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Comparison of methods to assess psychiatric medication adherence in methadone-maintained patients with co-occurring psychiatric disorder

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ABSTRACT

Background: Adherence with psychiatric medication is a critical issue that has serious individual and public health implications. This is a secondary analysis of a large-scale clinical treatment trial of co-occurring substance use and psychiatric disorder.
Method: Participants ($n = 153$) who received a clinically-indicated psychiatric medication ≥30 days during the 12-month study and provided corresponding data from Medication Event Monitoring System (MEMS) and Morisky Medication Taking Adherence Scale (MMAS) self-report adherence ratings were included in the analyses. Accuracy in MEMS caps openings was customized to each participant's unique required dosing schedule.
Results: Consistent with expectations, MEMS-based adherence declined slowly over time, though MMAS scores of forgetting medication remained high and did not change over the 12-month study. MEMS caps openings were not significantly impacted by any baseline or treatment level variables, whereas MMAS scores were significantly associated with younger age and presence of an Axis I disorder and antisocial personality disorder, or any cluster B diagnoses.
Conclusions: Results suggest that MEMS caps may be a more objective method for monitoring adherence in patients with co-occurring substance use and psychiatric disorder relative to the MMAS self-report. Participants in this study were able to successfully use the MEMS caps for a 12-month period with <1% lost or broken caps, suggesting this comorbid population is able to use the MEMS successfully. Ultimately, these data suggest that an objective method for monitoring adherence in this treatment population yield more accurate outcomes relative to self-report.

1. Introduction

More than 20% of adults in the United States have been prescribed at least one psychotropic medication (Medco Health Solutions, 2011). Psychiatric medication treatments are generally chronic treatment regimens, which have an increased opportunity for poor medication adherence to develop, and psychotropic medications are not taken as prescribed approximately 30–46% of the time (Bulloch and Patten, 2010). Poor medication adherence has been associated with poor outcomes and increases in medical costs and rehospitalizations in general medical conditions (Svarstad et al., 2001; Sokol et al., 2005), and in patients with serious mental illness specifically (Sun et al., 2007), and can obscure or confound the results of clinical trial evaluations of new medications or treatment indications (Blaschke et al., 2012; Vrijens and Urquhart, 2014). The World Health Organization has called poor medication adherence a worldwide problem of striking magnitude (World Health Organization, 2003; Sajatovic et al., 2010), yet efforts to measure adherence are hampered by the absence of universally accepted standards for defining and measuring adherence.

Up to 50% of patients entering methadone maintenance (MM) for the treatment of opioid use disorder suffer with a co-occurring psychiatric disorder (Brooner et al., 1997; McGovern et al., 2006). Psychiatric disorders in this population have been associated with impairments in patient psychosocial functioning and quality of life (Cacciola et al., 2001; Compton et al., 2003; Carpentier et al., 2009), and illicit drug use has been associated with poor medication adherence (Keck et al., 1997; Olfson et al., 2000; Magura et al., 2002; Lacro et al., 2002; Weiss, 2004). Thus, methods to measure and ultimately increase adherence to psychiatric medications are especially important for these patients. Only one study has compared

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different methods to assess medication adherence in MM patients; patients ($n = 53$) completed five concurrently administered self-report measures of antiretroviral adherence and rates of perfect adherence ranged from 22–58% across the measures (Berg et al., 2012). No studies have compared different methods for measuring adherence to psychiatric medication within MM patients. One reason for this may be the diverse nature of the medications prescribed in clinical settings. For instance, in contrast to participants in randomized clinical trial evaluations of medication efficacy, clinical MM patients with co-occurring psychiatric disorder are often prescribed myriad psychiatric medications that entail different dosing schedules and frequencies.

There is value in identifying effective methods to measure adherence with psychiatric medications in MM patients for both research and clinical settings. Self-report measures are conventional strategies that ask patients to recall their level of adherence over a period of time. These measures are relatively brief and inexpensive to administer, however results may be subject to problems with recall bias and are highly dependent upon the specific questions asked (Berg et al., 2012). A more advanced method is electronic adherence monitoring, which has been endorsed by the treatment community and Food and Drug Administration (Osterberg and Blaschke, 2005; Food and Drug Administration (FDA), 2012). The Medication Event Monitoring System (MEMS^{TM}; WestRock), an electronic prescription bottle cap that records all bottle openings as a proxy measure of adherence, is one example of this technology. Though MEMS cannot certify that the correct amount of medication was extracted and consumed during each opening, blood plasma levels of drugs can be accurately predicted by the number of MEMS openings (Vrijens et al., 2005), which supports its use as a proxy measure.

