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Change in symptoms of erectile dysfunction in depressed men initiating buprenorphine therapy[☆]

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Abstract

Aims—The aim of this study is to describe the change in erectile dysfunction (ED) symptoms in the first 12 weeks of outpatient buprenorphine therapy.

Background—Erectile dysfunction is highly prevalent in men who use illicit opioids when compared with the general population. To date, no study has examined ED symptoms over time in men initiating buprenorphine therapy for opioid dependence.

Methods—A randomized, double blind, placebo-controlled trial was conducted to determine whether escitalopram treatment of depressive symptoms begun 1 week prior to buprenorphine induction would improve treatment retention. Male patients completed the International Index of Erectile Function scale at baseline prior to induction and monthly thereafter. A score of 25 or less on the erectile function domain (range 1–30) is considered indicative of erectile dysfunction.

Findings—A total of 111 male subjects enrolled: mean age 38.5 ($\pm$ 9.7) years, 80.1% non-Hispanic Caucasian; 67.3% reported heroin as their opioid of choice. Mean IIEF at baseline was 20.4 ($\pm$ 10.5). At baseline, 44.1% of the entire cohort had erectile dysfunction; among those who identified as sexually active at baseline, 26.1% had ED. Baseline erectile function was inversely and significantly correlated with age ($r = -.27$, $p = .006$), but was not associated significantly with race, heroin use, years of opioid use, smoking, or hazardous use of alcohol. Compared to baseline, mean erectile function was significantly improved ($p = .001$) at 3 months, and sexual desire ($p = .002$) improved significantly at both 2- and 3-month assessments.

Conclusion—Erectile dysfunction is highly prevalent in depressed males using illicit opioids. Men who remain in buprenorphine treatment for 3 months show improvement in erectile function and sexual desire.

Keywords

Opioid dependence; Buprenorphine; Erectile dysfunction

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1. Introduction

Erectile dysfunction (ED), defined as the inability to achieve or maintain an erection satisfactory for the completion of sexual activity (National Institutes of Health, 1993), is a prevalent health condition affecting males in the United States (Selvin, Burnett, & Platz, 2007). Men who chronically use opioids report an unexpectedly high prevalence of erectile dysfunction and at younger ages compared to the general population. Across several published reports, in opioid-dependent males with a mean age ranging from 28 to 49 years, prevalence rates of ED averaged 21–52% (Bang-Ping, 2009; Brown, Balousek, Mundt, & Fleming, 2005; Cioe, Friedmann, & Stein, 2010; Hallinan et al., 2008; Hanbury, Cohen, & Stimmel, 1977; Quaglio et al., 2008).

Two cross-sectional studies have examined ED in men using illicit opioids who were not in treatment (Bang-Ping, 2009; Cioe et al., 2010). Erectile dysfunction preceded agonist therapy in these men and both studies noted an ED prevalence of 34–44%. ED was not associated with smoking status, duration of drug use, or total testosterone levels (Cioe et al., 2010), but was associated with older age. Heroin users had a higher risk of ED (OR 4.8; 95% CI; 2.9–7.8) compared to other non-opioid illicit substances (amphetamines and MDMA), and heroin use frequency was a predictor of ED (Bang-Ping, 2009).

The frequency of sexual dysfunction in men maintained on methadone or buprenorphine maintenance therapy has been compared in three cross-sectional studies. These studies found lower rates of ED in the men taking buprenorphine (Bliesener et al., 2005; Hallinan et al., 2008; Quaglio et al., 2008). Quaglio et al. found an overall ED prevalence of 42%, however the men receiving buprenorphine had lower rates of ED than those on methadone maintenance (36.3 versus 50.6%). Higher depression scores and lack of a steady partner were associated with ED; dosage of buprenorphine and methadone, duration of treatment, age, and education level were not (Quaglio et al., 2008). Similarly, Hallinan et al. found a lower prevalence of ED in the men being treated with buprenorphine than those receiving methadone therapy. Older age and depression symptoms were associated with ED (Hallinan et al., 2008). Lastly, Bliesener et al. found that only 12% of buprenorphine patients reported diminished erectile potency while 72% of methadone patients reported the same. Mean depression scores in the methadone and buprenorphine groups, measured by the Beck Depression Inventory, were similar (21.5 versus 16.4, respectively, $p > .05$).

