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Correlates of long-term opioid abstinence after randomization to methadone versus buprenorphine/naloxone in a multi-site trial

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Abstract

Opioid use disorder (OUD) is a chronic, relapsing condition with severe negative health consequences. Previous studies have reported that 5-year opioid abstinence is a good predictor of reduced likelihoods of relapse, but factors that shape long-term opioid abstinence are poorly understood. The present study is based on data from a prospective study of 699 adults with OUD who had been randomized to either methadone or buprenorphine/naloxone and who were followed for at least 5 years. During the 5 years prior to the participants' last follow-up interview, 232 (33.2%) had achieved 5-year abstinence from heroin. Of those 232, 145 (20.7% of the total) had remained abstinent from both heroin and other opioids (e.g., hydrocodone, oxycodone, other opioid analgesics, excluding methadone or buprenorphine). Compared to non-abstinent individuals, those in both categories of opioid abstinence had lower problem severity in health and social functioning at the final follow-up. Logistic regression results indicated that cocaine users and injection drug users were less likely to achieve 5-year heroin abstinence, whereas Hispanics (vs. whites) and those treated in clinics on the West Coast (vs. East) were less likely to achieve 5-year abstinence from heroin and other opioids. For both abstinence category groups, abstinence was positively associated with older age at first opioid use, lower impulsivity, longer duration of treatment for OUD, and greater social support. Reducing cocaine use and injection drug use and increasing social support and retention in treatment may help maintain long-term abstinence from opioids among individuals treated with agonist pharmacotherapy.

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Compliance with Ethical Standards

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

1. Introduction

Opioid use disorder (OUD) is a chronic relapsing condition associated with extensive co-morbidity, mortality, and negative social consequences (Hser et al. 2015). In the United States, deaths associated with prescription opioid and heroin use have quintupled since 1999 and reached a record high of more than 42,000 in 2016 (Centers for Disease Control and Prevention 2017). The escalating rates of OUD and overdose deaths have become a public health crisis.

The field of addiction treatment in general recognizes OUD as a chronic disorder with cycles of opioid use, treatment, relapse, and recovery, often protracted over many years (Hser et al. 2015). In addition to promoting abstinence from opioids, the ultimate aim of OUD treatment is to reduce negative consequences of OUD and enable patients to recover and attain a better life. Our previous work has suggested that maintaining opioid abstinence for at least five years substantially increases the likelihood of future stable abstinence (Hser, 2007). However, studies examining opioid use and abstinence have often been limited by the short observation periods, defining opioid abstinence as no use of opioids for as little as 1-3 months, with few studies examining use for as long as 12 months (Darke et al. 2007; Hser et al. 2001; Soyka et al. 2017; Weiss et al. 2015). The present study aimed to identify correlates associated with five years of opioid abstinence.

Methadone and buprenorphine are the most commonly used medications for treating OUD (Bart 2012; Kampman et al. 2015), and numerous studies have demonstrated they are effective medication treatments (Darke et al. 2007; Weiss et al. 2015; Apelt et al. 2013; Wittchen et al. 2008). Despite the benefits of medication treatment, many patients struggle to abstain from using opioids while in treatment and most relapse after they discontinue treatment (Bart 2012; Bentzley 2015). The few studies that have examined correlates of sustained opioid abstinence suggest that it is more likely to occur among women (Darke et al. 2015), older adults (Dreifuss et al. 2013; Naji et al. 2016), and those with more social and spiritual support (Dennis et al. 2007; Flynn et al. 2003) or who are employed (Flynn et al. 2003; Dennis et al. 2007; McKeganey et al. 2006; Nosyk et al. 2013). In contrast, barriers to sustained abstinence from opioids include several factors that are generally considered to be proxies for a more severe OUD, including injection drug use (Naji et al. 2016), polysubstance use (e.g., cocaine, benzodiazepine) (Naji et al. 2016; Dreifuss et al. 2013; Nosyk et al. 2013), many prior treatment experiences (Dreifuss et al. 2013; Darke et al. 2015), and involvement with the criminal justice system (McKeganey et al. 2006; Nosyk et al. 2013; Dennis et al. 2007; Scott et al. 2011). Other factors that may negatively influence sustained abstinence, such as younger age at first opioid use, minority race/ethnicity, lower education level, and preexisting physical or mental disorders, have not been thoroughly studied.

