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A smoking cessation intervention for the methadone-maintained

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ABSTRACT

Aim To test, in combination with the nicotine patch, the incremental efficacy of a maximal, tailored behavioral treatment over a minimal treatment for smoking cessation. **Design** Randomized clinical trial with 6-month follow-up. **Setting** Five methadone maintenance treatment centers in Rhode Island. **Participants** Three hundred and eighty-three methadone-maintained smokers. **Intervention** Participants were assigned randomly to nicotine patch (8–12 weeks) plus either (1) a baseline tailored brief motivational intervention, a quit date behavioral skills counseling session and a relapse prevention follow-up session (Max) or (2) brief advice using the National Cancer Institute's 4 As model (Min). An intent-to-treat analysis with those lost to follow-up assumed to smoke was used. **Measurements** Carbon monoxide (CO)-confirmed 7-day point smoking cessation prevalence at 3 and 6 months, and self-reported numbers of cigarettes smoked per day. **Findings** Participants had a mean age of 40 years, were 53% male, 78% Caucasian, smoked 26.7 (± 12.2) cigarettes/day and had a mean methadone dose of 95.5 mg. At 3 months, 317 (83%) were reinterviewed; at 6 months, 312 (82%) were reinterviewed. The intent-to-treat, 7-day point prevalence estimate of cessation was 5.2% in the Max group and 4.7% in the Min group ($P = 0.81$) at 6 months. In logistic models with treatment condition, age, gender, race, Fagerström Test for Nicotine Dependence and cigarettes per day as covariates, males were more likely to be abstinent at 3 months (OR 4.67; $P = 0.003$) and 6 months (OR 4.01; $P = 0.015$). **Conclusion** A tailored behavioral intervention did not increase quit rates over patch and minimal treatment. Smoking cessation rates in methadone-maintained smokers are low, with men having greater success.

Keywords Methadone maintenance, motivational intervention, smoking cessation.

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INTRODUCTION

Cigarette smoking rates among methadone-maintained opiate-dependent people far exceed the general population [1,2]. Across studies, at least 80% of methadone patients smoke, despite being well aware of the health risks of smoking and having motivation to quit [3,4]. Given the significant rates of tobacco-related morbidity and mortality in long-term narcotic users, finding effective interventions in stabilized methadone maintenance treatment (MMT) patients who are not experiencing the difficulties of opiate withdrawal may be an important goal of public health efforts [5,6].

In the general population, nicotine replacement has demonstrated greater efficacy than placebo in helping individuals to quit smoking [7,8]. Multi-component interventions, which include nicotine replacement plus behavioral therapies, have generally had superior outcomes and are well suited for highly dependent smokers [8–10] such as those in methadone maintenance treatment.

None the less, there is only a single randomized trial of a combined intervention among MMT patients, a population with high levels of nicotine dependence and low access to nicotine replacement. Shoptaw *et al.* tested recently relapse prevention and contingency management for optimizing smoking cessation during 12 weeks of nicotine replacement therapy in this population [11]. All study participants met with research staff three times a week for carbon monoxide (CO) testing, and the partic-

ipants in the relapse prevention group received up to 12 intervention sessions. Methodologically, this high number of interactions makes the study difficult to generalize.

None the less, during treatment those receiving contingency management had higher rates of smoking abstinence (25–33% versus 12% for patch only), but these effects were not maintained following the removal of contingencies. At 6 months, only 2–10% of participants had ceased smoking in both groups.

In the current study, we tested another form of combined behavioral/pharmacological treatment for methadone-maintained smokers. We utilized a higher and longer dose of nicotine replacement than Shoptaw *et al.* for the heaviest methadone-maintained smokers [11]. Our choice of a brief, individually tailored motivational therapy as our behavioral intervention component was based on the growing use of this method [12] and the success of this technique in other populations with substance use disorders [13,14]. The purpose of this study was to test, in combination with the nicotine patch, the incremental efficacy of a tailored behavioral treatment over a minimal treatment for smoking cessation among methadone-maintained people.

METHODS

Case identification and recruitment

Between February 2002 and May 2004, methadone-maintained smokers were recruited at five methadone maintenance treatment program (MMTP) clinics in the greater Providence, RI, area for a randomized clinical trial to test the incremental efficacy of an individually tailored behavioral treatment in combination with the nicotine patch. Individuals who expressed an interest in the study met briefly with a research assistant (RA) who explained the study and assessed eligibility. To be eligible for the study, participants were: (1) aged 18 years or older, (2) current, regular smokers of at least 10 cigarettes per day for the past 3 months, (3) English-speaking and (4) enrolled in MMTP for at least 6 months. However, participants did not have to agree to try to quit smoking or to use the nicotine patch.