Two longitudinal studies have examined ED symptoms over time in opioid-dependent men begun on methadone maintenance therapy (Brown et al., 2005; Chen et al., 2012). Participants were followed for 60 days (Brown et al., 2005) and 3-months (Chen et al., 2012) without statistically significant improvement in the prevalence of ED symptoms. ED symptoms were noted to become more severe over time in one study (Chen et al., 2012) and were associated with the dosage of methadone treatment in both studies (Brown et al., 2005; Chen et al., 2012).

Opioids affect the hypothalamic–pituitary–gonadal (HPG) axis and may interfere with the biological production of sex hormones, potentially contributing to erectile dysfunction (Katz, Kennedy, & Rizvi, 2009). Endogenous and exogenous opioids bind to mu receptors

in the hypothalamus, decreasing the release of gonadotropin releasing hormone (GnRH). This results in a decrease in the release of luteinizing and follicle-stimulating hormone from the pituitary, and a reduction in gonadal steroid production (testosterone and estradiol). Opioids also increase the release of prolactin from the pituitary and alter the production of dehydroepiandrosterone (DHEA) in the adrenal glands, both affecting the production and release of testosterone.

While it is clear that opioids affect the endocrine system (Katz et al., 2009; Vuong, Van Uum, O'Dell, Lutfy, & Friedman, 2010) and male sexual function (Mirin, Meyer, Mendelson, & Ellinboe, 1980), it is not clear whether these effects are dose- or substance-dependent. Additionally, the effect of partial opioid agonists, such as buprenorphine, may differ from full opioid agonists or antagonists. In rat studies, it appears that different opioids affect testosterone levels differently (Ceccarelli, Depadova, Fiorenzani, Massafra, & Aloisi, 2006). Brain levels of testosterone did not appear to be affected by the administration of buprenorphine, however, other opioids tested (morphine and fentanyl) affected both brain and plasma testosterone levels. Buprenorphine is a partial agonist at the mu receptor and it has been suggested that buprenorphine has an attenuated effect on hormonal levels (Bliesener et al., 2005).

The purpose of this study is to examine the change in symptoms of erectile dysfunction over time in men initiating buprenorphine therapy and to identify factors associated with ED among opioid-dependent men.

2. Methods

A randomized, double blind, placebo-controlled trial was conducted to determine whether escitalopram treatment of depressive symptoms begun 1 week prior to induction and continued during 12 weeks of buprenorphine treatment would improve treatment retention (Stein et al., 2010). Symptoms of erectile dysfunction were concurrently measured in male participants.

2.1. Study sample

Participants were recruited through community advertising, physician referrals and word-of-mouth. Interested individuals called the study phone to complete a brief, anonymous screen assessing basic demographics, current drug use, current depressive symptoms and current use of antidepressant medications. Potentially eligible individuals were given an appointment to complete the informed consent process in the study office. The study was approved by the Rhode Island Hospital and Butler Hospital Institutional Review Boards.

Study inclusion criteria included: age over 18 years, a SCID (*DSM-IV*) diagnosis of opioid dependence, a score on the Modified Hamilton Depression Revised Scale (MHDRS) greater than 14, the absence of significant suicidal ideation, willingness to complete 3 months of buprenorphine treatment, no medical contraindications to taking buprenorphine, no history of bipolar disorder or schizophrenia, not currently prescribed psychotropic medications, no previous non-response to escitalopram, and the ability to complete the study assessment in English.

2.2. Procedure

One hundred forty-seven persons enrolled in the study; 111 were male. No participants were using medications for erectile dysfunction at the time of enrollment. During the initial week, participants completed a baseline interview, and at its conclusion, each participant was randomized and provided study medication (10 mg of escitalopram or placebo). Participants returned for buprenorphine induction 5 days later. Dose adjustments were made based on continued opioid use, craving, and reported withdrawal symptoms. Buprenorphine doses ranged from 12 to 24 mg/day, with most participants receiving 16 mg daily. Urine specimens were obtained for toxicology testing at each study visit.

Participants had follow-up interviews at weeks 1, 2, 4, 6, 8, 10 and 12 post-enrollment; the interviews at weeks 4, 8 and 12 included a measurement of erectile function. All participants received buprenorphine/naloxone medication at no cost during their study participation.