To provide new data on long-term outcomes of opioid agonist therapy for OUD, the Clinical Trials Network (CTN) of the National Institute on Drug Abuse (NIDA) conducted a follow-up study of a previous CTN trial, Starting Treatment with Agonist Replacement Therapies (START). The START Follow-up Study was designed to examine the course of opioid use among START participants with OUD who had been randomized to either methadone

(MET) versus buprenorphine/naloxone (BUP). We previously reported that both MET and BUP were associated with a significant reductions in opioid use (Hser et al. 2016), and there were distinctive trajectories of opioid use over time (Hser et al. 2017).

In the present article, we report on findings from secondary analyses of the original START data plus data from the Follow-up Study, which included three follow-up interviews, to investigate the prevalence of sustained, long-term opioid abstinence and its correlates. We examined opioid abstinence according to two categories: (1) individuals who were abstinent from heroin only and (2) individuals who were abstinent from opioids, including both heroin and other opioids (e.g., hydrocodone, oxycodone, other opioid analgesics, excluding methadone or buprenorphine). We defined long-term opioid abstinence as abstinence for at least 5 consecutive years prior to the last follow-up assessment. We focused on heroin because most START participants were originally seeking treatment for their heroin use in the methadone clinics. We further considered other opioids in addition to heroin due to the recognition of adverse effects of use of prescription opioids as well as of heroin. We compared abstinent and non-abstinent participants to ascertain if long-term opioid abstinence is associated with improved functioning in other life domains. We then included baseline characteristics as well as correlates collected during the follow-up period to identify phenomena associated with long-term opioid abstinence. Specifically, we aimed to determine (1) the proportion of participants who achieved abstinence from heroin and other opioids for at least 5 years, (2) the correlates of long-term opioid abstinence with functioning in other key life domains, and (3) baseline characteristics and other correlates associated with long-term opioid abstinence.

2. Methods

2.1 Study design and participants

The original START study was a multi-site trial that randomized 1,269 opioid-dependent individuals to receive BUP (n=740) or MET (n=529) in nine sites during 2006–2009. Details of the study are available elsewhere (Saxon et al. 2013). The START Follow-up Study was conducted during 2011-2016 with three assessments one year apart (Hser et al. 2016; Hser 2017). Two sites (n=189) were dropped from the Follow-up Study due to small sample sizes and difficulty conducting follow-up. Among 1,080 participants remaining, 797 (73.8%) completed the first follow-up interview (Visit 1), 728 (67.4%) completed Visit 2, and 647 (60.0%) completed Visit 3; 699 had a follow-up period of 5 + years after the START study randomization and were included in the study. The mean length of the follow-up period among 699 OUD participants was 6.7 years (SD=1.0). Characteristics of the analysis group (n=699 with 5+ years of follow-up) and the omitted group (n=381 with <5 years of follow-up) were not statistically different at baseline (e.g., age, race/ethnicity, site, randomization to START medication condition, use of tobacco, alcohol, and other substances), except that the analysis group included more women (34.8% vs. 28.6%).

2.2 Procedures

Research staff at each START study site conducted informed consent and completed the first follow-up interview in-person (Visit 1) from August 2011 to April 2014. The assessment

interview took approximately 1.5–2 hours. Two yearly follow-up phone interviews, Visit 2 (from August 2012 to June 2016) and Visit 3 (from December 2013 to June 2016 as the final follow-up interview) were conducted by UCLA staff, each lasting approximately 1.5–2 hours. Participants were compensated $50 for Visits 1 and 2, and $70 for Visit 3. All study procedures were approved by the IRB at UCLA and by the local IRB overseeing each study site. A federal Certificate of Confidentiality was obtained to protect against disclosure of sensitive participant information.

2.3 Main measures

Long-term opioid abstinence.—Timeline follow-back (TLFB) (Sobell et al. 1992) was used to collect self-reported days of drug use per month from enrollment to the follow-up interviews. Among 699 participants with 5+ years of follow-up, 647 completed Visit 3. So, we defined long-term abstinence as no opioid use in the past 5 years prior to the participants' last self-reported record from the TLFB. We considered opioid abstinence in two ways. For heroin abstinence, we considered only days of heroin use. For abstinence from all opioids, we included use of heroin and use of other opioids (e.g., hydrocodone, oxycodone, other opioid analgesics) excluding opioid agonist treatment medications for OUD.

Problem severity.—The Addiction Severity Index (ASI) (Mclellan et al. 1992) was used to assess problem severity in seven key life domains that are potentially affected by OUD. It is a widely used instrument in addiction research and in clinical practice (Bray et al. 2017). Higher composite scores (range: 0 to 1) indicate greater problem severity. We used ASI composite scores from Visit 3 as another long-term outcome in the analysis.