Procedure

Initial assessment

The RA first administered the Rhode Island Hospital IRB-approved informed consent procedure. The participants then completed a questionnaire assessing socio-demographic information, aspects of smoking history (e.g. years, quit attempts, etc.) and methadone dose and duration. The RA also assessed the participants' CO concentration via a breath sample using the Bedfont EC_{50} Micro III Smokelyzer (Kent, UK). The time to complete the introduction, consent, questionnaire and breath sample averaged 45 minutes.

After a participant completed the baseline questionnaire, the RA introduced the participant to one of two PhD-level study interventionists. At this point, randomization and group assignment occurred. The study interventionist then performed either the minimal or the maximal treatment. At the end of this first session, all participants were offered the opportunity to set a quit date. This date could be as soon as the following day or as many as 90 days later. Participants were instructed not to smoke on their quit date, and were told they would receive their nicotine patches at the quit date appointment. Follow-up research assessments were performed at 1, 3 and 6 months after study enrollment by research assistants blinded to participant group assignment. CO breath samples were taken at all follow-up interviews where the participant reported not smoking.

Methadone clinic staff were also made aware of the study and were free to encourage participants to try to quit smoking or reinforce abstinence at visits. However, no specific training was provided to the MMTP staff with respect to addressing smoking cessation at regular MMTP visits.

Patch dose

The patch dose (Nicoderm®; GlaxoSmithKline, Pittsburgh, PA, USA), was based on the participant's baseline smoking level. For participants smoking up to one pack a day, the following 8-week protocol was as follows: 21 mg for the first 4 weeks, 14 mg for the next 2 weeks and 7 mg for the final 2 weeks. For participants smoking at least two packs a day, the following 12-week protocol was followed: 42 mg for the first 4 weeks, 35 mg for weeks 5 and 6, 28 mg for weeks 7 and 8, 21 mg for weeks 9 and 10, 14 mg for week 11 and 7 mg for the last week. For participants smoking between one and two packs a day, the 8-week protocol was initiated. Patches were given in 1-month supplies; participants needed to refill these supplies on a monthly basis.

Interventions

Minimal treatment

Participants assigned to this group received up to two visits, an individual session with a study interventionist at the end of their baseline interview and on the quit date (if they chose to set one). At the first session, participants received advice to quit smoking and self-help materials. The advice to quit smoking message (≤ 3 minutes) followed the National Cancer Institute's 4 As model for smoking cessation counseling [15]. This is a simple smoking cessation strategy with four discrete components: (1) *A*sk about smoking at every opportunity; (2) *A*dvise the

participant to quit smoking; (3) *A*ssist the participant in quitting; and (4) *A*rrange follow-up. The study interventionist was trained to provide the brief intervention, based on the 4 As in a standardized fashion. Participants were then asked if they were interested in setting a quit date. On this quit date, the interventionist dispensed the patch and described its proper use, i.e. placement, use of one patch a day, importance of not smoking while using the patch and tapering of patches. Interventionists described potential side effects and participants were provided with a handout specifying the health benefits related to quitting smoking. Participants not setting a quit date received only the initial session with the study interventionist.

Maximal treatment

Participants in this condition received up to three visits: (a) an initial motivational interviewing session with the study interventionist; (b) a session with the study interventionist on the quit date (if one was set) for skills training; and (c) a follow-up session. For participants who set a quit date within the first 3 months, this follow-up session focused on reinforcing skills training. For participants who did not set a quit date, the follow-up session was linked to the 1-month follow-up assessment interview and was designed to enhance the participant's motivation to quit. All participants were able to contact study staff throughout the study if they had any problems with the patch or withdrawal symptoms.

Initial motivational session

The motivational intervention was intended to minimize participant resistance and increase response-efficacy and self-efficacy by providing a set of alternative response strategies [12]. The interventionist's role was to raise the participant's awareness of the pros and cons of smoking and to clarify the conflicting motivation governing the decision to change. For participants who lacked motivation to quit smoking, more time was spent on exploring motivation for smoking cessation and on creating cognitive dissonance regarding continued smoking. For more motivated smokers, more time was spent on goal setting and discussing strategies to prepare for quitting smoking.

Information from the participant's breath sample, along with a feedback report culled from the baseline interview and including information regarding the participant's level of motivation, level of smoking, prior quit attempts, environmental factors and perceived vulnerability to smoking-related illnesses (from the baseline assessment), served as the basis for the 30-minute motivational intervention session. Feedback took the form of a dialogue between the study interventionist and the participant designed to increase dissonance between the individual's current behavior and the target behavior. The goals of the session were to: (1) discuss perceived vulnerability to smoking-related illnesses and the role this perception plays in smoking and in quitting; (2) elucidate any cognitive dissonance regarding continued smoking; (3) help the participant re-evaluate the role smoking plays in their life; (4) increase self-efficacy; and (5) set goals regarding changes in smoking behavior (e.g. cutting down, nicotine fading, setting a quit date). The participant was given a copy of this feedback report.