2.3. Measures

Demographic data including age, race/ethnicity, and smoking status were collected. A substance abuse history assessed the participants' current opioid of choice and total years of use, as well as use of other illicit drugs and alcohol in the past 30 days.

Erectile function was measured using the International Index of Erectile Function (Rosen et al., 1997). This validated scale includes five domains of sexual function, including (National Institutes of Health, 1993) erectile function, (Selvin et al., 2007) sexual desire, (Bang-Ping, 2009) orgasmic function, (Brown et al., 2005) intercourse satisfaction, and (Cioe et al., 2010) overall satisfaction. Within the six-item erectile function domain, scores range from 1 to 30 and ED severity is indicated as follows: no ED (score 26–30), mild ED (score 22–25), mild to moderate ED (score 17–21), moderate ED (score 11–16), and severe ED (score 1–10). Determination of recent (last 4 weeks) sexual activity is indicated by responses to questions 1 and 2 on the erectile function scale. The sexual desire subscale contains two items and total scores for this domain range from 2 to 10 (higher scores indicate greater sexual desire). The current analyses focus on the erectile function and sexual desire domains of the scale.

The Beck Depression Inventory II (BDI) was used to measure depressive symptoms Beck, Ward, Mendelson, Mock, & Erbaugh, 1961. BDI scores of 14 or less were interpreted as representing minimal depressive symptoms, scores of 14–19 indicated mild depressive symptoms, 20–28 indicated moderate depression, and scores of 29 or higher indicated severe depression.

2.4. Statistical analysis

All statistical analyses were performed using Stata 10.1 (Statacorp, 2009). Descriptive statistics including means, proportions and standard deviations were calculated. Logistic regression was used to determine if subject attrition was associated significantly with erectile function or sexual desire at baseline. Fixed effects regression was used to evaluate changes in erectile function and sexual desire over time (Allison, 2005). The fixed-effects estimator (sometimes called the within estimator) controls between subject heterogeneity on

all time-invariant characteristics. Random effects panel regression models were used to estimate the association of potential predictor variables on erectile function. Evaluated baseline (time invariant) predictors included age, race/ethnicity, opioid of choice, years of opioid use, alcohol use, cigarettes per day, and intervention group. Time-varying predictors assessed at baseline and each monthly follow-up included the BDI, and opiate and cocaine urine toxicology tests. All models also included the linear effect of time and were estimated by maximum-likelihood which generates unbiased parameter estimates when data are missing at random or completely at random.

With appropriate coding, time-varying predictors can be decomposed into uncorrelated within-subject and between-subject effects. The within-subject effect captures the degree to which within-subject changes in the predictor are associated with within-subject changes in the response variable over time. The between-subject effects capture the stable between person differences attributable to different levels of the covariate.

3. Results

Demographic and clinical characteristics of the sample are presented in Table 1. Participants averaged 38.5 ($\pm$ 9.7) years of age and 89 (80.1%) identified as non-Hispanic Caucasian. Most participants (90%) identified as current smokers. Overall, participants averaged 9.2 ($\pm$ 21.4) alcohol drinks in the 30 days prior to baseline. More than half (53.2%) reported no alcohol consumption during that period. Diabetes was reported by three (2.7%) of participants. The mean BDI-II score at baseline was 28.24 ($\pm$ 9.3). Two men reported sexual activity with other men in the past month.

At study entry, 74 (67.3%) of the participants identified heroin as their opioid of choice. Participants also reported preferred use of oxycodone (n = 28; 19%), hydrocodone (n = 13; 8.8%), and other opioids (n = 13; 8.8%). Seventeen participants (15.3%) were enrolled in methadone maintenance at the time of study entry. Mean duration of opioid use was 9.6 ($\pm$ 8.1) years. At baseline, participants' toxicology tests were positive for cocaine (29.7%), benzodiazepines (25.9%), cannabis (37.3%), and amphetamines (0.9%).