Months of treatment and incarceration during follow-up.—We summed the number of months of medication treatment for OUD and of incarceration during the 5-year period prior to the final follow-up interview, as collected by TLFB methods, to measure total exposures during the follow-up period.

Social support.—Social support was measured with the Texas Christian University (TCU) short forms, which gauged the degree of personal support received by family and friends for their treatment and recovery efforts (Garner et al. 2007). Scores ranged from 10 to 50, with higher values indicating more social support. The measure was collected at Visit 1 and Visit 3, and the average score was used in analyses.

Impulsiveness.—The Barratt Impulsiveness Scale is a 30-item questionnaire designed to assess impulsivity, defined as the deficient control of behaviors and inadequate decision-making (Reise et al. 2013). Scores ranged from 30 to 120 on a Likert scale, with higher summed scores indicating greater impulsiveness. The measure was collected at Visit 1 and Visit 3, and we took the average value in the analysis.

2.5 Statistical analyses

We examined differences in baseline characteristics between the two abstinence classification groups (defined by long-term abstinence separately for heroin only and for all opioids) using Wald chi-square tests for categorical variables and two-tailed independent t-

tests for continuous variables. We also compared the ASI composite scores at the final follow-up interview for abstinent participants and non-abstinent participants using two-tailed independent t-tests.

We used a series of logistic regression models to examine incremental contributions of correlates of each abstinent category. In Model I, we included only baseline variables, specifically demographics, study site, the number of diseases, alcohol and other substance use, and the randomization condition. In Model II, we added to Model I months of treatment and incarceration during the follow-up period. Finally, in Model III, we included additional measures (age at first opioid use, employment status, social support and impulsivity collected during the follow-up periods) to investigate their relationships with consistent, long-term abstinence. Finally, built upon Model III, we further conducted stratified analyses to investigate if age and gender are moderators in the relationships between opioid abstinence and impulsivity as well as between opioid abstinence and social support. Mean levels were used to dichotomize social support (1= ≥40 vs. 0= <40) and impulsivity (1= <60 vs. 0= ≥60) in stratified analyses. We calculated odds ratios (ORs) and 95% confidence intervals (CIs).

All tests were two-tailed with $\alpha<0.05$, indicating statistical significance. SAS version 9.4 was used for all analyses.

3. Results

3.1 Long-term opioid abstinence and baseline differences

Over an average 6.7 years of follow-up, 232 (33.2%) achieved 5-year abstinence from heroin, and 145 (20.7%) achieved 5-year abstinence from all opioids, including heroin. Demographics and other baseline characteristics are shown in Table 1. For both abstinence classification groups, fewer individuals in the abstinent group, compared to the non-abstinent group, were treated in clinics on the West Coast (vs. East: 53.0% vs. 65.7% for heroin, 47.6% vs. 65.2% for opioids) and injected drugs at baseline (48.9% vs. 74.1% for heroin, 54.9% vs. 68.6% for opioids).

Participants in the heroin-abstinent group, compared to the non-abstinent participants, were less like to have been randomized to BUP (vs. MET: 50.4% vs. 59.7%) or to use tobacco (84.9% vs. 91.9%) or cocaine (23.3% vs. 38.1%). Participants in the group that was abstinent from heroin and other opioids, compared to the non-abstinent participants, were significantly younger (M= 35.4 vs. 37.9 years), had fewer psychiatric disorders (2.01 vs. 2.35), and were less likely to be Hispanic (2.8% vs. 13.7%).

3.2 Health and social functioning and treatment status at Visit 3

At the final (Visit 3) follow-up interview, an assessment of addiction severity, health, and social functioning was administered with 609 (87%) participants using the ASI composite scores. Abstinent participants compared to those not abstinent had significantly lower addiction severity (Table 2). Participants in the heroin-abstinent group, compared to those in the non-abstinent group, reported less severe problems in the domains of drug use (0.1 vs. 0.18), employment (0.52 vs. 0.65), social and family relationships (0.07 vs. 0.11), legal

status (0.02 vs. 0.09) and psychiatric health (0.15 vs. 0.21). Participants abstinent from heroin and other opioids, compared to those in the non-abstinent group, experienced significantly less severe problems regarding drug use (0.09 vs. 0.17), employment (0.49 vs. 0.64), social and family relationships (0.06 vs. 0.11), legal status (0.01 vs. 0.08), and psychiatric health (0.14 vs. 0.21).