Quit date

Participants met with their study interventionist on their scheduled quit date. During this cognitive–behavioral skills training visit (15–30 minutes) the interventionist reinforced quitting efforts, described proper use of the patch and potential side effects and answered any questions the participant posed. Additionally, the session focused on setting and developing concrete strategies for meeting goals. The session was guided in part by a self-help manual, which presented strategies for maintaining smoking abstinence. In addition, cognitive behavioral skills training was emphasized, with a focus on removing barriers to remain abstinent, identifying trigger situations and using stimulus control techniques to manage trigger situations, managing stress via relaxation, making positive life-style changes (e.g. exercise) and increasing social support for not smoking. Relapse prevention and recovery strategies were also discussed, with an emphasis on identifying high-risk situations for relapse, developing effective strategies for coping in high-risk situations and avoiding the abstinence violation effect in the event of a lapse to smoking.

Follow-up session

Only participants in the maximal treatment condition met with their study interventionist at the time of their 1- or 3-month assessment visit (depending on timing of the quit date). The purpose of this session was to check on proper patch use and side effects, to reinforce abstinence and if the participant experienced difficulty quitting smoking to problem-solve and encourage setting another quit day for themselves.

Participants who were *not* ready to quit and therefore did not set a quit date received an in-person follow-up visit with the study interventionist concurrent with their 1-month follow-up assessment. This visit was targeted to the participant's level of motivation for smoking cessation. Counseling focused on reactions to the initial motivational intervention session. The counseling session (15 minutes) presented the idea that quitting smoking is a long-term process, and that even though the participant was not motivated currently to quit smoking it could be helpful to them to learn about specific methods and coping skills for quitting, or to consider taking some interim steps by changing their smoking pattern or their

life-style so as to increase the chances of quitting in the future. Thus, the cognitive–behavioral skills were offered in a more informational manner as strategies that may be utilized once the participant becomes ready to quit, as opposed to the implementation-oriented approach taken during a quit date. Participants were also offered suggestions about interim steps which they might consider, such as gaining knowledge about trigger situations, gradually fading the number of cigarettes smoked, beginning to exercise or using stress management techniques. For participants who were closer to taking action, this session focused upon setting goals, especially setting a quit date and developing concrete strategies for meeting those goals.

For those participants who became ready to set a quit date and use the patch within the next 30 days progress towards cessation was reviewed, and a quit date with the interventionist was then scheduled. This quit date session proceeded as noted above. If participants did not wish to set a quit date, they were informed that that they had until their 3-month follow-up to call the study RA to schedule a quit date appointment. If they did not call to schedule a quit date, this 1-month session was the final treatment contact point.

Therapist adherence

A modification of the Motivational Interviewing Skill Code 1.0 (MISC) was used both to train the two study interventionists, provide structured feedback, to monitor motivational interviewing skills and document interventionist adherence to MI during biweekly supervision [16]. We were not interested in evaluating psychotherapy process issues [17]. Therefore, we modified the MISC 1.0 in the following ways to address these goals (see [18] for similar decision rules). As recommended, we used a starting point of a score of 4 on a scale of 1–7 to indicate the presence of MI skills. Scores below a 4 suggested that the interventionist was not exhibiting MI skills. However, we coded only those codes relevant to the interventionist's behavior (six global therapist rating scales and two global interaction rating scales from the first pass), and did not code elements related to client behavior or specific interventionist behaviors (e.g. second or third pass codes). In addition, we listened to the full session and not only a 20-minute section of the session to allow a general assessment of the interventionist's skills, in keeping with recent work highlighting the value of attending to the full session to capture key aspects of MI, such as change talk [19] and the value of measuring interventionist behavior alone to assess treatment integrity [20].

Three raters, trained in MI and with established inter-rater reliability (mean intraclass coefficients range: 0.40–0.66), coded a 10% random sample of both control and intervention sessions (all sessions were audiotaped). Control sessions were coded 1 if no MI elements existed in the session, or 2 if some MI elements existed. Mean scores for control sessions were 1.13 (SD 0.35), 1.25 (SD 0.46) and 1.25 (SD 0.46) for the three raters. Intervention sessions were coded on the seven-point MISC scale. Scores ranged from 4 to 7 for all three raters; mean scores across the eight global scales for the intervention sessions were 5.65 (SD 0.54), 5.54 (SD 0.51) and 5.82 (SD 0.78) for the three raters.

Variables

The time-line follow-back (TLFB) technique [21] assessed smoking and nicotine replacement therapy (NRT) use at follow-up. TLFB data were collected at both the 3- and 6-month assessments. Some participants lost to follow-up at 3 months were assessed at 6 months; they were asked to provide a complete record of daily smoking and NRT use going back to the baseline interview.

