

Comparative effectiveness of motivation phase intervention components for use with smokers unwilling to quit: a factorial screening experiment

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ABSTRACT

Aims To screen promising intervention components designed to reduce smoking and promote abstinence in smokers initially unwilling to quit. **Design** A balanced, four-factor, randomized factorial experiment. **Setting** Eleven primary care clinics in southern Wisconsin, USA. **Participants** A total of 517 adult smokers (63.4% women, 91.1% white) recruited during primary care visits who were willing to reduce their smoking but not quit. **Interventions** Four factors contrasted intervention components designed to reduce smoking and promote abstinence: (1) nicotine patch versus none; (2) nicotine gum versus none; (3) motivational interviewing (MI) versus none; and (4) behavioral reduction counseling (BR) versus none. Participants could request cessation treatment at any point during the study. **Measurements** The primary outcome was percentage change in cigarettes smoked per day at 26 weeks post-study enrollment; the secondary outcomes were percentage change at 12 weeks and point-prevalence abstinence at 12 and 26 weeks post-study enrollment. **Findings** There were few main effects, but a significant four-way interaction at 26 weeks post-study enrollment ($P = 0.01$, $\beta = 0.12$) revealed relatively large smoking reductions by two component combinations: nicotine gum combined with BR and BR combined with MI. Further, BR improved 12-week abstinence rates ($P = 0.04$), and nicotine gum, when used without MI, increased 26-week abstinence after a subsequent aided quit attempt ($P = 0.01$). **Conclusions** Motivation-phase nicotine gum and behavioral reduction counseling are promising intervention components for smokers who are initially unwilling to quit.

Keywords Chronic care smoking treatment, comparative effectiveness, factorial experiment, motivational interviewing, Multi-phase Optimization Strategy (MOST), nicotine replacement therapy, Phase-Based Model, primary care, smoking cessation, smoking reduction.

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Submitted 4 February 2015; initial review completed 21 April 2015; final version accepted 8 September 2015

INTRODUCTION

More than 40 million Americans continue to smoke [1], despite the enormous harms of tobacco use [2]. More smokers would quit if a greater proportion were offered and accepted evidence-based treatment during their health-care visits [3]. However, only about 5–20% of smokers initiate cessation treatment during a health-care visit (e.g. [2,4–6]), in part because the vast majority

(70–90%) are not willing to commit to quitting smoking at a given clinic visit [5–7]. Because so few smokers are ready to quit at any given time, typical smoking treatments offered by health-care systems (i.e. cessation treatments) are unused by the majority of smokers; i.e., those unwilling to quit. Even when smokers do receive cessation treatment, only a minority succeed in quitting long-term [3]. Thus, two critical public health goals are to: (1) successfully recruit smokers who are unwilling to quit into evidence-

based smoking reduction treatment at health-care visits and (2) increase the success of their quit attempts. This research addresses both goals.

This research was guided by the Multiphase Optimization Strategy (MOST [8–11]) and the Phase-Based Model (PBM) of smoking treatment [12–14]. MOST is a research strategy that uses efficient designs (e.g. factorial experiments [11]) to screen multiple intervention components to identify those warranting further investigation. The PBM holds that there are different phases of smoking cessation (i.e. motivation, preparation, cessation, maintenance and relapse recovery), each presenting its own challenges and opportunities, and emphasizes the need to identify components that work especially well at each phase. This is one of four linked papers. One [12] reviews the theory and methods behind this research. The others report factorial experiments of intervention components for the motivation (this experiment) [15], the preparation/cessation [16], and maintenance [17] phases of smoking treatment.

The current experiment screens intervention components for smokers in the motivation phase of smoking intervention—those initially unwilling to quit. These components are designed to engage smokers in treatment, help them reduce their smoking and enhance their success if they ultimately attempt to quit. MOST and PBM are complementary; MOST affords the evaluative screening of multiple intervention components, and the PBM suggests the types of components that should be screened [12]. Together, they can be used to identify effective components for each phase of chronic care smoking treatment.

As per the PBM, we first identified chief challenges of the motivation phase, ones that reduce either the likelihood of initiating quitting or success in quitting once a quit attempt is made. These challenges include: (1) heavy smoking (although data are mixed [18–23], (2) motivation to smoke that outweighs motivation to quit [18,19,24,25], (3) environmental obstacles to cessation (e.g. smokers in the home [18,26]); and (4) low quitting self-efficacy [18,24,27,28]. On this basis, we identified four motivation-phase intervention components: nicotine patch, nicotine gum, motivational interviewing, and behavioral reduction counseling. All the components were designed for translation into real-world health-care settings, consistent with a pragmatic research approach [29–31].

Nicotine patch and gum might help smokers to: (1) reduce their smoking [32–34] which, over time, would reduce withdrawal and dependence [35,36]; (2) reduce smoking-environment and smoking-reward contingencies (e.g. [37]); and (3) enhance quitting self-efficacy by providing pre-quit practice, blunting withdrawal and providing a coping response [38], all of which will encourage more successful quit attempts (e.g. [33,39]; although see [40]).

Two types of nicotine replacement therapy (NRT) were selected so that we could examine whether they yield different effects, and also whether they interact.

Motivational interviewing (MI) was selected to increase intrinsic and personally relevant motives for quitting [3,41]. There is substantial evidence that MI can increase quit rates when provided during cessation [42–44]; it is much less clear that MI increases quit rates among smokers in the motivation phase who are initially unwilling to quit [42,43,45–47].

