

## ORIGINAL INVESTIGATION

# Early Quit Days Among Methadone-Maintained Smokers in a Smoking Cessation Trial

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## ABSTRACT

**Introduction:** Methadone maintenance treatment (MMT) patients have an exceedingly high prevalence of tobacco use, and interventions that have been specifically developed for this vulnerable subpopulation have struggled to attain even modest rates of cessation. A significant barrier has been an inability to initiate a quit attempt early in the treatment process and adherence to treatment.

**Methods:** This study examined the extent to which self-efficacy, medication adherence, and other demographic and smoking variables predicted an early quit day in a sample of MMT smokers ( $n = 315$ ) enrolled in a smoking cessation pharmacotherapy trial. Using logistic regression, we estimated the association of having an early quit day—24 hr without smoking during the first month of treatment.

**Results:** Only 35.2% of participants reported a successful early quit day. The likelihood of an early quit day increased significantly (odds ratio [OR] = 1.39, 95% CI = 1.04–1.86,  $p < .05$ ) with education level and if a quit attempt was made in the past year (OR = 2.27, 95% CI = 1.33–3.87,  $p < .01$ ). Compared to the placebo arm, those randomized to either nicotine replacement therapy (OR = 3.25, 95% CI = 1.30–8.10,  $p < .01$ ) or varenicline (OR = 3.16, 95% CI = 1.26–7.92) were significantly more likely to have an early quit day. The likelihood of an early quit day was also positively associated with adherence to the medication protocol (OR = 2.05, 95% CI = 1.52–2.76).

**Conclusions:** Difficulty in achieving an early quit attempt may help explain the very low cessation rates found in studies of MMT smokers.

## INTRODUCTION

Despite decades of tobacco use decline in the United States, significant health disparities in smoking prevalence and tobacco-related illnesses exist among certain subpopulations of smokers (Fiore et al., 2008). Substance abusers, particularly those who are opioid dependent and undergoing methadone maintenance treatment (MMT), are one such group. Studies have shown that up to 85%–98% of individuals involved in MMT treatment smoke cigarettes, which is more than three times the rate of the general population (Clarke, Stein, McGarry, & Gogineni, 2001; Richter, Gibson, Ahluwalia, & Schmelzle, 2001). A nicotine/methadone interaction has been proposed as a likely explanatory feature of the high rate of smoking in MMT populations (see review by Zirakzadeh, Shuman, Stauter, Hays, & Ebbert, 2013). The interaction between methadone and nicotine has been shown to decrease both opioid and nicotine withdrawal, increase the pleasurable effects of each substance, and

decrease methadone metabolism resulting in a more extended and enhanced opioid experience (Zirakzadeh et al., 2013). Tobacco smokers who are receiving MMT are known to be at high risk for developing tobacco-related illnesses and have a mortality rate that is four times greater than their nonsmoking MMT peers (Hser, McCarthy, & Anglin, 1994).

Consequently, there has been considerable interest in targeting MMT smokers with cessation interventions that can potentially be incorporated into MMT. Yet, all of the smoking cessation pharmacotherapies that have been tested in opioid-dependent persons have far lower quit rates (Mooney et al., 2008; Okoli et al., 2010; Reid et al., 2008; Shoptaw et al., 2002; Stein et al., 2006) than those reported in trials of nondrug users (Hurt et al., 1994; Mooney et al., 2008; Okoli et al., 2010; Reid et al., 2008; Shoptaw et al., 2002; Stead et al., 2008; Stein et al., 2006). Over the last two decades, there have been four fully powered randomized clinical trials (RCTs) involving smoking cessation interventions specifically with MMT smokers (Haug,

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Svikis, & Diclemente, 2004; Shoptaw et al., 2002; Stein et al., 2006, 2013; Story & Stark, 1991).