Our primary outcome was defined as CO confirmed [(scores < 8 parts per million (p.p.m.)] self-reported abstinence on the 7 days immediately prior to the 3- and 6-month assessments. CO as breath samples was analyzed using the Bedfont EC_{50} Micro III Smokealyzer. We also present data using 7-day self-report (not confirmed by CO testing) abstinence. We augmented our primary analysis with two secondary outcomes, setting a specific quit day (yes or no) and time (number of days) to first cigarette after the quit day. Other covariates included age in years, gender, race, average number of cigarettes per day during the 28 days prior to baseline assessment, age at which participants started smoking daily and readiness to change smoking behavior using a 10-point ladder [22]. STATA version 8.2 was used for all analyses [23].

Analysis plan

Our original power estimates assumed post-treatment abstinence rates of 0.04 and 0.12 in the control and intervention groups, respectively. Using the arcsine transformation of P described by Cohen [24], this difference represents a standardized effect of approximately 0.30. Following Cohen, we estimated that $n_1 = n_2 = 180$ would be sufficient to detect a difference this large with power = 0.80 and the two-tailed probability of Type I error = 0.05.

Our primary analysis used an intent-to-treat approach, with missing individuals presumed to have continued or resumed smoking. We report means and percentages to describe the sample. We used t-tests for differences in means and Pearson's χ^2 of independence to compare treatment groups on background characteristics and smoking history variables. We present contingency tables and associated statistics to describe and test for bivariate effects of intervention on our primary outcome variables. Logistic regression was used to estimate the adjusted effect of treatment controlling for potential

confounds. We present the median number of days to first cigarette following the quit date, and use the log-rank test to compare survivor functions by treatment assignment. All analyses adopted an alpha of 0.05. Tests of significance were two-tailed.

RESULTS

Most participants were Caucasian (78.3%), 53.0% were male and they averaged 40.1 (± 8.4) years of age (Table 1). The mean age at which participants started smoking regularly was 16.3 (± 5.1) years. During the 28 days prior to baseline, participants smoked an average of 26.7 (± 12.2) cigarettes per day. The mean score on the readiness to change ladder was 6.5 (± 1.5) on the readiness to change ladder; 282 participants had scores of 6, 'I plan to quit smoking in the next 6 months', or higher. The follow-up rate at 3 and 6 months were 82.8% and 81.5%, respectively; 289 (75.5%) of the participants completed both 3- and 6-month follow-ups, 28 (7.3%) completed only the 3-month follow-up, 23 (6.0%) completed the 6-month but were not assessed at the 3-month follow-up and 43 (11.2%) were lost to follow-up at both 3 and 6 months; 340 (88.8%) provided time-line follow-back data at either 3 or 6 months.

The treatment groups did not differ significantly with respect to demographic characteristics, methadone dose at baseline, mean age at which daily smoking was initiated, the average number of cigarettes smoked per day prior to baseline or the number of days on which they used NRT during the follow-up period (Table 1). Participants randomized to maximum intervention had higher mean scores on the readiness to change ladder (6.6 versus 6.3; $P = 0.05$). There was no evidence of differential subject loss; follow-up rates were similar in both treatment arms at 3- and 6-month follow-ups. Participants receiving maximal treatment attended, on average, 2.23 MI sessions; control participants attended 1.88 sessions.

Overall rates of self-reported and CO confirmed 7-day smoking abstinence are given in Table 2. Sixty-five

Table 1 Background characteristics by treatment condition.

	Total (n = 383)	*Maximum (n = 191)*	*Minimum (n = 192)*	*t (P)*
Age	40.1 (± 8.4)	39.9 (± 8.3)	40.3 (± 8.6)	0.47 (0.633)
Cigs/day	26.7 (± 12.2)	26.3 (± 13.3)	27.2 (± 10.9)	0.68 (0.494)
Methadone dose (mg)	95.2 (± 44.4)	94.9 (± 41.6)	95.6 (± 47.1)	0.14 (0.888)
Age reg. smoke	16.3 (± 5.1)	16.1 (± 5.2)	16.4 (± 5.1)	0.75 (0.452)
RTC ladder	6.5 (± 1.5)	6.6 (± 1.5)	6.3 (± 1.5)	1.97 (0.050)
				χ^2 (*P*)
% Male	203 (53.0%)	99 (51.8%)	104 (54.2%)	0.21 (0.647)
% White	300 (78.3%)	145 (75.9%)	155 (80.7%)	1.31 (0.253)
% Completed 3 months	317 (82.8%)	162 (84.8%)	155 (80.7%)	1.12 (0.290)
% Completed 6 months	312 (81.5%)	156 (81.7%)	156 (81.3%)	0.01 (0.915)

Table 2 Seven-day abstinence at 3- and 6-month follow-ups by intervention.