Behavioral reduction (BR) counseling was intended to enhance quitting success by reducing cigarette consumption, reducing exposure to cigarette cues (e.g. by increasing smoke-free environments) and encouraging coping practice. These effects might enhance coping skills and quitting self-efficacy, and perhaps decrease the severity of withdrawal during quit attempts. Both smoking reduction and a lower density of environmental smoking cues predict later quitting success [48–50]. However, little evidence exists on the effectiveness of BR counseling alone during the motivation phase. Similar counseling has typically been paired with pharmacotherapy in research designs that do not permit disentangling the effects of the two strategies [33,34,51] (relevant non-experimental data exist [52]).

In sum, this study used efficient research methods [8] to screen four intervention components (nicotine patch, nicotine gum, MI and BR counseling) designed to engage smokers in treatment, reduce smoking heaviness (primary outcome), enhance quitting success and be translated easily into health-care settings [53]. The main and interactive effects of these components were evaluated in this screening experiment to identify promising motivation-phase components for smokers initially unwilling to quit. Thus, this research yields valuable comparative effectiveness data on multiple intervention components that will help guide future treatment development (via additional factorial experiments or a randomized clinical trial (RCT) that evaluates a package of intervention components as a multi-component treatment [12,13]).

METHODS

Procedure

From June 2010 to October 2013, participants were recruited from 11 primary care clinics in two health-care systems in southern Wisconsin using indigenous medical assistants who were prompted by electronic health record (EHR) technology. During clinic visits, identified smokers were invited to participate in a research program to help them to reduce their smoking [54]. Interested patients were referred electronically to the research office. Research staff contacted interested patients and assessed eligibility. The inclusion criteria were: aged ≥ 18 years; smoked ≥ 5

cigarettes/day for the previous 6 months; had no interest in quitting in the next 30 days but willing to cut down; were able to read, write and speak English; agreed to complete assessments; planned to remain in the area for at least 6 months; not currently taking bupropion or varenicline; agreeing to use only study smoking medication during the study if reported current NRT use; no medical contraindications to NRT use; and, for women of childbearing potential, agreement to use an approved birth control method.

Eligible patients were invited to return to their primary care clinic to learn more about the study and provide written informed consent.¹ A customized research database program then created a schedule of intervention and assessment contacts, which guided treatment delivery by case managers. The case managers in this study were bachelor's level research staff supervised by licensed clinical psychologists.

There was an initial 6-week motivation-phase treatment period, and participants could choose to extend the same treatment for another 6 weeks. Participants who chose to extend the treatment continued to receive the same components to which they were initially assigned randomly. In addition, participants could elect to receive cessation-phase treatment at any point throughout the 6-month study period. Cessation-phase treatment was identical for all participants and consisted of 8 weeks of nicotine patch + gum, and two brief phone counseling sessions. Finally, at 12 and 26 weeks following study enrollment, all participants received a 15-minute follow-up assessment call.

Participants were randomized to treatment conditions using stratified permuted, computer-generated block randomization; we stratified by gender and clinic with a fixed block size of 16 based on the 16 unique possible combinations of intervention components (in random order within each block). Staff were blinded to randomization until eligibility was confirmed but not beyond that point; participants were blinded until consent was provided.

Experimental design

This 2 × 2 × 2 × 2 factorial experiment had four factors each comprising an active (On) condition and control (Off) condition: (1) nicotine patch; (2) nicotine gum; (3) MI; and (4) BR counseling, yielding 16 unique experimental conditions. Participants were randomized to one of the 16 experimental conditions (see Supporting Information, Table S1) within each participating clinic. Intervention components were designed to be compatible with one another, and to be delivered with fidelity across all treatment combinations using database prompts.

¹Although there are three related studies (this study and [16,17]), each is based on an independent sample. There was no cross-over in study participation among the three studies.

Table 1 Demographic and smoking history characteristics.

	Total sample		Nicotine patch		Nicotine gum		Motivational interviewing		Behavioral reduction Counseling	
	On	Off	On	Off	On	Off	On	Off	On	Off
Women (%)	63.4	63.5	63.4	63.2	63.6	63.6	63.2	63.6	62.7	64.2
Health system A (%)	55.1	55.2	55.1	56.5	53.8	52.7	57.7	52.7	57.7	52.5
High school diploma or GED only (%)	38.4	30.7	45.7	38.5	38.4	36.7	40.2	36.7	40.2	36.7
At least some college (%)	61.6	69.0	54.0	61.5	61.6	63.3	59.8	63.3	63.3	63.3
White (%)	91.1	90.5	91.7	91.7	90.5	91.7	90.5	91.7	92.3	89.9
African American (%)	4.8	5.6	4.2	4.3	5.3	4.9	4.7	4.9	4.6	5.1
Hispanic (%)	1.0	.8	1.9	1.2	1.6	0.8	2.1	0.8	0.8	2.0
Age (mean, SD)	47.0 (14.4)	47.0 (14.15)	47.1 (14.15)	47.5 (14.4)	46.6 (14.6)	47.5 (14.4)	46.3 (4.8)	47.7 (14.2)	46.3 (14.5)	47.7 (14.2)
Cigs/day (mean, SD)	17.5 (7.8)	16.4 (7.5)	18.3 (8.4)	16.9 (8.2)	17.9 (7.8)	17.3 (8.3)	17.3 (8.3)	17.4 (7.7)	17.0 (8.1)	17.8 (8.0)
FTND (mean, SD)	4.8 (2.1)	4.6 (2.0)	4.9 (2.1)	4.9 (2.0)	4.7 (2.2)	4.8 (2.1)	4.8 (2.1)	4.8 (2.01)	4.8 (2.1)	4.8 (2.0)
Heaviness of Smoking Index (mean, SD)	3.1 (1.4)	3.1 (1.4)	3.0 (1.4)	3.1 (1.4)	3.0 (1.4)	3.1 (1.4)	3.0 (1.6)	3.1 (1.2)	3.1 (1.5)	3.0 (1.2)
Baseline CO (mean, SD)	21.3 (11.8)	21.1 (12.9)	21.6 (10.2)	23.2 (12.3)	19.0 (10.8)	20.2 (13.0)	20.2 (13.0)	22.2 (10.7)	18.4 (10.6)	23.9 (12.3)

CO = carbon monoxide; SD = standard deviation; FTND = Fagerström Test for Nicotine Dependence; GED = general educational development. On = factor was present; Off = factor was not present.