The four existing smoking cessation RCTs that have focused on MMT populations have had poor long-term outcomes. In Shoptaw et al. (2002), four-group trial testing NRT, relapse prevention plus NRT, contingency management plus NRT, and all three treatments combined, 12-month carbon monoxide (CO)-confirmed abstinence rates were below 10% in all four groups and there were no significant treatment group differences found. In the trial by Stein et al. (2006) comparing Motivational Interviewing (MI) plus NRT to brief advice and patch, the intent-to-treat CO-confirmed 7-day point prevalence estimate of cessation were 5.2% in the MI group and 4.7% in the brief advice group at 6 months. Subsequent trial by Stein et al. (2013) testing NRT, varenicline, and varenicline placebo also showed poor rates of CO-confirmed 7-day abstinence rates at 6-month follow-up (5.4%) and there were no treatment group differences found (varenicline group abstinence = 3.7%, placebo 2.2%, and NRT 8.3%). Similarly, in the trial by Haug et al. (2004), there were no treatment group difference between the Motivational Enhancement Therapy group and the standard care control in abstinence rates at follow-up (1–3 months).

Findings from these RCTs underscore the challenge of achieving acceptable rates of cessation at follow-up. Despite promising rates of abstinence at the conclusion of treatment, the rate of cessation at 6 or more months of follow-up in such studies has not gone beyond 6% irrespective of the treatments being tested (Dunn et al., 2010). A number of factors have been examined as possible contributors to the poor rate of smoking cessation among MMT patients including the high comorbidity of mental health problems and nonopioid substance use among MMT patients (Dunn et al., 2010; Rosen, Smith, & Reynolds, 2008; Story & Stark, 1991).

### Quit Initiation and Treatment Adherence

An obvious precursor of successful long-term smoking cessation is whether an individual initiates a period of abstinence during treatment. Such *quit attempts* or *quit initiations*, as they are known in the smoking cessation literature, are a fundamental first step in achieving smoking cessation (Fiore et al., 2008; Haug et al., 2004). Logically, individuals who set a quit day and have success in not smoking for at least 24hr are more likely to achieve abstinence at follow-up (Fiore et al., 2008). Studies that have examined the initial period of tobacco abstinence have shown that 60% of all relapses occur within the first 2 weeks (Garvey, Bliss, Hitchcock, Heinhold, & Rosner, 1992) of a quit attempt and initiating a quit attempt is a robust predictor of smoking abstinence at follow-up (Hajek, Tønnesen, Arteaga, Russ, & Tonstad, 2009; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). If smokers in MMT are unable to achieve even 1 day of abstinence, prolonged cessation will remain out of reach. Quit initiation is an area that has not been well studied among MMT smokers. As noted previously, the existing RCTs of smoking cessation among MMT populations report on longer term follow-up outcomes and do not emphasize the early stages of the quitting in their analyses (Haug et al., 2004; Shoptaw et al., 2002; Stein et al., 2006, 2013), which will be examined in the current investigation.

Furthermore, the extent to which an individual adheres to smoking cessation treatment medications has also been shown to be a critical factor in determining successful cessation among

smokers (Blak, Wilson, Metcalfe, Maguire, & Hards, 2010; Catz et al., 2011, Cummings, Hyland, Ockene, Hymowitz, & Manley, 1997, Halperin et al., 2009, Lam, Abdullah, Chan, & Hedley, 2005, Piper et al., 2009; Shiffman, Sweeney, Ferguson, Sembower, & Gitchell, 2008). In studies of MMT smokers, poor medication adherence has been identified as a significant barrier to successfully quitting (Frosch, Nahom, & Shoptaw, 2002; Mooney et al., 2008; Richter et al., 2001; Stein et al., 2006, 2007).

In our current study, we surmise that the poor smoking cessation treatment outcomes of MMT smokers may be a consequence of problems in initiating an early quit attempt and adhering to the treatment medication and we seek to explore this gap in the MMT smoker literature. In the general smoking literature, there has been a significant amount of research focusing on identifying the most salient predictors of quit attempts (see Vangeli, Stapleton, Smit, Borland, & West, 2011 for review). In addition to demographic and smoking severity characteristics, an individual's self-efficacy about quitting has been linked to quit attempts (Vangeli et al., 2011). Quitting self-efficacy, or an individual's belief in their ability to perform the behaviors that will lead to quitting (Gwalter et al., 2009), has been shown to be predictive of quit initiation and cessation at follow-up (Vangeli et al., 2011).