7-Day abstinence outcome	*Total*	*Maximum*	*Minimum*	χ^2*(P =)*	*OR (95% CI)*
Observed at 3 months (*n* = 317)					
Self-reported (3 months)					
Yes	65 (20.5%)	30 (18.5%)	35 (22.6%)	0.80 (0.371)	0.78 (0.45–0.35)
CO_2 confirmed (months)					
Yes	27 (8.5%)	11 (6.8%)	16 (10.3%)	1.27 (0.260)	0.63 (0.28–0.41)
Observed at 6 months (*n* = 312)					
Self-reported (6 months)					
Yes	35 (11.2%)	16 (10.3%)	19 (12.2%)	0.28 (0.590)	0.82 (0.41–0.67)
CO_2 confirmed (6 months)					
Yes	19 (6.6%)	10 (6.4%)	9 (5.8%)	0.06 (0.813)	1.12 (0.44–0.83)
Intent-to-treat (*n* = 383)					
CO_2 confirmed (3 months)					
Yes	27 (7.1%)	11 (5.8%)	16 (8.3%)	0.97 (0.325)	0.67 (0.30–0.49)
CO_2 confirmed (6 months)					
Yes	19 (5.0%)	10 (5.2%)	9 (4.7%)	0.06 (0.805)	1.12 (0.45–0.83)

(20.5%) participants reported they had not smoked cigarettes in the 7 days immediately prior to 3-month assessment; only 27 were confirmed abstinent by CO testing. Only 35 (11.2%) of the participants observed at 6 months said they had not smoked a cigarette in the 7 days prior to assessment; of these only 19 were confirmed abstinent by CO testing.

While 7-day abstinence rates (especially CO confirmed abstinence) were low, we observed large and statistically significant reductions in cigarette use during the course of the study. To illustrate these reductions we compared the average number of cigarettes smoked in the 28 days prior to baseline and 3- and 6-month follow-ups. While participants averaged 26.7 cigarettes per day on the 28 days prior to baseline, they averaged only 9.7 cigarettes per day on the 28 days prior to the 3-month assessment, a reduction (64%) that was statistically significant ($t_{317} = 21.03$, $P < 0.001$). Average daily smoking was slightly higher at 6 months than at 3 months (11.4 cigarettes per day on the 28 days prior to 6-month assessment) but remained significantly lower than at baseline ($t_{312} = 20.01$, $P < 0.001$). The 309 participants who set a quit date used nicotine replacement therapy on an average of 42.98 (± 23.37; median = 45) days. Daily smoking was associated strongly with nicotine replacement therapy; participants averaged 10.23 fewer cigarettes on days when a 7 mg or stronger patch was used.

The percentage of participants who set a quit date did not vary significantly ($\chi^2 = 0.05$, $P = 0.815$) by treatment assignment; 81.2% of those randomized to intervention set a quit day and 80.2% of those randomized to control set a quit date.

Table 2 gives comparisons of 7-day smoking abstinence rates by treatment assignment. We present analyses using only the observed data with 317 and 312 observations at 3 and 6 months, respectively. Additionally we provide an intent-to-treat analysis ($n = 383$) in which observations lost to follow-up were assumed to have continued or resumed smoking. Observed bivariate treatment effects were substantively small, not statistically significant and not directionally consistent (Table 2). At 3 months, participants randomized to maximal treatment (6.8%) were slightly but not significantly ($\chi^2 = 1.27$, $P = 0.260$) less likely to have CO confirmed 7-day abstinence than controls (10.3%). The pattern for self-reported abstinence at 3 months is substantively similar (Table 2). Rates of self-report and CO confirmed smoking abstinence at 6 months were not different between the two treatment groups (Table 2). Participants randomized to intervention were slightly more likely to have CO confirmed 7-day abstinence (6.4% versus 5.8%), although they were slightly less likely to self-report 7-day abstinence (10.3% versus 12.2%).

Logistic regression models estimating the adjusted effects of intervention on 7-day CO confirmed smoking abstinence are given in Table 3. The results are substantively and statistically consistent with the bivariate analysis. The estimated effect of intervention on the odds of 7-day CO confirmed abstinence at three months was 0.61 ($P = 0.241$) indicating that those randomized to intervention were slightly less likely to be abstinent than controls. Those randomized to intervention were slightly more likely to have CO confirmed 7-day abstinence at 6-months (OR = 1.13, $P = 0.797$). Gender was a statistically significant predictor of CO confirmed smoking abstinence; at both 3 and 6 months, males were estimated to be more than four times more likely to be abstinent than females.

We used survival analysis to test for intervention effects on number of days to first cigarette following the quit date. This analysis was limited to the 309 participants who set a quit date. On average, participants were followed for 165.5 (median = 175) days. Fifteen (4.9%) of the 309 participants who set a quit day reported 0 smoking days during the entire follow-up period. The observed median number of days to first cigarette was slightly shorter among those randomized to intervention (4 days) than controls (4.5 days), although the survival function did not differ significantly by treatment group (log-rank $\chi^2 = 1.64$, $P = 0.200$).