At baseline, 49 (44.1%) participants in the entire cohort (N = 111) reported scores consistent with erectile dysfunction (score 25 or less on erectile function domain) and the mean erectile function score was 20.42 ($\pm$ 10.47). Twenty-nine (26.1%) participants had scores that indicated moderate or severe erectile dysfunction. Twenty study participants (18%) were not sexually active at baseline. When we examined only those participants who were sexually active at baseline (n = 91), we found that 29 (26.1%) had a score consistent with erectile dysfunction.

The mean score on the sexual desire scale was 5.9 ($\pm$ 2.4) at baseline. Baseline erectile function was inversely correlated with age (r = $-.26$, p = .006), but was not significantly associated with race, heroin use, years of opioid use, cigarette smoking, or hazardous use of alcohol.

Study follow-up rates were 86.5% at 1-month, 72.1% at 2-months, and 62.2% at 3-months. Loss to follow-up at 1-month (OR = 1.01, z = 0.57, p = .567), 2-months (OR = 1.03, z =

1.43, $p = .152$), and 3-months (OR = 1.01, $z = 0.65$, $p = .517$) was not associated significantly with baseline erectile function. Similarly, baseline sexual desire was also not a significant predictor of follow-up loss at 1-month (OR = 0.92, $z = -0.78$, $p = .436$), 2-months (OR = 1.13, $z = 1.33$, $p = .185$), or 3-months (OR = 1.08, $z = 0.86$, $p = .389$).

3.1. Change in erectile function and sexual desire over time

Both erectile function and sexual desire improved significantly during the 3-month course of buprenorphine treatment. Using fixed-effects regression, we found significant differences in mean erectile function ($F_{3,241} = 4.55$, $p = .004$) and mean sexual desire by month ($F_{3,241} = 3.93$, $p = .009$). Relative to baseline, mean erectile function scores at 1-month ($b = -0.31$, $t = -0.30$, $p = .764$) and 2-months ($b = 1.78$, $t = 1.78$, $p = .180$) were not significantly different. However, at 3-months, mean erectile function scores were 3.6 ($t = -3.09$, $p = .010$) points higher than at baseline. Mean sexual desire scores at 1-month were not significantly different than baseline ($b = 0.26$, $t = 1.16$, $p = .249$); however, mean sexual desire was significantly higher at both 2-months ($b = 0.74$, $t = 3.07$, $p = .002$) and 3-months ($b = 0.65$, $t = 2.56$, $p = .011$) compared to baseline.

Operationally, the erectile function scale defines persons not sexually active as having severe erectile dysfunction. We were concerned that floor effects could effectively drive overall changes in erectile function over time. Specifically, if those who were not sexually active at baseline became sexually active at follow-up, overall changes in observed erectile function scores would be biased upward. Fig. 1 plots mean erectile function scores in the full cohort ($N = 111$), and separately for those not sexually active at baseline ($n = 20$), those with moderate or more severe ED at baseline ($n = 29$) and for those with normal erectile function at baseline ($n = 62$).

Among those not sexually active at baseline, five were sexually active at 1-month, six were sexually active at 2-months, and seven were sexually active at 3-months. Overall, 11 of the 20 persons who were not sexually active at baseline reported at least some sexual activity at one or more of the follow-up assessments. The mean erectile function scores of the men who were not sexually active at baseline increased from 3.4 (baseline) to 14.9 at 3-months (Fig. 1); this was in part due to this increase in sexual activity. The trend was approximately linear and statistically significant ($b = 4.71$, $t = 4.80$, $p < .001$).

Among those with moderate or severe ED at baseline, mean erectile function scores were 14.1 at baseline, 14.9 at 1-month, 19.3 at 2-months, and 19.5 at 3-months. Relative to baseline, mean erectile function scores were significantly higher at 2-months ($b = 5.43$, $t = 2.76$, $p = .008$) and at 3-months ($b = 5.73$, $t = 2.66$, $p = .010$) but not at 1-month ($b = 1.17$, $t = .059$, $p = .555$). Among those with normal erectile function at baseline, mean erectile function scores did not change significantly over the course of study.