Due to the fact that MMT smokers are a relatively understudied group, the impact of pretreatment self-efficacy on quit initiation has also not been well understood. Considering the difficulty in achieving prolonged abstinence among MMT smokers, investigating the role of self-efficacy on quit initiation can potentially elucidate the ways that smoking cessation treatment can be enhanced for MMT smokers. Therefore, our study aims focus on predictors of an early quit attempt. We utilize baseline and early treatment outcome data from a three-group randomized controlled trial testing the efficacy of varenicline against varenicline placebo and NRT (Stein et al., 2013). We will describe the incidence of early quit days and examine quitting self-efficacy, medication adherence, and other demographic and smoking variables as predictors of successful quit initiation. We hypothesize that greater quitting self-efficacy will significantly predict quit initiation in our sample of MMT smokers.

## METHODS

This study uses data from a three-group RCT of varenicline (Chantix), varenicline placebo, and combination nicotine replacement patches plus *ad libitum* nicotine rescue gum (Stein et al., 2013). The data of 315 methadone-maintained cigarette smokers from nine methadone treatment programs in Rhode Island were used in the current analysis. Inclusion criteria were (a) 18 years of age or older, (b) current, regular smoker (at least 10 cigarettes per day for the past 3 months), (c) speak English, (d) methadone treatment for at least 1 month, and (e) willingness to set a smoking quit date within a week of medication initiation. Participants were excluded if they currently (a) were involved in another smoking cessation treatment (pharmacotherapy or behavioral), (b) used smokeless tobacco, (c) were pregnant or nursing, or (d) had a severe psychiatric condition that would interfere with treatment (e.g., schizophrenia or other psychotic disorder, bipolar disorder, suicidal ideation).

## Procedures

Study advertisements were posted at the nine participating clinics that were located in Southeastern New England. Participants were recruited directly by research staff in the methadone clinics during dosing hours. Of a total of 767 individuals screened for the study, 284 were ineligible (Stein et al., 2013). In total, 483 individuals were eligible for the study. Participants did not differ significantly from those ineligible and those not enrolled based on age, gender, race or ethnicity, or mean cigarettes per day. One hundred fifty-two eligible individuals did not attend the initial study visit; 331 individuals enrolled in the protocol. An additional 16 individuals were excluded, most often for not completing the baseline visit.

The final sample consisted of 315 persons who were randomized (3:1:3) to varenicline ( $n = 137$ ), placebo ( $n = 45$ ), and combination nicotine replacement ( $n = 133$ ). Participants were informed of the chance of being assigned to study conditions in the consent form prior to enrollment. The study protocol was approved by the Butler Hospital Institutional Review Board.

### Minimal Behavioral Intervention

Regardless of group assignment, participants met with a study interventionist. At this 15-min session, participants received standardized advice to quit smoking that followed the National Cancer Institute's 5 A's model for smoking cessation counseling (Fiore et al., 2008). Before receiving medication, participants also received education about how and when to use the assigned medication; medication adherence was emphasized and the potential for side effects explained. Participants were asked to set a quit date 8 days after this initial visit. Study visits were scheduled monthly, coinciding with refills of medication/NRT.

### Varenicline Condition

Participants were instructed to begin with one capsule (0.5 mg) with food the evening of the baseline visit. This dose was continued for 3 days, then increased to two 0.5 mg pills a day for 4 days, increasing to 1 mg twice daily after 1 week (as per the varenicline package insert) (Pfizer Inc., 2013). Participants were urged to call the study staff or seek medical support if they experienced adverse effects. The importance of adherence was emphasized at all medication dispensing visits. Medication was dispensed at 4-week intervals for up to a 24-week course of therapy. Interviews at 2- and 4-week visits assessed only adherence and side effects.