Table 3 Logistic regression models testing the effect of intervention and selected covariates on the odds of 7-day CO_2 confirmed smoking abstinence at 3- and 6-month follow-ups.

	3 Months (n = 317)			*6 Months (n = 312)*		
Predictor	*OR*	*P*	*95% CI*	*OR*	*P*	*95% CI*
Age	1.03	0.306	0.98–1.08	1.00	0.872	0.94–1.05
Gender (male)	4.67	0.003	1.68–12.98	4.01	0.015	1.31–12.78
Race (Caucasian)	0.38	0.035	0.16–0.93	1.31	0.652	0.41–4.22
Cigs/day	1.00	0.797	0.96–1.03	0.97	0.175	0.92–1.02
Age daily smoking	1.00	0.987	0.91–1.09	1.02	0.709	0.93–1.12
RTC ladder	0.99	0.917	0.75–1.29	1.08	0.641	0.78–1.49
Condition (maximun)	0.61	0.241	0.26–1.40	1.13	0.797	0.44–2.94

DISCUSSION

In this, the second large-scale randomized trial of smoking cessation among methadone-maintained people, we found extremely low quit rates both at the end of treatment and 3 months later. We evaluated a three-session, brief tailored motivational intervention in combination with high-dose nicotine replacement and found that it produced quit rates no different from a minimal behavioral intervention plus nicotine replacement. Our findings are consistent with the perception that tobacco smoking may be more difficult to quit than opiate use [25].

In the only other randomized controlled trial among methadone-maintained people, 12 weeks of contingency management therapy (plus nicotine replacement) assisted twice as many participants to achieve smoking abstinence compared to a no-contingency condition during treatment [11]. During the follow-up period, however, the erosion of treatment effects were significant. Our brief intervention and Shoptaw's more intensive contact within a contingency management program produced quit rates at 6 months that were nearly identical. In our sample of 383, only 15 people quit and remained quit during the entire follow-up period, an astonishingly low percentage of 3.9%. The challenge of achieving prolonged smoking cessation among the methadone-maintained suggests that novel strategies will be needed to enhance outcomes in this understudied and difficult-to-treat population [26].

The difficulty of quitting smoking during a cessation program may have broader implications for methadone-maintained individuals. Previous studies have documented both retrospectively and prospectively that those who fail to achieve tobacco abstinence are more likely to use cocaine than those who stop smoking successfully [27–30]. This suggests that there may be important interactions between psychoactive substances at the cellular level, particularly those substances which share nicotine brain pathways [31,32], and thus continued basic science research is critical.

Most study participants set a quit date and reported stopping cigarettes for at least 24 hours, which is in keeping with the relatively high baseline readiness to quit scale scores. Extrapolating from other trials with substance users, we included a 'booster session' consisting of relapse prevention techniques during the period of pharmacotherapy [14]. While participation in the therapy sessions was high, the behavioral counseling added neither short- nor long-term benefit compared to minimal advice plus nicotine replacement. Therefore, the need for and optimal timing of multiple behavioral therapy sessions (whatever the content) remains to be determined for this population.

Participants were able to reduce their cigarette use significantly during the intervention. On days when participants used nicotine replacement they smoked at notably lower levels, providing support for the use of nicotine replacement therapy. Although participants did not return to baseline levels of smoking following the intervention, average daily smoking was slightly higher at the 6-month assessment compared to the end of treatment.

As in most smoking cessation studies, we used a biological marker to confirm participant self-reports of abstinence. One notable finding in this methadone-maintained population was the discrepancy between self-report and CO confirmation of smoking cessation rates. Across conditions and assessments, participants reported 7-day abstinence rates that were up to 2.5 times the CO confirmed prevalence rates. In future cessation trials with the methadone-maintained, biological monitoring (CO or urine cotinine) is warranted.

Our sample had nearly equal gender representation, and men had significantly better quit rates than women. There was no evidence for an intervention × gender interaction. We do not know the reasons for this gender difference, but we speculate that women in this population may be more likely to have certain characteristics associated with poorer smoking cessation outcomes such as recurrent depression or chronic health problems [33]. Other studies have reported that women respond poorly to nicotine replacement therapy compared to men [34]. Importantly, women who continue to smoke have similar lung cancer and cardiovascular disease mortality to men [10].

There are several limitations to this study. First, although not advertised expressly as a smoking cessation study, it probably attracted those methadone clients most interested in trying to quit. Secondly, there may be distortion in the reports of cigarettes use per day and the lack of biochemical data suggests the need for caution regarding claims of smoking reduction. Finally, future work should examine the factors affecting relationship between level of tobacco smoking and illicit substance use, which in turn may help to elucidate the dynamics of addiction more broadly.