Table 2 Self-reported mean cigarettes per day (CPD) percentage reduction and point-prevalence abstinence rates at 12 and 26 weeks post-study enrollment.

Factor	Mean % CPD reduction at 12 weeks (SD)		Mean % CPD reduction at 26 weeks (SD)		% Abstinent at 12 weeks		% Abstinent at 26 weeks	
	On	Off	On	Off	On	Off	On	Off
Nicotine patch	37.0 (34.6)	37.6 (36.4)	38.7 (36.2)	38.9 (37.1)	5.7	11.1	9.4	12.3
Nicotine gum	37.7 (35.0)	36.9 (35.9)	37.4 (36.2)	40.2 (36.9)	8.7	7.9	9.1	12.6
Motivational interviewing	35.3 (35.9)	39.2 (34.9)	37.2 (35.6)	40.2 (37.5)	8.3	8.3	9.1	12.5
Behavioral reduction counseling	38.4 (36.2)	36.2 (34.6)	38.6 (36.3)	38.9 (36.9)	10.8	5.8	10.8	10.9

On = factor was present; Off = factor was not present; SD = standard deviation.

Experimental factors

The intervention components were designed to address phase-specific challenges and opportunities, and to be readily translatable to real-world practice. See Supporting Information, Tables S2 and S3 for outlines of counseling protocols and review of fidelity assessments.

Nicotine patch versus no patch

Participants in the On (active) condition were instructed to use 14-mg patches daily for the 6-week intervention period.

Nicotine gum versus no gum

Participants in the On condition were instructed to use 2-mg gum for the 6-week intervention period (\geq nine/day, one piece/1–2 hours) in place of smoking.

MI versus no MI

Participants in the On condition received an initial 20-minute in-person counseling session followed by three biweekly, 10-minute counseling calls over the 6-week intervention period. Based on Miller & Rollnick [55,56], the counseling sessions included motivation-building exercises to reinforce intrinsic motivation and to help participants overcome ambivalence about quitting.

Behavioral reduction (BR) versus no BR

Participants in the On condition received an initial 20-minute in-person counseling session followed by six weekly 10-minute counseling calls. During these sessions, participants set smoking reduction goals and developed reduction strategies (e.g. delaying smoking, eliminating smoking in specific situations). Participants were also instructed to record daily smoking, which case managers used to identify successes and challenges.

Assessments

Participants completed baseline assessments of vital signs, demographics and smoking history and dependence (e.g. the Fagerström Test for Nicotine Dependence [FTND] [57]). During study visits, adverse events, medication adherence and smoking in the past week were assessed.

Outcome measures

The primary outcome was percent change in cigarettes smoked per day (CPD) at 26 weeks relative to baseline CPD. CPD change was chosen as the primary outcome because it reflects both smoking reduction and abstinence, and thus captures the net impact of treatment, and because smoking reduction is a valid predictor of future cessation [50,58]. Percentage change also permitted comparison with prior research and controlled for baseline differences in CPD [33]. The secondary outcomes were percentage change in CPD at 12 weeks and 7-day point-prevalence abstinence at 12 and 26 weeks.² Assessors were not involved in treatment but were not blind to treatment assignment.

Analytical plan

Analyses were conducted using SPSS [59]. Initial analyses examined treatment adherence, safety and patterns and associations with missing data. We computed separate models using effect coding (each coded -1 = Off condition; $+1$ = On condition) testing main and interactive effects. We computed separate regression models for the CPD percentage change outcome at weeks 12 and 26; models were computed with and without adjusting for a predetermined set of covariates (see below). Participants who did not provide outcome information for the percentage change primary outcome were assumed to be smoking at their baseline CPD rate. Sensitivity analyses with multiple imputation for missing outcome data [60] yielded similar results. Therefore, we present results from analyses where missing = baseline CPD (see Supporting information, Table S4 for sensitivity analyses).

²Based upon reviewer recommendations, the designation of outcomes was altered from what was listed in trial registration materials.

Table 3 Unadjusted and adjusted regression analyses for percentage change in cigarettes smoked per day in the past week at weeks 12 and 26 post-study enrollment.