### Varenicline-Placebo Condition

The double-blind varenicline-placebo control condition consisted of 24 weeks of placebo tablets (compounded to be identical in appearance to varenicline capsules) using an identical dosing, dispensing, and interview schedule as the active varenicline group.

### Combination Nicotine Replacement Condition

For participants assigned to combination NRT condition, research staff dispensed the nicotine patch and described its proper use: placement, daily dosage, importance of not smoking while using the patch, and tapering of patches. Participants were urged to call if they experienced adverse effects. The importance of adherence was emphasized at all medication dispensing visits. The Nicoderm® patch (GlaxoSmithKline

Inc., 2013) was given at 4-week intervals for up to 24 weeks of therapy. For participants who smoked >30 cigarettes per day, the treatment began at 42 mg, and for participants smoking <30 cigarettes per day, the treatment began at 21 mg.

In addition to using daily nicotine patch, participants received a 4-week supply of 4 mg nicotine gum (Nicorette; GlaxoSmithKline Inc., 2013) at the baseline visit. Participants were instructed to chew gum when experiencing craving and felt that they were likely to restart smoking. Patients were instructed to chew up to 1–2 pieces of gum per hour but no more than 24 pieces of gum per day. Participants were provided refills of the nicotine gum at their request at any time during the treatment phase.

### Medication Recycling

We encouraged smokers with lapses to restart treatment at any point during the 24 weeks. Research staff contacted all persons who did not come to their expected monthly medication pickup dates to seek additional study medication when needed. At these visits, if participants reported smoking, research staff performed the 5 A's counseling strategy again and suggested restarting the assigned study medication.

### Participant Retention and Follow-up

Research assessments were performed at 2 and 4 weeks (focused on side effects and adherence) and at 24 weeks after study enrollment by research assistants blinded to participant group assignment. Participants were compensated \$30 to complete the baseline assessment and \$40 for the 6-month assessment.

## Measures

Demographic characteristics (e.g., age, gender, ethnicity, and race) were assessed at baseline using a self-report demographic survey. Tobacco dependence was evaluated using the Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991). FTND scores range from 1 to 10 and the following scoring ranges were used to interpret nicotine dependence level: 1–2 (*low dependence*), 3–4 (*low to moderate dependence*), 5–7 (*moderate dependence*), and 8 or more (*high dependence*) (Heatherton et al., 1991). Quitting self-efficacy was measured with a single item from the *Thoughts About Abstinence* scale (Marlatt, Curry, & Gordon, 1988). For this item, participants were asked to rate their current quitting efficacy (projected chances of success) on a 10-point scale with 1 representing the lowest degree of efficacy and 10 representing the greatest degree of efficacy.

Self-reported cigarette use was also assessed using the timeline followback (TLFB; Sobell & Sobell, 1992). The TLFB is a calendar-based interview that asks participants to recall the frequency of substance use. The TLFB has been used extensively in assessing the use of a variety of substances as well as health behaviors (Sobell, & Sobell, 1992). We also collected study medication adherence data using the TLFB interview. In the NRT group, a day of adherence was defined as applying a patch. For the oral medication groups (varenicline and varenicline placebo), a day of adherence was defined as taking both prescribed doses (unless it was during the first 3 days of treatment when only one dose is taken). An early quit day was defined as at least 24 hr without smoking during the first month of treatment as self-reported on the TLFB.

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### Analytic Strategy

We present descriptive statistics to summarize the characteristics of the sample. We used logistic regression to estimate the unadjusted and adjusted association of having an early quit day with evaluated baseline correlates. Continuous predictor variables were standardized to zero mean and unit variance prior to estimation; the associated coefficients give the expected change in odds of early quit day for a 1-SD increase corresponding predictor. To determine if the effect of adherence on early quit was conditioned by treatment, we also estimated a model testing the treatment by adherence interaction. Statistical analyses were conducted using StataCorp 10.1. (2010).