Why is it so difficult for methadone-maintained people to quit smoking? Some studies have implicated methadone as the cause. Several authors have demonstrated that increases in methadone dose lead to increases in smoking, as well as greater tobacco craving and withdrawal symptoms [25,35]. Even if such effects habituate at higher doses of methadone [36], the relationship of methadone to tobacco abstinence is complex [37], and suggests that methadone somehow affects the severity of nicotine dependence. The effects of methadone on the rate and pathway of nicotine metabolism or the sensitivity of nicotine receptors remains understudied.

Alternatively, the reinforcing effects of nicotine, which may include enhancement of cognitive performance, may be more profound among methadone users. In addition, the lives of people with opiate dependence are often stressful [38]; they may be psychologically and socially different from other populations of dependent smokers and smoking may be an important method of blunting stress for this population.

More extensive physiological investigation is necessary to explore the biological basis of methadone-maintained smokers' behavior. Greater understanding of the causes for such low quit rates among opiate dependent smokers is necessary. Before the widespread implementation of smoking cessation programs at methadone maintenance programs can be expected to have success, novel therapeutic approaches will have to be developed.

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References

1. Clarke, J., Stein, M. D., McGarry, K. & Gogineni, A. (2001) Interest in smoking cessation among injection drug users. *American Journal of Addiction*, **10**, 159–166.
2. Chait, L. D. & Griffiths, R. R. (1984) Effects of methadone on human cigarette smoking and subjective ratings. *Journal of Pharmacology and Experimental Therapeutics*, **229**, 636–640.
3. Shadel, W. G., Stein, M. D., Anderson, B. J., Herman, D. S., Bishop, S., Lassor, J. A. *et al.* (2005) Correlates of motivation to quit smoking in methadone-maintained smokers enrolled in a smoking cessation trial. *Addictive Behaviors*, **30**, 295–300.
4. Clemmey, P., Brooner, R., Chutuape, A. M., Kidorf, M. & Stitzer, M. (1997) Smoking habits and attitudes in a methadone maintenance population. *Drug and Alcohol Dependence*, **44**, 123–132.
5. Hser, Y. I., McCarthy, W. J. & Anglin, M. D. (1994) Tobacco use as a distal predictor of mortality among long-term narcotic addicts. *Preventive Medicine*, **23**, 61–69.
6. Engstrom, A., Adamsson, C., Allebeck, P. & Rydberg, U. (1991) Mortality in patients with substance abuse: a follow-up in Stockholm County, 1973–84. *International Journal of Addictions*, **26**, 91–106.
7. Ahluwalia, J. S., McNagny, S. E. & Clark, W. E. (1998) Smoking cessation among inner city African Americans using the nicotine transdermal patch. *Journal of General Internal Medicine*, **13**, 1–8.
8. Fiore, M. C., Kenford, S. L., Jorenby, D. E., Wetter, D. W., Smith, S. S. & Baker, T. B. (1994) Two studies of the clinical effectiveness of the nicotine patch with different counseling treatments. *Chest*, **105**, 524–533.
9. Daughton, D., Susman, J., Sitorius, M., Belenky, S., Millatmal, T., Nowak, R. *et al.* (1998) Transdermal nicotine therapy and primary care. Importance of counseling, demographic, and participant selection factors on 1-year quit rates. *Archives of Family Medicine*, **7**, 425–430.
10. Anthonisen, N. R., Skeans, M. A., Wise, R. A., Manfreda, J., Kanner, R. E. & Connett, J. E. (2005) The effects of a smoking cessation intervention on 14.5 years mortality. *Annals of Internal Medicine*, **142**, 233–239.
11. Shoptaw, S., Rotheram-Fuller, E., Yang, X., Frosch, D., Nahom, D., Jarvik, M. E. *et al.* (2002) Smoking cessation in methadone maintenance. *Addiction*, **97**, 1317–1328.
12. Miller, W. R. & Rollnick, S. (2002) *Motivational Interviewing: Preparing People for Change*, 2nd edn. New York: Guilford Press.
13. Dunn, C., Deroo, L. & Rivara, F. P. (2001) The use of brief interventions adapted from motivational interviewing across behavioral domains: a systematic review. *Addiction*, **96**, 1725–1742.
14. Stein, M. D., Charuvastra, A., Maksad, J. & Anderson, B. J. (2002) A randomized trial of a brief alcohol intervention for needle exchangers (BRAINE). *Addiction*, **97**, 691–700.
15. Manley, M., Epps, R. P., Husten, C., Glyn, T. & Shopland, D. (1991) Clinical interventions in tobacco control. A National Cancer Institute training program for physicians. *JAMA*, **266**, 3172–3173.
16. Miller, W. (2000) *The Motivational Interviewing Skill Code (MISC) Manual*, version 1. Available at: http://casaa.unm.edu/download/misc1.pdf. Accessed 15 February 2001.
17. Moyers, T., Miller, W. & Hendrickson, S. (2005) How does motivational interviewing work? Therapist interpersonal skill predicts client involvement within motivational interviewing sessions. *Journal of Consulting and Clinical Psychology*, **73**, 590–598.
18. Miller, W., Moyers, T., Ernst, D. & Amrheim, P. (2003) *The Motivational Interviewing Skill Code (MISC) Manual*, version 2.0. Available at: http://casaa.unm.edu/download/Miscellaneouspdf. Accessed 29 September 2005.
19. Amrhein, P., Millwe, W., Yahne, C., Palmer, M. & Fulcher, L. (2003) Client commitment language during motivational interviewing predicts drug use outcomes. *Journal of Consulting and Clinical Psychology*, **71**, 862–878.
20. Moyers, T., Martin, T., Manual, J., Hendrickson, S. & Miller, W. (2005) Assessing competence in the use of motivational interviewing. *Journal of Substance Abuse Treatment*, **28**, 19–26.
21. Sobell, L. C. & Sobell, M. B. (1992) Timeline follow-back: a technique for assessing self-reported ethanol consumption. In: Allen, J. & Litten, R. Z., eds. *Measuring Alcohol Consumption: Psychosocial and Biology Methods*, pp. 41–72. New Jersey: Humana Press.
22. Biener, L. & Abrams, D. B. (1991) The contemplation ladder: validation of a measure of readiness to consider smoking cessation. *Health Psychology*, **10**, 360–365.
23. StataCorp (1993) *Stata Statistical Software*, release 8.2. College Station, TX: Stata Corporation.
24. Cohen, J. (1988) *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn. New Jersey: Lawrence Erlbaum Publishers.
25. Story, J. & Stark, M. J. (1991) Treating cigarette smoking in methadone maintenance clients. *Journal of Psychoactive Drugs*, **23**, 203–215.
26. Campbell, B. K., Wander, N., Stark, M. & Holbert, T. (1995) Treating cigarette smoking in drug-abusing clients. *Journal of Substance Abuse Treatment*, **12**, 89–94.