Model effect	12 weeks						26 weeks					
	Unadjusted			Adjusted ^a			Unadjusted			Adjusted ^a		
	β	<i>t</i>	<i>P</i>	β	<i>t</i>	<i>P</i>	β	<i>t</i>	<i>P</i>	β	<i>t</i>	<i>P</i>
Nicotine patch	-0.01	-0.19	0.85	0.01	-0.14	0.89	-0.00	-0.03	0.98	-0.00	-0.05	0.96
Nicotine gum	0.01	0.25	0.80	0.01	0.17	0.87	-0.04	-0.84	0.40	-0.05	-1.07	0.29
BR	0.03	0.74	0.50	0.02	0.54	0.59	-0.00	-0.01	0.99	-0.01	-0.17	0.87
MI	-0.05	-1.23	0.22	-0.06	-1.35	0.18	-0.04	-0.97	0.33	-0.05	-1.06	0.29
Patch×gum	-0.04	-0.79	0.43	-0.03	-0.76	0.45	-0.04	-0.82	0.41	-0.04	-0.81	0.42
Patch×BR	-0.08	-1.80	0.07	-0.08	-1.73	0.09	-0.07	-1.51	0.13	-0.06	-1.40	0.16
Patch×MI	-0.07	-1.54	0.12	-0.06	-1.27	0.21	-0.01	-0.15	0.88	0.00	-0.00	0.99
Gum×BR	0.007	0.15	0.88	0.01	0.12	0.91	0.03	0.77	0.44	0.03	0.76	0.45
Gum×MI	-0.08	-1.92	0.06	-0.09	-1.96	0.05	-0.05	-1.10	0.27	-0.06	-1.34	0.18
BR×MI	0.02	0.36	0.72	0.01	0.20	0.84	0.01	0.15	0.89	0.00	0.04	0.97
Patch×gum×BR	0.02	0.50	0.62	0.02	0.43	0.67	0.07	1.51	0.13	0.06	1.45	0.15
Patch×gum×MI	0.00	0.03	0.98	0.01	0.15	0.88	0.02	0.43	0.67	0.03	0.59	0.56
Patch×BR×MI	0.00	0.08	0.93	0.00	0.03	0.98	0.02	0.37	0.71	0.02	0.35	0.73
Gum×BR×MI	0.01	0.33	0.75	0.02	0.37	0.71	-0.04	-0.99	0.32	-0.04	-1.00	0.32
Patch×gum×BR×MI	0.11	2.51	0.01	0.11	2.58	0.01	0.12	2.65	0.01	0.12	2.66	0.01

Bold type indicates $P < 0.05$. ^aAdjusted model controlled for gender, race (white versus non-white), age, education (up to high school diploma versus at least some college), health-care system (A versus B), Heaviness of Smoking Index and baseline carbon monoxide. BR=behavioral reduction; MI=motivational interviewing.

Table 4 Unadjusted and adjusted logistic regression analyses for 7-day point-prevalence abstinence at weeks 12 and 26 post-study enrollment ($n = 517$).

Model effect ^a	12 weeks				26 weeks			
	Unadjusted		Adjusted ^b		Unadjusted ^b		Adjusted	
	<i>b</i>	<i>P-value</i>	<i>b</i>	<i>P-value</i>	<i>b</i>	<i>P-value</i>	<i>b</i>	<i>P-value</i>
Nicotine patch	-0.45	0.03	-0.38	0.06	-0.21	0.26	-0.17	0.38
Nicotine gum	-0.03	0.89	-0.04	0.84	-0.28	0.15	-0.30	0.12
Behavioral reduction	0.42	0.04	0.42	0.04	0.08	0.68	0.07	0.72
Motivational interviewing (MI)	-0.03	0.88	-0.04	0.83	-0.30	0.11	-0.30	0.12
Patch×gum	-0.11	0.57	-0.14	0.49	-0.06	0.72	-0.08	0.67
Patch×BR	0.16	0.42	0.20	0.34	-0.25	0.14	-0.22	0.20
Patch×MI	-0.01	0.96	-0.01	0.97	-0.10	0.54	-0.11	0.53
Gum×BR	0.12	0.54	0.13	0.51	0.45	0.02	0.49	0.01
Gum×MI	-0.10	0.61	-0.08	0.70	-0.40	0.04	-0.41	0.04
BR×MI	0.15	0.43	0.12	0.53	0.24	0.20	0.24	0.21
Patch×gum×BR	0.30	0.13	0.27	0.19	0.18	0.30	0.19	0.29
Patch×gum×MI	-0.05	0.78	-0.03	0.89	0.13	0.49	0.13	0.50
Patch×BR×MI	-0.10	0.60	-0.07	0.72	-0.09	0.62	-0.07	0.71
Gum×BR×MI	-0.04	0.82	-0.06	0.74	0.05	0.78	0.03	0.87

Bold type indicates $P < 0.05$. ^aThe model included effects up to a three-way interaction because higher-order interactions did not converge. ^bAdjusted model controlled for gender, race (white versus non-white), age, education (up to high school diploma versus at least some college), health-care system (A versus B), Heaviness of Smoking Index and baseline carbon monoxide. BR=behavioral reduction; MI=motivational interviewing.

Logistic regression was used to analyze 7-day point-prevalence abstinence at 12 and 26 weeks (0 = smoking 1 = abstinent). Participants who did not provide outcome information were assumed to be smoking (i.e. missing = smoking). All CPD change and abstinence analyses were

conducted with and without adjusting for covariates: gender, race (white versus non-white), age, education (up to high school versus at least some college), the Heaviness of Smoking Index [61], baseline exhaled carbon monoxide and health-care system. We discuss results