### RESULTS

Participants averaged 39.9 ( $\pm 9.7$ ) years of age, 156 (49.5%) were male, 250 (79.4%) were non-Hispanic White, 8 (2.5%) were Black, 38 (12.1%) were Hispanic, and 19 (6.0%) were of other racial or ethnic origins (Table 1). Ethnicity was dichotomized to contrast non-Hispanic Whites to all racial or ethnic minorities in subsequent analyses. Mean years of education was 11.8 ( $\pm 2.1$ ) and mean methadone dose at baseline was 108.7 mg ( $\pm 63.1$ ). On average, participants smoked 19.6 ( $\pm 10.4$ ) cigarettes/day during the month prior to baseline and their mean FTND score was 5.7 ( $\pm 2.2$ ). Participants were adherent to the medication treatment protocol on 63.7% ( $\pm 39.0$ ) of the days during the 1-month follow-up; adherence rates were 65.0% ( $\pm 40.0$ ), 63.7% ( $\pm 37.3$ ), and 59.6% ( $\pm 42.1$ ) in the NRT, varenicline, and placebo arms, respectively ( $F_{2,312} = 0.32, p = .724$ ). Including the 22 (7.0%) persons lost to follow-up and who were defined as not having a quit attempt, only 111 (35.2%) of the participants reported a successful early quit day. Quit day

**Table 1. Background Characteristics (n = 315)**

|                                  | M (SD) or n (%)      |
|----------------------------------|----------------------|
| Age, years                       | 39.9 ( $\pm 9.6$ )   |
| Gender (male)                    | 156 (49.5%)          |
| Ethnicity                        |                      |
| Non-Hispanic Caucasian           | 250 (79.4%)          |
| Black                            | 8 (2.5%)             |
| Hispanic                         | 38 (12.1%)           |
| Other                            | 19 (6.0%)            |
| Years of education               | 11.8 ( $\pm 2.1$ )   |
| CES-D                            | 12.0 ( $\pm 6.3$ )   |
| Methadone dose                   | 108.7 ( $\pm 63.1$ ) |
| Mean cigarettes/day              | 19.6 ( $\pm 8.5$ )   |
| Quit self-efficacy (1–10)        | 8.1 ( $\pm 2.0$ )    |
| Quit attempt past 12-month (yes) | 118 (37.5%)          |
| FTND                             | 5.7 ( $\pm 2.2$ )    |
| Mean % days adherent to protocol | 63.7 ( $\pm 39.0$ )  |
| Early abstinence (yes)           | 111 (35.2%)          |
| Intervention condition           |                      |
| NRT                              | 133 (42.2%)          |
| Varenicline                      | 137 (43.4%)          |
| Placebo                          | 45 (14.3%)           |

Note. CES-D = Center for Epidemiological Studies Depression Scale; FTND = Fagerström Test for Nicotine Dependence; NRT = nicotine replacement therapy.

rates were 40.6%, 35.7%, and 17.8% in the NRT, varenicline, and placebo arms, respectively ( $\chi^2 = 7.70, df = 2, p = .021$ ).

After adjusting for all other model covariates, the likelihood of an early quit day increased significantly (odds ratio [OR] = 1.39, 95% CI = 1.04–1.86,  $p < .05$ ) as education increased (Table 2). Having a quit attempt in the past year was associated with a 2.27 (95% CI = 1.33–3.87,  $p < .01$ ) fold increase in the expected odds of an early quit. Compared to the placebo arm, those randomized to either NRT (OR = 3.25, 95% CI = 1.30–8.10,  $p < .01$ ) or varenicline (OR = 3.16, 95% CI = 1.26–7.92,  $p < .05$ ) were significantly more likely to have an early quit day. As evidenced by the similar adjusted odds ratios, substantive differences between active treatment arms were not statistically significant ( $\chi^2 = 0.01, df = 1, p = .919$ ). The likelihood of an early quit was also associated positively (OR = 2.05, 95% CI = 1.52–2.76) with adherence to the medication protocol. The first-order treatment condition by adherence interaction effect (not shown in Table 2) was not statistically significant ( $\chi^2 = 0.72, df = 2, p = .699$ ). Having an early quit day was not associated with any of the other correlates evaluated in Table 2 including self-efficacy, one of our primary hypothesized predictive variables of interest.