27. Frosch, D. L., Shoptaw, S., Nahom, D. & Jarvik, M. E. (2000) Associations between tobacco smoking and illicit drug use among methadone-maintained, opiate-dependent individuals. *Experimental and Clinical Psychopharmacology*, **8**, 1–7.
28. Shoptaw, S., Jarvik, M. E., Ling, W. & Rawson, R. A. (1996) Contingency management for tobacco smoking in methadone-maintained opiate addicts. *Addictive Behaviors*, **21**, 409–412.
29. Lemon, S. C., Friedmann, P. D. & Stein, M. D. (2003) The impact of smoking cessation on drug abuse treatment outcome. *Addictive Behaviors*, **28**, 1323–1331.
30. Stein, M. D. & Anderson, B. J. (2003) Nicotine and drug interaction expectancies among methadone maintained cigarette smokers. *Journal of Substance Abuse Treatment*, **24**, 357–361.
31. Pontieri, F. E., Tanda, G., Orzi, F. & Di Chiara, G. (1996) Effects of nicotine on the nucleus accumbens and similarity to those of addictive drugs. *Nature*, **382**, 255–257.
32. Reid, M. S., Mickalian, J. D., Delucchi, K. L. & Berger, S. P. (1999) A nicotine agonist, mecamylamine, reduces cue-induced cocaine craving in cocaine-dependent subjects. *Neuropsychopharmacology*, **20**, 297–307.
33. Covey, L. S., Glassman, A. H., Stetner, F. & Becker, J. (1993) Effect of history ofalcoholism or major depression on smoking cessation. *American Journal of Psychology*, **150**, 1546–1547.
34. Perkins, K. A. (2001) Smoking cessation in women: special consideration. *CNS Drugs*, **15**, 391–411.
35. Schmitz, J. M., Grabowski, J. & Rhoades, H. (1994) The effects of high and low doses of methadone on cigarette smoking. *Drug and Alcohol Dependence*, **34**, 237–242.
36. Stark, M. J. & Campbell, B. K. (1993) Cigarette smoking and methadone dose levels. *American Journal of Drug and Alcohol Abuse*, **19**, 209–217.
37. Spiga, R., Schmitz, J. & Day, J. (1998) Effects of nicotine on methadone self-administration in humans. *Drug and Alcohol Dependence*, **50**, 157–165.
38. Hayaki, J., Stein, M. D., Lassor, J. A., Herman, D. S. & Anderson, B. J. (2005) Adversity among drug users: relationship to impulsivity. *Drug and Alcohol Dependence*, **78**, 65–71.