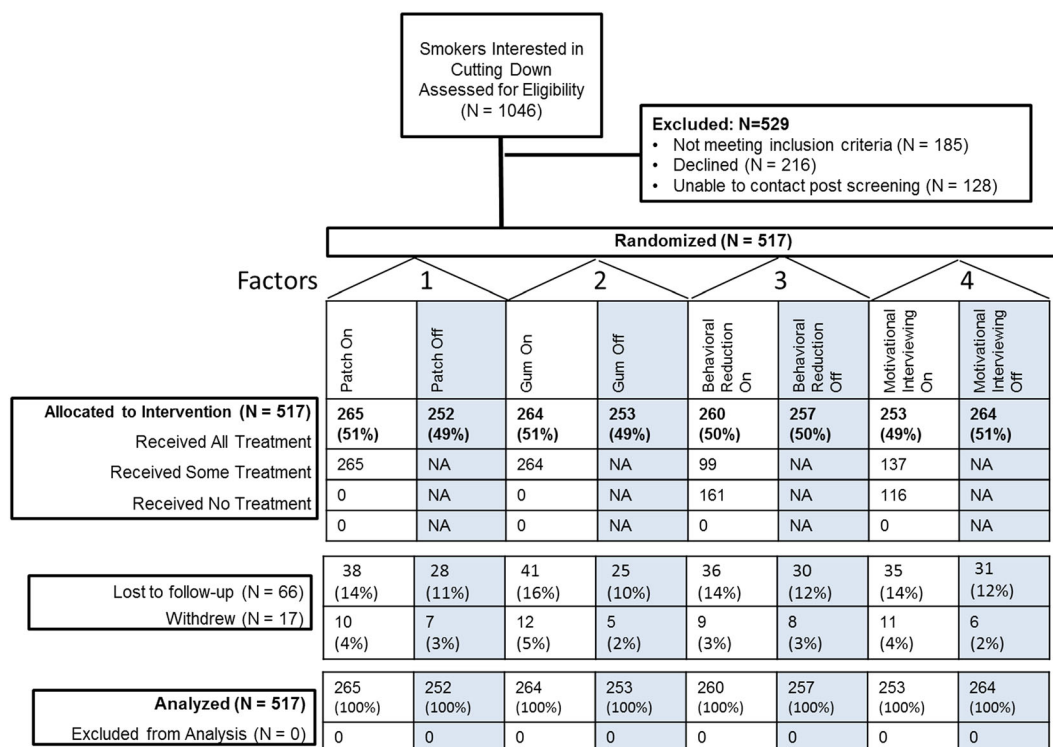


Figure 1 Consolidated Standards of Reporting Trials (CONSORT) diagram. NA = not applicable.

from the unadjusted models only; patterns of statistical significance were consistent across both unadjusted and adjusted models.

RESULTS

Participants

Of the 1046 smokers who expressed initial interest, 517 provided consent [see Fig. 1 for Consolidated Standards of Reporting Trials (CONSORT) diagram and Supporting information materials for sample size justification]. Each clinic recruited 23–89 participants. Table 1 provides descriptions of demographic and tobacco dependence characteristics.

Treatment participation

On average, participants in the MI condition attended a mean of 3.16 [standard deviation (SD)=1.06] of four counseling sessions. Participants in the BR condition attended a mean of 5.31 (SD = 1.86) of seven sessions. Participants in the patch condition used an average of 4.94 patches/week (SD = 2.09), and those in the gum condition used an average of 3.61 pieces of gum/day (SD = 2.10). In addition, 75 (15%) chose to receive a second 6 weeks of the same motivation-phase treatment to which they had been

randomized, and 100 (19%) chose to receive cessation-phase treatment.

Safety

There were no serious adverse events related to study participation. The most common adverse events/condition were nausea (11%: gum), vivid dreams (20%: patch) and skin rash (26%: gum + patch).

Missing data

The percentage of participants with missing CPD data decreased from 26% at week 6 to 13% at week 26. At week 26, 44 participants (9%) were missing point-prevalence abstinence data. There were no significant differences in missing data across the contrasting levels of each intervention factor.

Change in cigarettes smoked per day outcome

Table 2 presents the CPD percentage change for each factor level at 12 and 26 weeks post-study enrollment. No treatment main effects were found but a statistically significant four-way interaction (patch × gum × BR × MI) was found at both weeks 12 and 26, $P_s = 0.01$ (see Table 3).³ When effect coding is used, a four-way interaction means that a

³Significant four-way interactions at weeks 12 and 26 were found among a subset of participants who had not quit smoking ($P_s = 0.02$ and 0.01 , respectively). Thus, the same reduction effects were found when cessation contributed to the effect, and when it did not. Moreover, the same pattern of significant findings emerged when length of motivation-phase treatment (6 versus 12 weeks) was entered as a covariate into the model.

three-way interaction involving three experimental factors varies depending on the level of a fourth factor.

As shown in Fig. 2a and b, results of the four-way interaction for the percentage CPD change model showed a pattern where some combinations of two components produced substantial reductions in smoking, but only when used with no other components. Across both time-points: (1) the combination of gum and BR, without

other components, produced consistent mean CPD reduction (48% smoking reduction at week 12; 50% reduction at week 26); and (2) the combination of BR with MI, without other components, also produced substantial mean CPD reductions at both time points (48% at week 12; 49% at week 26). While there was a tendency for BR and MI to perform well together, MI did not yield promising effects when used with additional components