Based on the participants' last record of treatment status from the TLFB, 374 (53.5 %) were receiving medication treatment for OUD; there were no differences in treatment status between the abstinent and non-abstinent groups defined by heroin use (58.2% versus 51.2%), but more individuals who achieved long-term abstinence from both heroin and other opioids were in treatment, compared to the non-abstinent group (63.5% vs. 50.9%, p<.01).

3.3 Logistic regression predicting long-term opioid abstinence

Baseline characteristics and measures collected during the follow-ups were examined in separate logistic regression analysis (Table 3). Series models with increasing numbers of covariates were tested, with Model I including only baseline characteristics, Model II adding measures of treatment and incarceration during the follow-up period, and Model III further incorporating additional potential correlates measured at the follow-ups. Because the findings are largely consistent across the three models, we describe results based on Model III. For long-term heroin abstinence, positive correlates included older age at first opioid use (OR: 1.03; 95% CI: 1.00, 1.05), higher social support (OR: 1.06; 95% CI: 1.02, 1.10), and more months in treatment (OR: 1.02; 95%CI: 1.01, 1.03), and negative correlates included cocaine use (OR:0.54; 95%CI:0.37, 0.80), injection drug use (OR: 0.41; 95%CI: 0.28, 0.59), and high impulsivity (OR: 0.96; 95%CI: 0.94, 0.98). For long-term abstinence from heroin and other opioids, older age (OR: 1.03; 95% CI: 1.00, 1.06), higher social support (OR: 1.06; 95% CI: 1.02, 1.11), and more months in treatment (OR: 1.03; 95%CI: 1.02, 1.04) were significant positive correlates, while high impulsivity (OR: 0.96; 95% CI: 0.93, 0.98) was a negative correlate. Furthermore, Hispanics (relative to white, OR: 0.23; 95%CI: 0.08, 0.68) and West Coast clinic sites (relative to East Coast, OR=0.63; 95%CI: 0.40, 0.99) were associated with a lower likelihood of long-term abstinence from heroin and other opioids.

In stratified analyses, we detected heterogeneity of the associations between impulsivity and heroin abstinence across age group strata (p for heterogeneity =0.03), and between impulsivity and abstinence from heroin and other opioids across the gender strata (p for heterogeneity =0.04; Table 4). While lower impulsivity was associated with higher likelihood of abstinence from heroin for both males (OR=1.69; 95%CI=1.02, 2.78) and for females (OR=2.78; 95%CI=1.43, 5.56), the difference in this association for men and women was not statistically significant. In contrast, the associations between low impulsivity and heroin abstinence were stronger for the younger (OR=2.70; 95%CI: 1.35, 5.26 for 18-30; OR=2.27; 95%CI: 1.03, 5.00 for 31-50) than for the older (OR=1.47; 95%CI: 0.74, 2.94 for 50+). The significant association between impulsivity and abstinence from heroin and other opioids was also found for females (OR=3.33; 95%CI: 1.47, 7.69), but not for males (OR=1.72; 95%CI: 0.98, 3.03).

In addition, we observed the heterogeneity of the associations between social support and abstinence from heroin and other opioids across the age group strata (p for heterogeneity

=0.03). The association between social support and abstinence from heroin and other opioids for the younger participants (OR=2.42; 95%CI: 1.09, 5.36 for 18-30; OR=1.70; 95%CI: 0.65, 4.49 for 31-50) was stronger than those for the older participants (OR=1.41; 95%CI: 0.57, 3.52 for 50+).

4. Discussion

The present study found that among individuals seeking medication treatment for OUD as participants in a clinical trial and followed for at least 5 years, 33.2% achieved stable abstinence from heroin for at least 5 years, and 20.7% were abstinent from heroin and other opioids. Compared to non-abstinent participants, those with long-term abstinence demonstrated lower problem severity at the final follow-up in many key life domains (i.e., drug use, employment, social/family, legal, and psychiatric areas for both abstinent classifications, with additional improvement in medical conditions for those with long-term abstinence from heroin and other opioids). Use of cocaine, injection drug use, and impulsivity were negatively associated with heroin abstinence, while being Hispanic (vs. white), on the West Coast (vs. East), and impulsivity were negatively associated with abstinence from heroin and other opioids. For both abstinence classifications, older age at opioid initiation, greater social support, and longer duration of treatment were positively associated with stable abstinence.