3.2. Predictors of erectile function and sexual desire

Random effects models were used to estimate the effect of selected predictor variables on erectile function and sexual desire (Table 2). Baseline predictors included age, ethnicity, opiate of choice, years of regular opiate use, cigarettes per day, and intervention group

(escitalopram versus placebo) assignment. The BDI score was included as a time-varying covariate. The linear effect of time was included as a covariate. Controlling for all other predictors included in the model, erectile function was inversely and significantly associated with age ($b = -0.27$, $z = -3.14$, $p = .002$), significantly higher among those with a preference for heroin ($b = 2.94$, $z = 2.31$, $p = .021$), and inversely associated with BDI score ($b = -0.13$, $z = -2.33$, $p = .020$). Sexual desire was inversely and significantly associated with age ($b = -0.04$, $z = -2.05$, $p = .040$) and BDI score ($b = -0.05$, $z = -4.57$, $p < .001$), but was not associated significantly with any of the other evaluated predictors.

Between-person differences in BDI scores were not associated significantly with erectile function (the product-moment correlation using only baseline data was $-.10$, $p = .404$). However, within-person increases in depression scores were associated significantly ($p < .05$) with decreases in erectile function. The linear effect of time was not significant in the full model; this term was significant in all models with the exception of those including the within-person effect of depression. Sexual desire was associated significantly with both the between ($p < .05$) and within person ($p < .05$) effects of depression (the p -value for the unadjusted effect was $.056$); persons with higher BDI scores had lower sexual desire, and, within persons, an increase in depression severity was associated with a decrease in sexual desire. Change in erectile function was not significantly associated with escitalopram treatment ($b = 4.17$, $t = 1.25$, $p = .214$).

4. Discussion

Our study examined the change in symptoms of erectile dysfunction in depressed men initiating buprenorphine treatment. Consistent with the literature, we found that erectile dysfunction was highly prevalent, and at younger ages, in men using opioids chronically. Examining symptom change over time, we found that erectile function and sexual desire improved significantly during the 3 months following buprenorphine initiation. Additionally, we found that an improvement in depressive symptoms was associated with improved erectile function.

This study provides additional evidence that younger men with opioid dependence have a notable prevalence of erectile dysfunction and that symptoms are often moderate to severe. These findings are similar to other reports in the literature that examine ED symptoms in men who use opioids. Prevalence rates of 21–52% have been reported among users of illicit opioids, methadone and buprenorphine; however, several cross-sectional reports demonstrated that buprenorphine users had consistently lower levels of dysfunction when compared to other opioids (Bliesener et al., 2005; Hallinan et al., 2008; Quaglio et al., 2008). Similar to other studies, baseline erectile function was inversely associated with age (Bang-Ping, 2009; Cioe et al., 2010; Hallinan et al., 2008) but not with duration of opioid use (Bang-Ping, 2009; Cioe et al., 2010; Quaglio et al., 2008) or cigarette smoking (Bang-Ping, 2009; Cioe et al., 2010). Sexual dysfunction in men is complex and can be attributed to biological etiologies—such as low testosterone or atherosclerosis. However, testosterone levels (which were not tested in this study) are unlikely to fully explain the high prevalence of ED found in this study and by others (Cioe et al., 2010; Hallinan et al., 2008). Opioid-related processes may contribute to sexual dysfunction in this population, including

sedation, satiety (Pfuas, 2009), and also the salience of substance use, aside from non-opioid factors including mood disorders.

To our knowledge, this is the first and only prospective study to examine symptoms of erectile dysfunction over time in men receiving buprenorphine therapy. Interestingly, unlike two longitudinal studies in men receiving methadone maintenance, our study found that ED symptoms significantly improved over time. Brown et al. (2005) and Chen et al. (2012) found that ED prevalence increased and the severity of symptoms worsened over time when men initiated methadone for opioid dependence treatment. Buprenorphine, unlike methadone, is a partial opioid agonist at the mu receptor and this may account for the difference seen in our study.

In the full cohort, we found a 3.6 point improvement in the mean score of the erectile function domain subscale over the 3-month period of follow-up; and while this was statistically significant, it is difficult to know if this level of change is clinically relevant. Rosen, Allen, Ni, and Araujo (2011) examined 17 clinical trials with 3345 patients treated with a phosphodiesterase type 5 inhibitor for 12 weeks to determine the “minimal clinically important difference” (MCID) in the erectile function domain of the IIEF. They concluded that the overall MCID was four, however it varied significantly by baseline severity and ranged from two, five, and seven, for mild, moderate and severe dysfunction, respectively. We found that there was significantly greater improvement over time in all groups who reported a score of 25 or less at baseline: within the full cohort, within those with erectile function at baseline, and within the men who were not sexually active at baseline (see Fig. 1). A longer period of follow-up may have shown further marked improvement, possibly reaching the MCID suggested by Rosen et al.