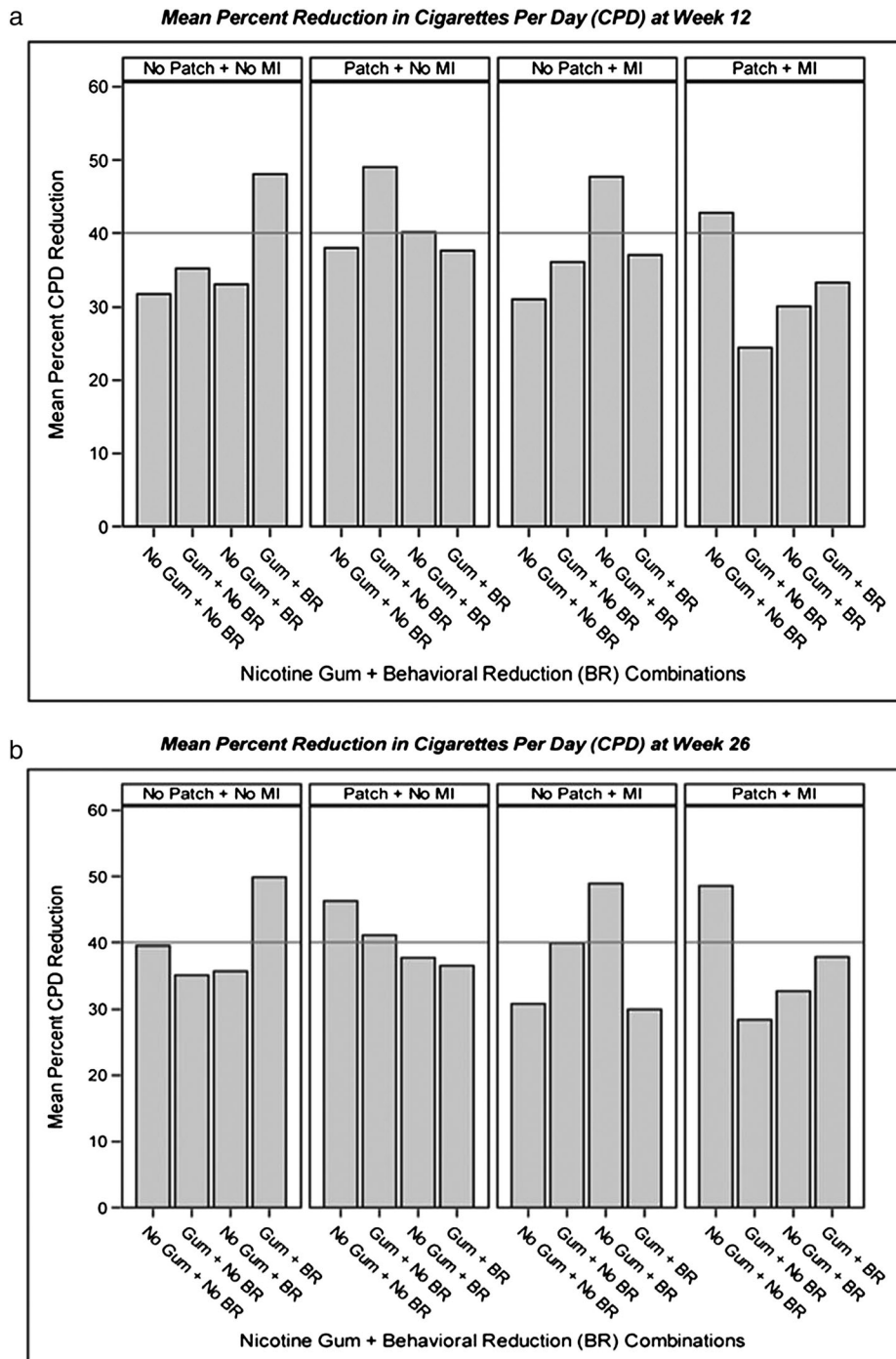


Figure 2 (a) Bar graph showing interactions for mean percentage reduction in cigarettes per day at 12 weeks post-study enrollment. (b) Bar graph showing interactions for mean percentage reduction in cigarettes per day at 26 weeks post-study enrollment. MI = motivational interviewing.

(e.g. MI + gum + BR or patch + MI + gum: see Fig. 2a,b). Figure 2 also suggests that, in general, combinations of three or four active components suppressed smoking less effectively than did pairs of components.

Finally, the percentage of participants reporting at least a 50% reduction in CPD (cf. [33]) at 12 and 26 weeks, depending on condition, ranged from approximately 27 to 59% across component combinations, with BR + gum and BR + MI (without other components) producing the greatest proportion who reduced by at least 50% (52% at week 12 and 59% at week 26; 50% at week 12 and 47% at week 26, respectively).

Cessation outcome

Table 2 presents self-reported 7-day point-prevalence abstinence rates for each factor level at 12 and 26 weeks post-study enrollment. There were significant main effects of patch and BR at week 12 (see Table 4); patch was associated with decreased abstinence at 12 weeks while BR was associated with increased abstinence rates. Moreover, there were two significant two-way interactions at 26 weeks: gum × BR and gum × MI (see Table 4 and Fig. 3). Participants receiving gum or BR alone attained the lowest abstinence rates, whereas those receiving neither attained the highest abstinence rates. Those receiving both gum + MI did particularly poorly relative to all other conditions.

We also analyzed 7-day point-prevalence abstinence among only those participants who elected to receive cessation-phase treatment ($n = 100$) (see Table 5). There was an antagonistic gum × MI interaction at 26 weeks.

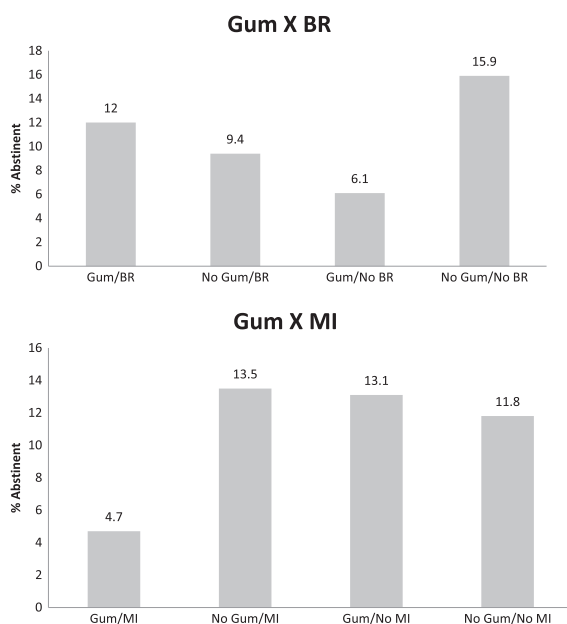


Figure 3 Bar graphs for gum × behavioral reduction (BR) and gum × motivational interviewing (MI) interactions for the 26-week point-prevalence abstinence model for the full sample ($n = 517$)

As Fig. 4 shows, gum with no MI increased abstinence, but this effect was reversed by adding MI. There was also a 26-week synergistic gum × BR interaction at $P = 0.06$, suggesting that gum improved abstinence when paired with BR, and reduced abstinence when not paired with BR (see Fig. 4).