The 5-year abstinence rates in the present study were lower than those reported by several earlier studies. A 33-year follow-up study in the U.S. (Hser et al. 2001) and a 11-year follow-up of the Australian Treatment Outcome Study (ATOS) (Darke et al. 2015) both found that approximately half of the treated heroin users maintained abstinence for at least 5 years. Compared to these two studies, the present study had a shorter follow-up period, a lower mortality rate (6.2%, vs. 48.9% in the 33-year study and 10.2% in ATOS), and younger age (M=44, vs. 57 in the 33-year study), all of which could contribute to the lower abstinence rates. Despite the short follow-up period, low mortality, and young ages, the current study did show that a proportion of OUD participants were able to achieve and maintain stable abstinence, although the low rates indicate there is considerable room for improvement.

Our study findings confirm that long-term opioid abstinence was associated with improvement in several key domains of health and social functioning, thus substantiating that long-term opioid abstinence is a good indicator of stable recovery (Laudet 2007; Substance Abuse and Mental Health Services Administration 2011; The Betty Ford Institute Consensus Panel 2007). There are a few exceptions to the overall recovery status of the START follow-up study sample, however; for example, there was no significant difference in alcohol composite scores for both abstinent classifications, suggesting that long-term opioid abstinence may not be contributory to reductions in alcohol use. Additionally, compared with the non-abstinent group, the medical composite score was significantly better among participants who maintained abstinence from all opioids, but not for those who were abstained only from heroin. The reason for this difference is not immediately clear. Many people use opioids for pain, but the severity of medical conditions at baseline did not differ between abstinent and non-abstinent groups for the opioid-abstinent classifications. Future

studies should be devoted either to replicating this finding or to investigating reasons for this difference.

Several baseline and follow-up predictors were associated with long-term opioid abstinence. In particular, baseline drug use patterns served as important markers for predicting long-term abstinence from heroin. The heroin-abstinent group had less cocaine use and injection drug use at baseline than did the non-abstinent group. These results remained even after including other follow-up variables in the model. The relationship between reduction of other substance use and heroin abstinence was also reported consistently in some studies (Darke et al. 2005; Williamson et al. 2007; Rosic et al. 2017). Hence, treatment and other interventions must specifically address use of other substances for poor outcomes.

For abstinence from heroin and other opioids, race/ethnicity and locations of clinic site were independent predictors. Hispanics had lower odds of achieving abstinence compared to whites, suggesting attention to other opioid use among Hispanics with OUD may be warranted (Alegría et al. 2006). Additionally, OUD participants treated in clinics on the West coast (California, Oregon, and Washington) had lower long-term abstinence than those on the East coast (Connecticut, Pennsylvania). The underlying reasons for this geographical variation are unknown, but previous studies have suggested several potential factors including characteristics of resident populations, their health care utilization, availability of heroin and other opioids, and prescription drug monitoring laws (McDonald et al., 2012). In addition, the difference also could be affected by different sub-cultural philosophies or relative emphasis on abstinence versus harm reduction among these clinics. This finding highlights the critical role of environmental factors beyond individual characteristics that influence individual health and public health and should be taken into consideration in overall strategies curbing the opioid epidemic and related negative consequences.

There are several consistent predictors of long-term abstinence across the abstinent classifications. Older age at first opioid use was positively associated long-term abstinence, and impulsivity was negatively associated with long-term abstinence, which are consistent with previous literature (Soyka et al. 2008; Su et al. 2015). Longer time in treatment increases the chance of achieving and maintaining treatment success. Consistent with previous studies, strong social support is a critical factor for sustained abstinence not only for heroin but also for other illicit opioids, which suggests the importance of establishing social networks for underpinning a drug-free life (Flynn et al. 2003).

We also observed significant differences in the associations between opioid abstinence and impulsivity as well as social support across age or gender strata. Impulsivity had stronger effects on abstinence from heroin and other opioids for females compared with males, and for younger individuals compared with older participants. Our study also found that the beneficial effect of social support on abstinence from heroin were stronger for females than for males, while it was of greater importance among the younger group than the older group on abstinence from heroin and other opioids. These findings suggest the differential impact of impulsivity and social support in achieving stable abstinence for groups of different gender and age. Clinicians may need to consider these factors in managing patients with OUD in order to maximize their likelihood of stable recovery.

The present study has several limitations. First, data on opioid use are self-reported and may be vulnerable to recall error or other bias; however, studies of drug users have consistently demonstrated adequate reliability and validity of such data in research settings (Fals-Stewart et al. 2000; Carey 1997). Specifically based on the 33-year follow-up study, test-retest reliability has been judged acceptable (e.g., 0.71 for opioid abstinence, 0.63 for daily use). Second, we only included participants with OUD who had a follow-up period of 5 years or more. The attrition analysis, as reported earlier, did not show differences in baseline characteristics, except for gender. Third, other potential correlates (e.g., treatment history, motivation for change) that may be associated with opioid abstinence were not available and therefore not included in this study. Finally, the clinical implications of the statistical significance found in the differences between the abstinent and non-abstinent groups need to be further ascertained.