With regard to depressive symptoms and erectile function, we report two interesting findings. In within-persons analyses, we observed that increases in depression scores were significantly associated with increases in erectile dysfunction, which is consistent with the literature. In the general population (Jeong et al., 2011; Lotti et al., 2012) and studies of opioid-dependent men (Hallinan et al., 2008; Quaglio et al., 2008), depressive symptoms are often associated with increased symptoms of erectile dysfunction. Although the exact mechanism for this is unknown, psychological causes have been postulated (Jeong et al., 2011).

In the United States, SSRIs are widely used for the treatment of depression and 30–60% of patients generally report sexual dysfunction as an adverse effect of their use (Gregorian et al., 2002; Kennedy & Rizvi, 2009). We found no statistically significant differences in erectile function between those randomized to treatment with an SSRI and those receiving placebo. Directionally, between group differences slightly favored those in the active intervention (escitalopram) arm. Our findings suggest that using escitalopram to treat depression in this population does not increase erectile dysfunction. The improvement in depressive symptoms may have had a beneficial effect on participants’ social function, thus increasing the potential for sexual activity and improved erectile function. Kennedy and Ritvi reported that while sexual dysfunction and depression often co-occur, they appear to be bidirectional, in that the treatment of one may alleviate or improve the symptoms of the

other (Kennedy & Rizvi, 2009). Additionally, in a meta-analysis of sexual dysfunction related to antidepressant medications, Serretti and Chiesa (2009) found that escitalopram was associated with less impact on sexual function compared to other frequently prescribed SSRIs (Serretti & Chiesa, 2009). Studies in patients treated with SSRIs often show that up to 90% of patients who report treatment-related sexual dysfunction are nonadherent with treatment due to this side effect (Nurnberg, 2008). The improvement in erectile function seen in our study is particularly promising because it has the potential to affect that subgroup of opioid dependent males who are also receiving treatment for depressive symptoms.

This study has limitations. The study had a modest sample size and there was significant dropout between baseline and 3 months. It is unknown whether those who dropped out experienced change in erectile dysfunction symptoms; however, baseline erectile dysfunction and sexual desire did not predict dropout. We have 12 weeks of follow-up and we are unable to project whether we would have seen continued improvement over a longer period of time. All males who entered this study had depressive symptoms at baseline and therefore our findings may not be generalizable to all men initiating buprenorphine for opioid dependence. Lastly, the IIEF instrument has not been tested in substance users and its reliability in this population is unknown. The instrument focuses specifically on one's ability to have sexual intercourse in measuring erectile function (Rosen, Cappelari, & Gendrano, 2002), potentially confounding partner status with erectile function. Participants who were not sexually active or did not have a partner at baseline may have had lower scores due to the lack of a sexual partner rather than to erectile dysfunction itself. Also, a change in partner status, such as might for happen with improved social function in the context of opioid pharmacotherapy, could potentially affect serial erectile function scores.

Patients with opioid dependence should routinely be screened for erectile dysfunction due to the high prevalence in this population. The findings of our study suggest that improvement in ED symptoms may be seen following buprenorphine initiation. Further research is needed to determine if buprenorphine treatment is more beneficial in improving sexual dysfunction symptoms when directly compared to other treatments that are used for opioid dependence. Also, studies of longer duration could demonstrate continued and further improvement over time in erectile dysfunction symptoms.

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Fig. 1.
Mean erectile function by month in the full cohort and by baseline erectile function classification.

Table 1Background characteristics ($N = 111$).