DISCUSSION

The goal of this screening experiment was to identify motivation-phase intervention components that yield patterns of promising effects on smoking reduction and abstinence when used in a primary care setting. None of the four intervention components (nicotine patch, nicotine gum, MI counseling, BR counseling) yielded significant main effects on percentage CPD change. However, a significant patch × gum × MI × BR interaction at both 12 and 26 weeks showed that component effectiveness was influenced by the co-occurrence of components (Fig. 2). In particular, gum + BR and BR + MI were relatively effective at reducing CPD at both 12 and 26 weeks. These results were obtained both when abstainers were, and were not, included in analyses. The results also showed that no combinations of three or more components were especially effective (Fig. 2a,b), suggesting a cost of treatment complexity [62,63]. Further, the percentage of participants showing meaningful reductions compared favorably with much longer trials of motivation-phase treatments. The Moore *et al.* meta-analysis [33] showed smoking reductions of $\geq 50\%$ at treatment end in about 22% of the participants receiving active treatment. Our results show that 27–59% of participants reported meaningful reductions ($> 50\%$), depending on condition, with some of this reduction reflecting cessation.

Motivation-phase intervention components appeared to influence cessation success. In the full sample, participants who received BR were more likely to be abstinent than those who did not receive BR, whereas the patch produced lower abstinence rates relative to no patch. Gum, depending on the components with which it was paired, produced especially low 26-week abstinence rates (Fig. 3). However, among participants who entered cessation-phase treatment, receiving gum during the motivation phase was related to the highest abstinence rates; pairing MI with gum reduced this benefit (gum + no MI = 58% abstinent versus gum + MI = 24%; see Fig. 4). Thus, the effectiveness of motivation-phase gum depended upon the components with which it was paired and the treatment phase in which it was used (i.e. motivation or cessation).

Even though the participants in this study were initially unwilling to quit, the point-prevalence abstinence rates among those who opted to receive formal cessation treatment were relatively high for a modestly intense cessation intervention (38% abstinent across all conditions: cf. [3]).

Table 5 Unadjusted and adjusted logistic regression analyses for 7-day point-prevalence abstinence at weeks 12 and 26 post-study enrollment among those who underwent an aided quit attempt ($n=100$)

Model effect ^a	12 weeks				26 weeks			
	Unadjusted		Adjusted ^b		Unadjusted		Adjusted ^b	
	<i>b</i>	<i>P</i> -value	<i>b</i>	<i>P</i> -value	<i>b</i>	<i>P</i> -value	<i>b</i>	<i>P</i> -value
Nicotine patch	-0.47	0.08	-0.47	0.11	-0.26	0.30	-0.30	0.29
Nicotine gum	0.33	0.23	0.22	0.46	0.14	0.60	0.09	0.77
Behavioral reduction	0.48	0.06	0.47	0.11	-0.14	0.62	-0.22	0.52
Motivational interviewing (MI)	0.15	0.57	0.29	0.35	-0.28	0.28	-0.39	0.20
Patch×gum	0.22	0.41	0.11	0.71	0.01	0.97	-0.02	0.95
Patch×BR	0.40	0.13	0.46	0.10	-0.01	0.99	0.10	0.76
Patch×MI	0.02	0.94	0.18	0.55	-0.38	0.16	-0.39	0.20
Gum×BR	-0.11	0.66	-0.14	0.59	0.61	0.06	0.64	0.06
Gum×MI	-0.28	0.24	-0.25	0.34	-0.84	0.01	-1.00	0.00
BR×MI	0.08	0.75	-0.03	0.92	0.46	0.15	0.45	0.19

Bold type indicates $P < 0.05$. ^aThe model included effects up to a two-way interaction because higher-order interactions did not converge. ^bAdjusted model controlled for gender, race (white versus non-white), age, education (up to high school diploma versus at least some college), health-care system (A versus B), Heaviness of Smoking Index and baseline carbon monoxide. BR=behavioral reduction; MI=motivational interviewing.

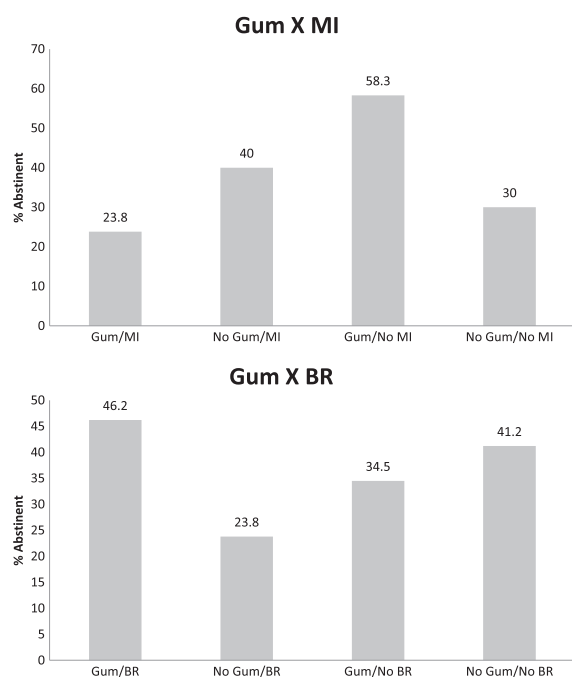


Figure 4 Bar graphs showing gum × motivational interviewing (MI) and gum × behavioral reduction (BR) interactions for the 26-week point-prevalence abstinence model among participants who received cessation treatment ($n = 100$)

