



Frequency and correlates of sleep disturbance in methadone and buprenorphine-maintained patients



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HIGHLIGHTS

- Large numbers of opioid maintenance treatment (OMT) patients suffer from sleep impairment.
- Levels of impairment were similar between methadone and buprenorphine-maintained patients.
- Impairment was associated with several concurrent problems suggestive of substantial distress.
- Research to reduce sleep impairment in OMT patients is warranted.

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ABSTRACT

Background: Opioid use disorder (OUD) is a significant public health problem, and opioid maintenance treatment (OMT) on methadone or buprenorphine is a common approach. This study characterized sleep impairment in patients maintained on methadone or buprenorphine, and evaluated its association with psychiatric and medical comorbidities.

Methods: Participants (N = 185) maintained on methadone (N = 125) or buprenorphine (N = 60) for OUD completed the Medical Outcomes Study Sleep Scale (MOS) to provide a point-prevalence assessment of sleep impairment. Measures of lifetime problems and current functioning were also examined and compared as both a function of OMT and level of sleep impairment.

Results: Participants reported high levels of sleep impairment on the MOS, including not getting the amount of sleep they needed (42.9%), not sleeping enough to feel rested (39.6%) and trouble falling asleep (23.3%) or falling back asleep after waking (25.8%). Few differences were observed between OMT groups, and psychiatric dysfunction emerged as the most robust predictor of sleep impairment ratings. Patients with sleep impairment, independent of OMT medications, also reported current opioid withdrawal, psychiatric impairment, negative affect, and pain.

Conclusions: Results demonstrate substantial and clinically-significant impairments in sleep that are associated with a variety of current problems that could impact OMT outcomes and decrease quality of life. Outcomes support the development of methods to improve sleep in OMT patients, and to examine the degree to which sleep improvements may be associated with improvements in mood and other health-related measures.

1. Introduction

Opioid misuse and abuse is a serious public health problem. Maintenance on an opioid agonist like methadone or buprenorphine is endorsed by the World Health Organization as an effective treatment for opioid use disorder (OUD) (World Health Organization, 2007) and is among the most common forms of treatment for this indication. > 78,000 people in the United States initiated opioid maintenance treatment (OMT) with one of those medications in 2012 (Substance Abuse and Mental Health Services Administration (SAMHSA), Center

for Behavioral Health Statistics and Quality, 2014). However, OMT patients continue to experience a host of concurrent psychiatric and medical comorbidities that may interfere with their treatment and/or increase their propensity for relapse, and there is value in understanding the breadth and severity of these issues to help develop supportive resources for this population.

Sleep disturbance is a primary characteristic of multiple substance use disorder syndromes, including OUD (Barth et al., 2013; Caviness, Anderson, de Dios, Kurth, & Stein, 2013; Garcia & Salloum, 2015). Relative to healthy controls (8.8%), significantly more individuals with

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OAD (80.6%) have ratings ≥ 5 on the Pittsburgh Sleep Quality Index, indicative of poor sleep quality (Hartwell, Pfeifer, McCauley, Moran-Santa Maria, & Back, 2014), which has also been verified objectively through polysomnography (PSG) testing (Kay, Eisenstein, & Jasinski, 1969; Kay, 1975; Xiao et al., 2010). Sleep disturbance is evident among patients who are newly enrolled into OMT (Burke et al., 2008; Nordmann et al., 2016), as well as long-term OMT patients (Stein et al., 2004). Longitudinal evaluations suggest sleep does not naturally improve over the course of methadone treatment (Nordmann et al., 2016; Peles, Schreiber, Hamburger, & Adelson, 2011) and that sleep may in fact worsen, with the development of central sleep apnea in some patients (Wang et al., 2005).

Previous studies of sleep in OUD patients have also reported associations between sleep impairment and psychiatric comorbidities (Peles, Schreiber, & Adelson, 2006; Stein et al., 2004), however those data were collected in the context of a single clinic and were restricted to methadone-maintained patients. To date, no studies have reported on the sleep characteristics and related comorbidities of buprenorphine-maintained patients. Maintenance medication type is an important distinction for several reasons. First, evidence suggests methadone and buprenorphine treatment modalities may draw different types of patients. Relative to methadone-maintained patients, buprenorphine-maintained patients are more likely to be male, employed, have health insurance, and have milder levels of OUD (e.g., shorter use and treatment histories, less injection drug use, primary prescription opioid users) (Fingerhood, King, Brooner, & Rastegar, 2014; Sullivan, Chawarski, O'Connor, Schottenfeld, & Fiellin, 2005). Second, the fact that buprenorphine is often prescribed from primary care settings suggests those patients may also have greater access to concurrent sleep treatments and pharmacotherapies. Finally, the pharmacological differences between methadone and buprenorphine could impact sleep quality. Specifically, methadone is a full agonist at the mu opioid receptor, whereas buprenorphine is a partial agonist at the mu opioid and ORL-1 receptors and a partial antagonist at the kappa receptor. Pre-clinical studies report that mu receptor agonists directly inhibit rapid eye movement (REM) (Cronin, Keifer, Baghdoyan, & Lydic, 1995) and slow wave (Dimsdale, Norman, DeJardin, & Wallace, 2007) sleep, so differences in mu receptor properties between methadone and buprenorphine could theoretically influence sleep quantity and quality.