### DISCUSSION

The inability of more than 60% of methadone-maintained smokers who voluntarily entered a smoking cessation trial to

**Table 2. Logistic Regression Models Estimating the Unadjusted and Adjusted Effects of Selected Predictors on the Likelihood of an Early Quit Day (n = 315)**

| Predictor                                | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|--|------------------------|----------------------|
| Age <sup>a</sup> , years                 | 1.07 (0.85–1.34)       | 0.95 (0.73–1.24)     |
| Gender (male)                            | 1.12 (0.70–1.78)       | 1.36 (0.80–2.32)     |
| Non-Hispanic Caucasian (yes)             | 0.84 (0.48–1.47)       | 0.82 (0.43–1.56)     |
| Years of education <sup>a</sup>          | 1.38* (1.07–1.78)      | 1.39* (1.04–1.86)    |
| CES-D <sup>a</sup>                       | 1.19 (0.94–1.49)       | 1.29 (0.98–1.68)     |
| Mean cigarettes/day <sup>a</sup>         | 0.82 (0.64–1.04)       | 0.83 (0.60–1.16)     |
| FTND <sup>a</sup>                        | 0.90 (0.71–1.13)       | 1.09 (0.78–1.52)     |
| Methadone dose <sup>a</sup>              | 1.16 (0.92–1.45)       | 1.15 (0.89–1.50)     |
| Quit attempt past 12-month (yes)         | 2.20** (1.37–3.54)     | 2.27** (1.33–3.87)   |
| Quit self-efficacy <sup>a</sup>          | 1.17 (0.92–1.49)       | 1.13 (0.87–1.47)     |
| % days adherent to protocol <sup>a</sup> | 1.99** (1.51–2.63)     | 2.05** (1.52–2.76)   |
| Intervention arm                         |                        |                      |
| NRT (patch)                              | 3.16** (1.37–7.31)     | 3.25* (1.30–8.10)    |
| Varenicline                              | 2.57* (1.11–5.97)      | 3.16* (1.26–7.92)    |
| Placebo [ref.]                           | [1.00]                 | [1.00]               |

Note. OR = odds ratio; CI = confidence interval; CES-D = Center for Epidemiological Studies Depression Scale; FTND = Fagerström Test for Nicotine Dependence; NRT = nicotine replacement therapy.

<sup>a</sup>Continuous variables were standardized to zero mean and unit variance prior to estimation. The associated coefficients give the expected change in the odds of an early quit attempt for each 1-SD increase in the predictor.

\* $p < .05$ , \*\* $p < .01$ .



complete a quit day during the first month of treatment was unexpected and noteworthy. Achieving an early quit attempt, not ordinarily reported in clinical trials, may in good part explain the very low cessation rate of 5.4% at 6 months found in the current study (Stein et al., 2013) and other studies with this population.

We can speculate why only 37% of participants had a quit day in the first month. It is possible that participants were not motivated to quit. Some may have enrolled for the study remuneration or even to sell study medication (in the case of NRT where treatment type was unblinded). Some may have been disappointed by the study group to which they were assigned (e.g., pill recipients might have preferred patch). Participants may also have viewed smoking reduction rather than abstinence as an acceptable endpoint; smoking even one cigarette did not qualify as a quit day. The intervention did not provide a quit day appointment, and without the accountability to staff, and the support such a visit might offer, participants simply did not quit. Medication adherence is critical for positive smoking outcomes, and adherence rates for the first month were low, which in this trial was not explained by reported side effects. We suspect that most nonadherence was intentional, and not a matter of misunderstanding or forgetfulness. Sustained adherence to pharmacotherapy beyond the first month remained a problem as well in this study (Stein et al., 2013).