The 26-week abstinence rate for the full sample, across all intervention conditions, was 11%, comparable to abstinence rates obtained with active motivation-phase intervention in other studies (7–20% [33,64,65]). However, those studies lasted typically for 6–24 months, versus 6–12 weeks in the current experiment. The current results may compare favorably to earlier, longer studies because

those studies did not provide a cessation intervention for smokers who had become ready to quit [3,66].

Although combination NRT and MI are proven interventions for both cessation and inducing quit attempts [3,33,43,67], in this motivation-phase experiment neither yielded meaningful benefit. For instance, MI reduced the beneficial effect of gum on abstinence rates (e.g. Fig. 4). Similarly, the patch and gum did not yield meaningful additive or synergistic effects in abstinence analyses with the full sample. These differences in intervention component effects across the motivation and cessation phases, if replicated, underscore the importance of experimentally evaluating components for each treatment phase [13]. This research also highlights the value of examining both main and interactive effects when developing integrated treatments [8]. The results suggest that component interaction effects of meaningful magnitude may occur; such effects would not have been detected in a typical RCT [68].

This research supports the feasibility of chronic care treatment for smoking [69,70]. A meaningful percentage of smokers in primary care who were initially unwilling to quit entered (30% [7]) and adhered to motivation-phase treatment with a reduction goal. Also, after brief motivation-phase treatment, 19% of participants opted for formal cessation-phase treatment, and prior exposure to particular motivation-phase intervention components was related especially to abstinence (e.g. gum when not accompanied by MI, and perhaps gum + BR). The latter finding does not permit strong inference, however, because the motivation-phase components might have affected either cessation ability itself, or participant self-selection into the cessation treatment.

One might question either the strength of the effects obtained or the strength of the evidence. For instance, in the overall sample, there were no significant main effects for intervention components with regard to percentage CPD change, although BR produced a main effect by enhancing abstinence rates. Moreover, it is difficult to draw strong inferences about particular components from higher order interactions, particularly those that were not hypothesized a priori. However, unlike interactions involving person factors that vary randomly, these interactions involve factors that have been manipulated experimentally in a controlled fashion, increasing the likelihood of replicability. Future research is required to determine whether the interactions we found will replicate. In addition, main effects might have been obtained with longer treatment duration or higher dosages of the NRT agents, features that are typical in prior research in this area (e.g. [33]). Also, this study specifically recruited smokers who were willing to cut down but not quit; the findings might not generalize well to other smokers (e.g. those not interested in cutting down). Finally, self-reports of abstinence were not biochemically confirmed. Future motivation-phase research should extend the length of motivation-phase treatment, explore other promising components (e.g. the five Rs [3,51]), and use a broader range of smokers who are unwilling to quit.

CONCLUSION

Using the Phase-Based Model of Smoking Intervention [13] and the Multiphase Optimization Strategy [8], this research found that two motivation-phase intervention components may be relatively effective with smokers who are willing to reduce their smoking but not quit: nicotine gum and behavioral reduction counseling. These components were present in combinations that produced the most consistent and marked reductions in smoking across time, and BR improved abstinence in the full sample. There was also evidence that gum, and possibly BR combined with gum, could enhance long-term abstinence among those making aided quit attempts. Results also revealed that the effectiveness of intervention components was often affected meaningfully by the components with which they were paired. The promising intervention components identified in this research should undergo further evaluation, including additional factorial experiments or an RCT that evaluates a package of intervention components.

Declaration of interests

This research was supported by grants 9P50CA143188 and 1K05CA139871 from the National Cancer Institute to the University of Wisconsin Center for Tobacco Research and Intervention and by the Wisconsin Partnership Program. This work was carried out in part while T.R.S.

was a Primary Care Research Fellow supported by a National Research Service Award (T32HP10010) from the Health Resources and Services Administration to the University of Wisconsin Department of Family Medicine. W.-Y.L. is also supported by NSF grant DMS-1305725. L. M.C. is also supported by NIH grants P50DA10075 and R01DK097364. J.W.C. is supported by Merit Review Award 101CX00056 from the US Department of Veterans Affairs. The authors have received no direct or indirect funding from, nor do they have a connection with, the tobacco, alcohol, pharmaceutical or gaming industries or anybody funded substantially by one of these organizations. W.-Y.L. is supported partially by a grant from Eli Lilly and Company for research that is unrelated to smoking or tobacco dependence treatment.

Clinical Trial Registration: NCT01122238

Acknowledgements

We would like to acknowledge the staff at Aurora Health Care, Deancare and Epic Systems Corporation for their collaboration in this research. We are very grateful to the staff and students at the Center for Tobacco Research and Intervention in the University of Wisconsin School of Medicine and Public Health for their help with this research.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web site:

Table S1 Experimental Conditions

Table S2 Overview of the Content Covered in Behavioral Reduction Counseling

Table S3 Overview of the Content Covered in Motivational Interviewing

Table S4 Regression Analyses for Percent Change in Cigarettes Smoked per Day (CPD) in the Past Week at 26 Weeks Under Different Missing Data Assumptions