Despite the potential for improved adherence monitoring, MEMS can be expensive and logistically complicated, so ensuring their use is necessary and appropriate for specific populations is important. Although a recent meta-analysis reported that MEMS and self-reported measures of adherence are highly correlated (Shi et al., 2010a), evidence suggests that patient population may significantly impact outcomes. For instance, some populations (*e.g.*, diabetes; pregnancy) show strong correspondence between MEMS and other methods of adherence monitoring, suggesting these patients may not incur any additional benefit from MEMS caps monitoring (Gonzalez et al., 2013; Bosman et al., 2014); whereas other populations (*e.g.*, depression, heart failure, schizophrenia) show major discrepancies between MEMS and other methods of adherence monitoring, suggesting these patients may benefit from MEMS caps over other monitoring approaches (Byerly et al., 2005; Parker et al., 2007; Wu et al., 2008; Lee et al., 2010; Nieuwenhuis et al., 2012). The degree to which MEMS and self-report measures are associated, and the degree to which MM patients with co-occurring psychiatric disorder can successfully utilize the MEMS caps, is currently unknown.

This is a secondary data analysis to compare medication adherence rates concurrently assessed using MEMS and a widely-used self-report measure of medication adherence among MM participants prescribed medication for a co-occurring psychiatric disorder. Psychiatric medications were prescribed as clinically indicated, which resulted in a range of different medications and dosing schedules, and patients were enrolled for a 12-month period, which provides a unique opportunity to compare the value of two adherence monitoring methods over an extended period of time in a real-world clinical setting. The study hypothesized that MEMS caps would provide a better method of tracking medication adherence in this population relative to self-report, and that participants would be able to successfully use the MEMS caps during the trial (*i.e.*, low rates of loss or broken MEMs caps). These data will help inform the field on the utility and merits of monitoring psychiatric medication adherence *via* electronic *versus* self-report methods in clinical populations with co-occurring substance use and other psychiatric disorder.

2. Methods

2.1. Participants

Participants ($n = 316$) were recruited from the Addiction Treatment Services (ATS) program in Baltimore, MD to participate in a randomized controlled comparison of on-site/integrated *versus* off-site/non-integrated substance abuse and psychiatric care (Brooner et al., 2013). All participants were receiving MM as part of their overall treatment plan. To be eligible for the study, participants had to meet DSM-IV criteria for opioid dependence and federal criteria for MM, meet DSM-IV criteria for a current psychiatric diagnosis that was eligible for treatment within Maryland's public mental health system, and to report an interest in receiving treatment for the psychiatric problem. Exclusion criteria were being pregnant, presence of an acute medical and/or psychiatric problem that required urgent attention, and presence of an organic mental disorder and/or other cognitive impairment that may interfere with comprehension of study procedures. For the purpose of these analyses, the two experimental groups were collapsed and only participants who received a MEMS cap for $\geq$30 days and had corresponding self-report data within the 12-month study period were evaluated. Reasons for not receiving a MEMS cap included never starting a psychiatric medication, treatment drop-out, or being prescribed a psychiatric medication not subject to tracking (*e.g.*, symptomatic medications used when needed). The Johns Hopkins Institutional Review Board reviewed and approved the study and all participants provided voluntary written consent to participate.

2.2. Study procedures

A full report of the study procedures and primary outcomes have been reported previously (Brooner et al., 2013); therefore, only procedures relevant to these analyses are described here.

Participants enrolled in this 12-month intervention completed assessments at screening and 30-day intervals. All participants were prescribed methadone for opioid use disorder as part of routine care and were provided with good and comparable access to prescribed psychiatric medications; medication costs for uninsured participants ($n = 158$; 50.0% of total sample) were paid by the study. Prescriptions for psychiatric medications were submitted to a single pharmacy and medication was delivered to the treatment clinic within 48-h. Participants who received medications were issued a wide-range of prescriptions with different dosing schedules, and it was possible for participants to have prescriptions that began and/or ended during the 12-month study.

2.3. Study measures

2.3.1. Self-report and observer-rated measures. The Structured Clinical Interview for DSM-IV (First et al., 1997, 2002) was administered by a trained staff member at screening to diagnose the presence of drug and/or alcohol dependence and other Axis I & II psychiatric disorders; diagnoses were confirmed by a board certified psychiatrist or clinical psychologist. Participants also completed the Symptom Checklist-90 (SCL-90), a 90-item self-report measure that assesses functioning in 9 psychiatric symptom domains and produces a global assessment of functioning (Global Severity Index; GSI), at screening and at 30-day intervals and each subscale was normalized for age and gender to yield a T-score value. Self-reported adherence with prescriptions was collected every 30-days using the Morisky Medication Taking Adherence Scale (MMAS; Morisky et al.,