	Mean ($\pm$ <i>SD</i>) or I (%)	Median	Range
Age (years)	38.51 ($\pm$ 9.74)	38.0	20–66
Race/ethnicity			
Caucasian (non-Hispanic)	89 (80.1%)		
African-American	4 (3.6%)		
Hispanic	13 (11.7%)		
Other minority	5 (4.5%)		
Beck Depression Inventory	28.24 ($\pm$ 9.28)	28	9–52
Erectile function	20.42 ($\pm$ 10.47)	27.0	1–30
Sexual desire	5.93 ($\pm$ 2.39)	6.0	2–10
Opioid of choice, heroin	74 (67.3%)		
Years of regular opioid use	9.57 ($\pm$ 8.07)	7.0	0–37
Cigarettes/day			
None	11 (10.1%)		
10	35 (32.1%)		
11–20	43 (39.5%)		
> 20	20 (18.3%)		
No. of alcohol drinks last 30 days	9.19 (21.36)	0.0	0–154
Cocaine+ at baseline	33 (29.7%)		
Current MMT enrollment (yes = 1)	17 (15.3%)		
Study follow-up rate, 1-month	96 (86.5%)		
Study follow-up rate, 2-months	80 (72.1%)		
Study follow-up rate, 3-months	69 (62.2%)		

Table 2

Random intercept models estimated the unadjusted^a and adjusted^a effects of selected predictor variables on erectile function and sexual desire.

	Erectile function		Sexual desire	
	Unadjusted <i>b</i> (95% CI)	Adjusted <i>b</i> (95% CI)	Unadjusted <i>b</i> (95% CI)	Adjusted <i>b</i> (95% CI)
Time-invariant predictors				
Age	−0.27** (−0.44; −0.11)	−0.31** (−0.50; −0.12)	−0.04* (−0.08; −0.01)	−0.04* (−0.08; −0.01)
Race (Caucasian)	0.33 (−3.92; 4.59)	−0.54 (−4.75; 3.67)	−0.16 (−1.07; 0.76)	−0.31 (−1.23; 0.60)
Opiate of choice (heroin)	2.94 (−0.58; 6.47)	3.00 (−0.70; 6.69)	0.16 (−0.60; 0.93)	−0.14 (−0.94; 0.67)
Years of regular opiate use	−0.09 (−0.30; 0.12)	0.07 (−0.17; 0.32)	−0.01 (−0.05; 0.36)	0.02 (−0.03; 0.07)
Cigarettes per day	0.02 (−1.55; 1.59)	0.51 (−1.00; 2.01)	−0.24 (−0.58; 0.10)	−0.19 (−0.52; 0.13)
Drinks last 30-days	−0.04 (−0.11; 0.04)	−0.02 (−0.10; 0.05)	−0.01 (−0.03; 0.01)	−0.01 (−0.03; 0.00)
Intervention (yes)	−0.02 (−3.36; 3.32)	0.09 (−3.08; 3.27)	0.06 (−0.65; 0.78)	0.05 (−0.64; 0.75)
Time-varying predictors				
Month	<i>b</i>	0.47 (−0.46; 1.41)	<i>b</i>	−0.06 (−0.26; 0.14)
BDI (between)	−0.00 (−0.19; 0.19)	−0.10 (−0.29; 0.09)	−0.04 (−0.08; 0.00)	−0.06** (−0.10; −0.02)
BDI (within)	−0.13* (−0.23; −0.02)	−0.14* (−0.25; −0.02)	−0.05** (−0.07; −0.02)	−0.05** (−0.07; −0.02)
Opiate+ (between)	4.02 (−0.32; 8.36)	2.79 (−1.97; 7.56)	0.37 (−0.58; 1.31)	0.60 (−0.43; 1.64)
Opiate+ (within)	1.00 (−1.50; 3.49)	1.47 (−1.10; 4.03)	0.20 (−0.34; 0.75)	−0.06 (−0.61; 0.50)
Cocaine+ (between)	2.89 (−1.64; 7.42)	0.95 (−3.59; 5.49)	0.86 (−0.17; 1.78)	0.58 (−0.41; 1.57)
Cocaine+ (within)	−1.37 (−4.19; 1.46)	1.23 (−1.64; 4.10)	−0.21 (−0.83; 0.40)	0.28 (−0.34; 0.90)
<i>SD</i> (intercept)	<i>b</i>	7.03** (5.8; 8.41)	<i>b</i>	1.53** (1.28; 1.84)

^a Models estimated unadjusted effects included only the relevant predictor, the linear effect of time, and the random intercept. Models estimating adjusted effects also included all predictors as covariates.

^b Estimates are not reported because they vary depending on which predictor variable was being evaluated.

* $p < .05$.

** $p < .01$.