



## Gender-Specific Predictors of Retention and Opioid Abstinence During Methadone Maintenance Treatment



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### ABSTRACT

**Aims:** Retention in methadone maintenance treatment (MMT) for 1 year is associated with positive outcomes including opioid abstinence, however, most studies have not investigated gender differences. We hypothesized that predictors of retention and opioid abstinence would differ between men and women, and aimed to determine which factors best predict retention and abstinence for each gender.

**Methods:** Data were available for 290 patients (173 M, 117 F) admitted to outpatient MMT. Regression analyses, stratified by gender, were conducted to identify unique predictors of MMT retention (<1 vs. >1 year) and opioid abstinence rate (proportion of opioid-free urine samples up to 1 year retention).

**Results:** Gender did not significantly predict treatment retention (mean = 231 days, 39% retained >1 year) or opioid abstinence (49% overall). For males, significant predictors of >1-year retention were urine samples negative for opioids (odds ratio [OR] = 6.67) and cannabinoids (OR = 5.00) during the first month, and not cocaine dependent (OR = 2.70). Significant predictors of higher long-term opioid abstinence were first-month urine samples negative for opioids and cocaine metabolites. For females, significant predictors of >1-year retention were first-month urine samples negative for cocaine metabolites (OR = 4.00) and cannabinoids (OR = 9.26), and no history of sexual victimization (OR = 3.03). The only significant predictor of higher opioid abstinence rate was first-month opioid-free urine samples.

**Conclusions:** These findings indicate gender-specific predictors of MMT retention and opioid abstinence. Future studies on MMT outcomes should examine each gender separately, and consider unique pathways by which females and males adhere to, and benefit from MMT.

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### 1. Introduction

Methadone maintenance treatment (MMT) remains the most common efficacious treatment for opioid dependence (Substance Abuse and Mental Health Services Administration, 2012). Success in MMT has been defined heterogeneously, e.g., continuous opioid abstinence based on negative urine drug screens (UDS); lower rates of arrest, HIV infection, and drug related deaths; and higher employment (Joseph, Stancliff, & Langrod, 2000). In one meta-analysis of retention in 29 outpatient MMT programs, half of patients remained in treatment for over a year (Simpson, Joe, Brown, & Barry, 1997). Rates of ≈ 60% were found in more recent studies (Himmelhoch et al., 2012; Kelly, O'Grady, Mitchell, Brown, & Schwartz, 2011; Villafranca, McKellar, Trafton, & Humphreys,

2006). Patients who remained in MMT for >1 year exhibited less heroin use, drug injection and jail time than those who did not remain in MMT for 1 year (Simpson et al., 1997). Patients' 1-year retention rate is a frequently used marker of treatment success (Peles, Schreiber, & Adelson, 2006; Simpson & Joe, 2004).

Despite the general effectiveness of MMT (Kreek, 1978), not all patients entering MMT reduce their drug use. Identifying treatment-resistant patients can allow treatment providers to support (e.g., by providing extra counseling sessions) those with high need to overcome barriers to recovery. Studies examining predictors of MMT retention have found that the most consistent predictor of retention in MMT is methadone dose: higher doses forecast longer retention and less drug use (Bao et al., 2009; Bart, 2012; Farré, Mas, Torrens, Moreno, & Camí, 2002; Joe, Simpson, & Hubbard, 1991; Kamal et al., 2007; Kelly et al., 2011; Peles, Linzy, Kreek, & Adelson, 2008; Villafranca et al., 2006). Other predictors of MMT retention have varied across studies, with some support for fewer years of drug use (Ball & Ross, 1991; Peles et al., 2008), lack of concurrent non-opioid drug use (Ball & Ross, 1991; DeMaria, Sterling, & Weinstein, 2000; Joe et al., 1991), and lack of comorbid psychiatric diagnoses (Marsch et al., 2005; McLellan, Luborsky, Woody, O'Brien, & Druley, 1983).

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Studies that investigated predictors of MMT retention typically included only or mostly males, or mixed samples that did not consider gender differences (Greenfield et al., 2007). When gender was included in models of MMT outcome, it was usually examined as a predictor of retention, rather than as a stratification variable by which other risk factors can be studied. Most studies have found no differences in length of time in treatment between genders (Kelly et al., 2011; Peles et al., 2008), and others found that females were more likely than males to be retained in treatment >1 year (Deck & Carlson, 2005; Hser, Anglin, & Liu, 1990). Interpretations for why females may remain in treatment longer than males include extra motivation to abstain from drug use to retain custody of children, and the finding that females tend to utilize support services such as group and individual therapy sessions more frequently than males (Barry et al., 2011; Schiff, Levit, & Moreno, 2007). Chronically heroin-dependent females (vs. males) have also been found to have poorer overall health status, more dysfunctional families of origin, and greater mental health problems (Chatham, Hiller, Rowan-Szal, Joe, & Simpson, 1999; Grella & Lovinger, 2012), perhaps motivating them to remain in care and use more treatment services.