5. Conclusion and implications

Findings from this study provide information leading to a better understanding of OUD treatment effects over the long term and offer insights into correlates of long-term opioid abstinence. Our results support the notion that maintaining long-term opioid abstinence is likely to lead to improvements in important life domains and areas of functioning. While long-term abstinence may be rare and cannot be expected for most individuals with OUD, our study does suggest that long-term opioid abstinence can be improved by addressing individuals' risk factors and enhancing their protective factors, as well as by attending to the larger environmental factors beyond individual personal characteristics. Our findings highlight the need of scaling up promising interventions targeting these abstinence-related factors.

Since remaining in treatment is a positive predictor of abstinence, maintenance treatment should be made more widely available, more easily accessible, and more patient-centered. Cocaine use was associated with inability to sustain abstinence from opioids following treatment. Contingency management for stimulant use has been widely implemented nationally across the Veterans Affairs Health Care System (Petry et al. 2014). To promote long-term abstinence from stimulants and opioids among people with OUD, contingency management should be implemented widely in all MAT programs. Medical and psychiatric conditions were associated with lower rates of long-term abstinence. Making treatment for these conditions more available and accessible for individuals with OUD would likely improve abstinence rates. Impulsivity was also related to lack of long-term abstinence. Impulsivity is a hallmark symptom of attention deficit hyperactivity disorder (ADHD), and addressing ADHD-related impulsivity may lead to higher long-term abstinence rates among OUD patients.

The findings reported here are important for several reasons. First, while patterns and correlates of heroin abstinence have been reported by many previous studies, those studies are limited by a short time period of observation. In addition, few studies considered non-medical use of prescription opioid medications (e.g. oxycodone, hydrocodone) when studying overall opioid abstinence (McDermott et al. 2015). Given the current opioid crisis, the present study contributes valuable information by identifying correlates of long-term

opioid abstinence that are important for efforts to facilitate stable recovery. The present study demonstrated the existence of common and distinctive predictors and correlates for abstinence from heroin and from other opioids, which further highlights the importance of considering non-medical use of prescription opioids in addition to use of heroin when investigating OUD.

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Table 1.

Baseline characteristics by long-term opioid abstinence groups (n=699)

	Abstinence from heroin		Abstinence from heroin and other opioids		Total
	Yes (n=232)	No (n=467)	Yes (n=145)	No (n=554)	(n=699)
Years of follow Up, Mean (SD)	6.9 (1.0)	6.6 (1.0)	6.9 (1.0)	6.6 (1.0)	6.7 (1.0)
Years of abstinence Mean (SD)	6.4 (1.0)	1.4 (1.5)	6.4 (0.9)	1.2 (1.4)	2.3 (2.5)
Age at baseline (%)					
18-24	16.0	15.9	20.0	14.8	15.9
25-34	37.1	29.1	37.2	30.3	31.8
35-44	16.8	23.1	14.5	22.7	21.0
45-54	23.7	25.7	21.4	26.0	25.0
55+	6.5	6.2	6.9	6.1	6.3
Age, Mean (SD)	36.4 (11.2)	37.9 (11.1)	35.4 (11.6)	37.9 (11.0) *	37.4 (11.2)
Gender (%)					
Female	39.7	32.3	33.8	35.0	34.8
Race/ethnicity (%)					
White	76.7	70.5	80.00	70.6 *	72.5
African American	8.2	10.1	7.6	9.9	9.4
Hispanic	7.3	13.5 *	2.8	13.7 **	11.4
Other	7.8	6.0	9.7	5.8	6.6
West coast (%)	53.0	65.7 **	47.6	65.2 **	61.5
Randomized to BUP (%)	50.4	59.7 *	49.7	58.5	56.7
Number of diseases, Mean (SD)					
Medical	1.5 (1.3)	1.6 (1.3)	1.4 (1.3)	1.6 (1.3)	1.5 (1.3)
Psychiatric	2.1 (1.6)	2.4 (1.7)	2.0 (1.6)	2.4 (1.7) *	2.3 (1.7)
Smoker at baseline (%)	84.9	91.9 **	85.5	90.6	89.6
In past 30 days, self-reported use of... (%)					
Alcohol	35.5	28.5	32.6	30.3	30.8
Drugs by injection	48.9	74.1 **	54.9	68.6 **	65.8
Opiates	97.4	99.1	97.9	98.7	98.6
Positive urine testing (%)					
Cocaine	23.3	38.1 **	28.3	34.5	33.2
Amphetamine	4.3	5.4	2.8	5.6	5.0
Cannabis	22.4	18.8	21.4	19.7	20.0