Unexpectedly, we did not find self-efficacy to be a significant predictor of quit initiation despite the well-established association seen in the more general smoking literature (Gwaltney, Metrik, Kahler, & Shiffman, 2009). Participants may have misjudged their capacity to quit even for 24 hr. Possibly, our measure of self-efficacy, the item from the *Thoughts about Abstinence Scale*, did not capture critical dimensions of self-efficacy associated with quit initiation among MMT smokers. Although the TAA self-efficacy item is widely used and has been substantiated as a predictor of treatment efficacy (Hall, Havassy, & Wasserman, 1991), the scale may not be optimally suited for this particular subpopulation of smokers or for predicting a quit initiation. In order to more fully understand this finding, future research in this area should consider validating the TAA among MMT smokers and also utilize other measures of self-efficacy that include contextual and situational domains for efficacy.

In our study, participants in the active medication groups (NRT or varenicline) were more likely to achieve a successful quit day. We attribute this finding to the fact that both medication groups received treatments that are known to physiologically decrease craving and withdrawal, which is a critical component of successful tobacco cessation (Hughes, 2007; Hughes, Gust, Skoog, Keenan, & Fenwick, 1991). The various symptoms associated with withdrawal and craving are known to be physiological and psychologically entrenched and serve to perpetuate and reinforce smoking behavior. Pharmacotherapy agents that relieve these negative states, such as the two employed in the current trial, offer smokers a means for circumventing this entrenched process so that daily functioning is not impacted severely and the individual can attend to other difficult aspects of the quitting experience. In keeping with this speculation, we found that individuals with greater adherence to their treatment were more likely to initiate a quit attempt.

Our study findings demonstrated that as education level increases, so does the likelihood of initiating and completing an early quit day among MMT smokers. This finding is

consistent with the broader smoking cessation literature that has noted a consistent relationship between education level and cessation outcomes (de Walque, 2007; Kaleta et al., 2012; Pierce, Fiore, Novotny, Hatziandreu, & Davis, 1989). Not only is education a known proxy for socioeconomic status, which has been shown to impact smoking cessation (Vangeli et al., 2011), but also it is believed that a greater level of education is associated with a greater awareness of the risks and dangers of smoking (Margolis, 2013). Furthermore, education level is also known to be correlated with a variety of intellectual and cognitive domains that can significantly impact one's ability to execute and sustain a tobacco quit attempt.

The limitations of this study must be carefully considered when interpreting our findings. First, our study relied on self-reported measures. Secondly, our study inclusion and exclusion criteria limit our ability to generalize our findings to the entire population of MMT smokers. For example, we excluded pregnant women, individuals who do not speak English, and light smokers (<10 cigarettes per day). Lastly, due to a lack of data, our study could not account for the impact of psychiatric diagnoses, length of MMT treatment, methadone dosage, and other substance use. Future studies should attempt to account for these important variables that are likely to impact smoking cessation quitting and adherence to medication.

Despite these study limitations, this is the first investigation that examined predictors of a successful early quit among MMT smokers. Our findings underscore the importance of medication adherence for initiating a quit attempt and demonstrate the significant impact that education can have on MMT smokers' attempts to quit smoking. Past quit attempts predict future quit attempts, and in future studies, a considerable effort should be placed on ways to increase adherence to pharmacotherapy, with special attention paid to early quit attempts. Our findings highlight the need for MMT providers to not only assess and offer pharmacological treatments for tobacco use but also there is a critical need for providers to remain steadfast beyond the assessment and initial treatment prescription phase. Behavioral interventions have much to offer in this domain and providers can work closely with patients to set and implement a quit date as well as target adherence. Moreover, quit date calls are fairly easy to implement and can be particularly helpful to patients in need of additional support and prompt in order to initiate the process of quitting. In terms of pharmacotherapy adherence, providers as well as future investigations can develop proactively strategies for addressing potential barriers to medication adherence and develop interventions that can be enacted prior to the quit attempts.

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## DECLARATION OF INTERESTS

*None declared.*

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