Counseling x Medication Duration	06	.51	06	.52	.03	.78	.04	.66	.02	.87	.02	.81

Note. **Bold** indicates p < .05.

** Models were adjusted for gender, race (White vs. non-White), age, education (high school or less vs. at least some college), healthcare system, Heaviness of Smoking Index, and baseline carbon monoxide (N = 631 due to missing covariates).