Note. Abstinence from heroin: no heroin use during five years prior to the participants' last self-reported record from the TLFB; Abstinence from heroin and other opioids: no heroin and other opioids use during the 5 years prior to the participants' last self-reported record from the TLFB. BUP: Buprenorphine/naloxone. Self-reported opiates in past 30 days at baseline: includes heroin, Demerol, Codeine, Dilaudid.

* $p<0.05$,

** p<0.01.

Table 2.

Health and social functioning by the long-term opioid abstinence group at the end of follow-up (n=609)

	Abstinence from heroin		Abstinence from heroin and other opioids		Total
	Yes (n=212)	No (n=397)	Yes (n=132)	No (n=477)	(n=609)
Addiction Severity Index composite score, Mean (SD)					
Alcohol	0.06 (0.11)	0.06 (0.14)	0.04 (0.08)	0.07 (0.14)	0.06 (0.13)
Drug	0.10 (0.1)	0.18 (0.14) **	0.09 (0.09)	0.17 (0.14) *	0.15 (0.13)
Employment	0.52 (0.34)	0.65 (0.33) **	0.49 (0.33)	0.64 (0.34) **	0.60 (0.34)
Social/Family	0.07 (0.14)	0.11 (0.18) **	0.06 (0.14)	0.11 (0.17) **	0.10 (0.17)
Legal	0.02 (0.07)	0.09 (0.17) **	0.01 (0.05)	0.08 (0.16) **	0.06 (0.15)
Medical	0.26 (0.35)	0.31 (0.36)	0.19 (0.30)	0.32 (0.36) **	0.30 (0.35)
Psychiatric	0.15 (0.20)	0.21 (0.23) **	0.14 (0.19)	0.21 (0.23) **	0.19 (0.22)

Note. Abstinence from heroin: no heroin use during five years prior to the participants' last self-reported record from the TLFB; Abstinence from heroin and other opioids: no heroin and other opioids use during the 5 years prior to the participants' last self-reported record from the TLFB.

* $p<0.05$,

** $p<0.01$.

Table 3.

Logistic regression predicting long-term opioid abstinence (n=699)

	Abstinence from heroin			Abstinence from heroin and other opioids		
Predictors	**Model I**	**Model II**	**Model III**	**Model I**	**Model II**	**Model III**
Age	1.01 (0.99, 1.02)	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)	1.00 (0.98, 1.02)	0.99 (0.97, 1.01)	0.99 (0.96, 1.01)
Gender (Male vs. Female)	0.76 (0.53, 1.09)	0.81 (0.56, 1.17)	0.91 (0.61, 1.36)	1.13 (0.75, 1.72)	1.24 (0.80, 1.90)	1.37 (0.86, 2.19)
Randomization (BUP vs. MET)	0.68 (0.48, 0.95) *	0.74 (0.52, 1.05)	0.72 (0.50, 1.03)	0.68 (0.47, 1.00)	0.79 (0.53, 1.18)	0.79 (0.52, 1.19)
Race (vs. White)						
Black	0.64 (0.33, 1.23)	0.68 (0.35, 1.31)	0.61 (0.31, 1.20)	0.64 (0.30, 1.37)	0.69 (0.32, 1.51)	0.61 (0.27, 1.37)
Hispanic	0.54 (0.30, 0.98) *	0.65 (0.35, 1.19)	0.64 (0.34, 1.23)	0.19 (0.07, 0.54) *	0.24 (0.08, 0.69) *	0.23 (0.08, 0.69) *
Other	1.39 (0.73, 2.66)	1.43 (0.74, 2.78)	1.21 (0.61, 2.42)	1.80 (0.90, 3.58)	1.94 (0.95, 3.94)	1.61 (0.77, 3.36)
Sites (West vs. East)	0.71 (0.49, 1.02)	0.72 (0.50, 1.05)	0.80 (0.54, 1.19)	0.54 (0.36, 0.82) *	0.56 (0.37, 0.86) *	0.63 (0.40, 0.99) *
Number of baseline diseases						
Medical	0.99 (0.86, 1.15)	1.02 (0.88, 1.18)	1.04 (0.89, 1.21)	0.94 (0.80, 1.11)	0.98 (0.83, 1.16)	1.00 (0.84, 1.19)
Psychiatric	0.91 (0.81, 1.02)	0.90 (0.80, 1.02)	0.96 (0.85, 1.09)	0.92 (0.81, 1.05)	0.91 (0.79, 1.04)	0.99 (0.85, 1.15)
Smoker at baseline	0.55 (0.33, 0.94) *	0.57 (0.34, 0.98) *	0.63 (0.36, 1.10)	0.60 (0.34, 1.06)	0.62 (0.34, 1.12)	0.76 (0.40, 1.44)
Past 30 days use of						
Alcohol	1.40 (0.97, 2.01)	1.35 (0.93, 1.95)	1.37 (0.93, 2.02)	0.98 (0.65, 1.49)	0.91 (0.59, 1.40)	0.93 (0.59, 1.45)
Drugs by injection	0.41 (0.28, 0.59) *	0.42 (0.29, 0.61) *	0.44 (0.30, 0.65) *	0.70 (0.47, 1.06)	0.76 (0.49, 1.16)	0.85 (0.54, 1.32)
Cocaine positive by urine test	0.54 (0.37, 0.80) *	0.57 (0.39, 0.85) *	0.58 (0.38, 0.87) *	0.79 (0.52, 1.22)	0.88 (0.56, 1.37)	0.96 (0.60, 1.53)
Ever employed during follow-up			0.78 (0.52, 1.16)			1.06 (0.67, 1.70)
Age at first opioid use			1.03 (1.00, 1.05) *			1.03 (1.00, 1.06) *