The present study sought to characterize the self-reported sleep profiles of community-based patients maintained on methadone or buprenorphine for the treatment of OUD and to examine the association between sleep impairment and psychiatric, drug use, and medical comorbidities. The study also examined whether associations varied systematically between methadone and buprenorphine-maintained participants. These data will help to further characterize the breadth and severity of sleep impairment among OMT patients.

2. Methods

2.1. Participants

Participants were recruited between 4/2012 and 2/2014 from eight different methadone and buprenorphine OMT providers in Baltimore, MD. Individuals who were under 18 years of age, not receiving methadone or buprenorphine for the treatment of OUD, or not fluent in English were excluded. A total of 201 individuals completed the survey; of these eight answered “yes” to the quality control question “Have you completed this survey before”, three did not indicate their OMT type, and five did not answer all questions on the MOS (preventing subscale calculations); resulting in a final sample size of 185. This study was approved by the Johns Hopkins IRB and a waiver of written informed consent was obtained.

2.2. Study procedures

Staff members set up stations within the OMTs that advertised a survey opportunity on health behaviors. Interested patients from within the OMT were provided with self-report surveys to complete, and were compensated up to \$10 in cash or giftcards for participation. Study staff were available to help answer questions and read items to participants with low literacy. All surveys were completed in a single session; patients were not allowed to take surveys home for completion. Measures collected information regarding lifetime history (demographics, medical/psychiatric diagnoses) as well as current (ranging from past 30-day to today) experiences.

2.3. Measures

2.3.1. Demographic and drug use questionnaire

Participants completed a brief demographic and drug use questionnaire to help characterize the sample. Past 30-day self-reported illicit drug use and OMT dose were collected but omitted from the analyses due to a large portion of participants not answering those questions.

2.3.2. Medical and psychiatric diagnoses

Participants were asked to indicate whether they had been diagnosed with one of 61 potential medical or psychiatric problems in their lifetime. The list of psychiatric diagnoses included mood and non-mood disorders that are known to have high prevalence in OMT patients but was not meant to be exhaustive. Diagnoses were categorized into systems and the dichotomous endorsement (yes/no) of any medical condition within each system was included in the analyses.

2.3.3. Medical Outcomes Study (MOS) Sleep Scale

The MOS Sleep Scale is a 12-item self-report measure that assesses sleep retrospectively over the past 30 days. Participants are asked how long it takes them to fall asleep on an ordinal scale and to write in the number of hours they slept each night. Ten additional questions are rated on a 6-point Likert scale (“All of the Time” to “None of the Time”). The MOS Sleep Scale yields a rating of hours slept per night and seven subscales: Sleep Disturbance, Snoring, Sleep Short of Breath or Headache, Sleep Adequacy, Somnolence, Sleep Problems Index I, and Sleep Problems Index II. The MOS Sleep Scale has strong psychometric properties that were derived from a representative sample of men and women in the United States (Allen, Kosinski, Hill-Zabala, & Calloway, 2009; Hays, Martin, Sesti, & Spritzer, 2005) and has been used previously to characterize sleep outcomes within methadone-maintained patients (Burke et al., 2008). Normative values are available and provided for each subscale (see Table 2), and more information regarding the constitution of specific scales are available in the MOS Scoring Manual (Hays et al., 2005).

2.3.4. Subjective Opiate Withdrawal Scale (SOWS) (Handelsman et al., 1987)

The SOWS is a self-report instrument that rates current opioid withdrawal across 16 potential symptoms using a 5-point Likert scale (“Not At All” to “Extremely”). Values are summed to create a total severity score (range 0–64). The SOWS was used to provide a point-prevalence assessment of acute opioid withdrawal and was evaluated as a potential correlate of sleep impairment.

2.3.5. Symptom-Checklist 10R (SCL-10R) (Rosen et al., 2000)

The SCL-10R is a brief self-report instrument derived from the SCL-90, and provides an assessment of past 30-day psychiatric functioning on a 5-point Likert scale (“Not At All” to “Extremely”). Values are summed to create a total severity score (range 0–40). The SCL-10R was used to provide a point-prevalence assessment of current psychiatric impairment, and was evaluated as a potential correlate with sleep

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