One of the few studies that examined gender-specific predictors of drug abstinence in substance abuse treatment found gender differences in which individual characteristics at intake predicted abstinence (Hser, Huang, Teruya, & Anglin, 2003). For males but not females, having a spouse who abused drugs predicted continued substance use. For females but not males, a history of polydrug use and lack of treatment readiness predicted continued substance use. That study combined results from outpatient, residential, detoxification, and MMT (21.8% of the sample) programs; thus, those results may not specifically apply to patients in MMT. Furthermore, patients' primary drug of abuse was not limited to opioids, and because more women than men reported cocaine or amphetamine as their primary abused drug this may bias conclusions about the effect of gender on predictors of treatment success.

Trauma exposure also appears to be an important factor in substance abuse treatment. For instance, post-traumatic stress disorder is associated with poorer adherence to MMT (Hien, Nunes, Levin, & Fraser, 2000), however, this has not been universally observed (Himelhoch et al., 2012). Furthermore, among cocaine dependent inpatients, severity of childhood trauma has been found to predict cocaine relapse among women but not among men (Hyman et al., 2008). MMT programs vary widely in the extent to which they provide treatments to address trauma exposure. An important step involves understanding the impact of trauma exposure on treatment outcomes for women and men.

The present study was conducted to determine whether predictors of MMT retention and opioid abstinence would differ between men and women, and which factors best predict outcomes for each gender. We hypothesized that, consistent with previous studies, higher methadone dose would predict higher retention and proportion of opioid-negative UDS. We further hypothesized that drug use (opioids, cocaine, cannabis, and benzodiazepines) within the first 30 days of treatment would be negatively associated with both outcome variables. Given the limited evidence on gender differences among individuals in MMT, we also hypothesized that trauma exposure (physical, sexual or emotional abuse) would specifically predict treatment outcomes for women.

## 2. Methods

### 2.1. Setting

The current study utilized data from an urban, university-affiliated MMT program, with services primarily funded through Block grant and Medicaid contracts. This clinic espouses a chronic care model focusing on retention, abstinence, harm reduction and recovery. In addition to using higher doses of methadone (when safe) to improve opioid abstinence, clinic procedures include contingency management to promote desired behavioral goals such as regular attendance at counseling

sessions (Rhodes et al., 2003), reduction of cocaine use (Tzilos, Rhodes, Ledgerwood, & Greenwald, 2009), and physician use of converging methods to reduce patients' misuse/diversion of prescribed drugs (Christensen et al., 2010).

At intake, all patients tested opioid-positive (>300 ng/ml) on their initial UDS and met criteria from the Diagnostic and Statistical Manual of Mental Disorders for a diagnosis of opioid dependence for >1 year prior to admission (DSM-IV-TR; American Psychiatric Association, 2000). All patients underwent medical and psychosocial evaluations. Patients were assigned an individual counselor with whom they were required to meet weekly for at least 30 minutes, and to a biweekly therapy group that incorporated cognitive/behavioral and interpersonal approaches.

Initial methadone doses for new patients were 30–40 mg, and titrated according to physician judgment, nursing observations and counselor input (e.g. based on opioid withdrawal signs/symptoms and drug use) in increments of 5-mg, no more frequently than every other day. Patients submitted randomly scheduled, visually monitored urine samples at least twice monthly for UDS. Upon evidence of success in maintaining abstinence (repeated opioid-negative UDS), some patients became eligible to take-home methadone doses, permitting these patients to attend the clinic less than daily. Clinical response to drug-positive UDS is generally problem-focused rather than punitive. However, heavy/persistent use of alcohol or benzodiazepines is grounds for methadone dose-reduction and potential discharge from the program (for safety reasons), although patients who demonstrate abstinence can reinstate their former status.

### 2.2. Participant selection

We screened data from medical records of 433 patients in opioid dependence treatment from 2002–2009 for inclusion in this study. Patients were excluded from analyses if: (1) their demographic/psychosocial intake data were missing ( $n = 32$ ); (2) they transferred to another MMT program ( $n = 54$ ), died ( $n = 14$ ), or were tapered off methadone before the 1-year retention mark ( $n = 3$ ); (3) they received buprenorphine instead of methadone ( $n = 31$ ); or (4) they were pregnant ( $n = 9$ ; because clinic policies differ for pregnant women). Following exclusion, data from 290 participants were retained for analysis.

### 2.3. Outcome variables

#### 2.3.1. Retention

Number of days in treatment was retrieved from each patient's electronic medical record. This raw value was transformed into a new dichotomous variable, reflecting fewer than 365 days (<1 year) or more than 365 days (>1 year).

#### 2.3.2. Proportion of opioid-negative UDS

All UDS were analyzed using radioimmunoassay methods for methadone, opioids, cocaine metabolites, cannabinoids and benzodiazepines at an off-site facility. We examined each participant's UDS results for the first year of treatment only. For each participant, the proportion of UDS results negative for opioids was calculated ( $\# \text{ opioid-negative} \div \text{total number of UDS}$ ) within the first year. Using this proportion eliminates variance due to differing numbers of UDS, which is influenced by length of time in treatment.

### 2.4. Predictor variables

Zero-order correlations (Pearson  $r$  for continuous measures, Kendall  $\tau$  for categorical measures) were calculated—separately for males and females—between outcome measures and demographic, substance use history, and psychological variables assessed at intake. Items correlated significantly ( $p < .05$ ) with either outcome measure were recoded as dichotomous (yes/no) variables for inclusion in regression analyses. The

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