	Abstinence from heroin			Abstinence from heroin and other opioids		
Predictors	**Model I**	**Model II**	**Model III**	**Model I**	**Model II**	**Model III**
Social support score			1.06 (1.02, 1.10) *			1.06 (1.02, 1.11) *
Barratt Impulsiveness Scale			0.96 (0.94, 0.98) *			0.96 (0.93, 0.98) *
Months of treatment during the past 5 years		1.02 (1.01, 1.03) *	1.02 (1.01, 1.03) *		1.03 (1.02, 1.04) *	1.03 (1.02, 1.04) *
Months of incarceration during the past 5 years		0.98 (0.96, 1.00)	0.99 (0.96, 1.01)		0.98 (0.95, 1.01)	0.99 (0.96, 1.02)

Note. Abstinence from heroin: no heroin use during five years prior to the participants' last self-reported record from the TLFB; Abstinence from heroin and other opioids: no heroin and other opioids use during the 5 years prior to the participants' last self-reported record from the TLFB; BUP: Buprenorphine/naloxone; MET: Methadone.

* The 95% confidence interval of odds ratio is statistically significant.

Table 4.

The associations between opioid abstinence and impulsivity, and between abstinence and social support, stratified by gender and age group (n=699)

		Odds Ratio (95% CI)	
Stratum		**Abstinence from heroin**	**Abstinence from heroin and other opioids**
Impulsivity (<60 vs. ≥60)			
Gender	Male	1.69 (1.02, 2.78) *	1.72 (0.98, 3.03)
	Female	2.78 (1.43, 5.56) *	3.33 (1.47, 7.69) *
	P †	0.06	0.04
Age group	18-30	2.70 (1.35, 5.26) *	2.78 (1.32, 5.88) *
	31-44	2.27 (1.03, 5.00) *	2.13 (0.81, 5.56)
	55+	1.47 (0.74, 2.94)	1.69 (0.72, 4.00)
	P †	0.03	0.06
Social support (≥40 vs. <40)			
Gender	Male	1.41 (0.85, 2.34)	1.53 (0.86, 2.73)
	Female	3.13 (1.50, 6.51) *	2.23 (0.90, 5.54)
	P †	0.05	0.61
Age group	18-30	1.96 (0.97, 3.99)	2.42(1.09, 5.36) *
	31-50	1.71 (0.77, 3.81)	1.70 (0.65, 4.49)
	50+	2.34 (1.12, 4.87) *	1.41 (0.57, 3.52)
	P †	0.70	0.03

Note. Abstinence from heroin: no heroin use during five years prior to the participants' last self-reported record from the TLFB; Abstinence from heroin and other opioids: no heroin and other opioids use during the 5 years prior to the participants' last self-reported record from the TLFB.

Model for each stratum: adjusted all covariates in model III except for the stratified variables.

* The 95% confidence interval of odds ratio is statistically significant

† P value of test for heterogeneity.