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Measurement of psychiatric treatment adherence

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Abstract

Objective: Nonadherence to medications for mental disorders substantially limits treatment effectiveness and results in higher rates of relapse, hospitalization, and disability. Accurate measurement of medication adherence is important not only in adherence research but also in clinical trials in which medications are being evaluated and in clinical practice where failure to detect nonadherence results in premature medication changes, unnecessary polypharmacy, and greater likelihoods of functional deteriorations and hospitalizations. This is a review of psychiatric treatment adherence methods and measures arising from a meeting on "Methodological Challenges in Psychiatric Treatment Adherence Research" held on September 27–28, 2007, in Bethesda, MD, and organized by the National Institute of Mental Health (NIMH). **Methods:** This paper reviews the range of modalities currently available for assessing adherence behavior including pill counts, pharmacy records, technology-assisted monitoring, biological assays, and a range of self-report and interviewer-rated scales. Measures of adherence attitudes are also reviewed. **Results:** Each of the adherence measures described are imperfect estimates of actual medication ingestion, but each provides informative estimates of adherence or the attitudinal factors associated with adherence. Measure selection depends on a range of factors including the patient sample, the context in which the measure is being used, and the clinical outcomes expected from various levels of nonadherence. The use of multiple measures of adherence is encouraged to balance the limitations of individual measures. **Conclusion:** While adherence assessment has become increasingly sophisticated in recent years, there remains a need for refinement and expansion on currently available methods and measures.

Keywords: Adherence; Assessment; Compliance; Measurement; Outcomes; Self-report

Introduction

The World Health Organization defines adherence as "the extent to which a person's behavior—taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care professional" [1]. Nonadherence is a serious problem in psychiatric treatment and compromises effectiveness [2–6]. In schizophrenia, full or partial nonadherence can exceed 60% [7–9] and is associated with relapse, hospitalization, and elevated health care costs [7,10,11]. In bipolar disorder, nonadherence ranges from 20% to 60% [2,12,13] and is associated with poorer outcomes, elevated rates of relapse, hospitalization, suicidal behavior, and greater costs of care [13–15]. Thirty percent of patients stop taking antidepressants after 1 month and 45–60% after 3 months. Inadequate adherence to antidepressants may lead to increased recurrence, severity, and disability, poorer responsivity to future treatment, and greater health care cost [16–22].

Reflecting an increasing awareness of the importance of treatment adherence on psychiatric populations, the National Institute of Mental Health (NIMH) assembled a group of experts in the area of mental health treatment research for a

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meeting on "Methodological Challenges in Psychiatric Treatment Adherence Research" held on September 27–28, 2007, in Bethesda, MD. During this meeting, the experts discussed and consolidated their experience based on the extant literature and their own research on mental health treatment adherence research methods and articulated a series of recommendations for future directions. This review is a product of the 2007 NIMH meeting. While other forms of adherence such as attending office visits are also important aspects of treatment for mental disorders, this review of psychiatric treatment adherence measures focuses on medication adherence.

The challenge of adherence measurement

Adherence is an observable behavior—we could continually observe an individual and record time, type, and number of pills taken and compare this to a prescribed regimen. Rules for determining mismatch between actual and prescribed use (e.g., what constitutes nonadherence) would need to be determined, but continually observing actual medication ingestion is the true gold standard of adherence measurement. Unfortunately, 24-hour observation of adherence behaviors is impractical. Such obtrusive monitoring would also prompt better adherence than would occur in unobserved contexts. Also, measuring adherence behavior does not reveal the reason(s) for nonadherence. Nonetheless, accurate assessment of adherence behavior is the foundation in which research on this topic becomes possible.

Thus, necessarily, the measures of medication-taking behavior that are currently used in research and clinical practice are inexact estimates of actual medication ingestion. Even technology-assisted methods such as Medication Event Monitoring (MEMS) caps and smart pill boxes that are often presented as a "gold standard" only monitor opening and closing of medication bottles, not actual drug ingestion.

Measures of medication adherence fall into two basic categories: (1) objective indicators of medication-taking such as pharmacy records, pills counts, electronic monitoring, and blood plasma levels, and (2) subjective measures of medication use via patient-report or interviewer ratings. In addition to measures of adherence behaviors, there are also measures of adherence attitudes. These typically assess proximal factors associated with nonadherence including illness insight and treatment attitudes.

Objective adherence measures

Objective adherence assessments are widely utilized, quantifiable measures of treatment adherence. One or more of these methods, sometimes in conjunction with standardized attitudinal and self-report scales, may be utilized in clinical studies that have a primary or secondary focus on adherence assessment.

Pill counts

Pill counts are a "low tech" method to measure adherence that may be applied to any patient or population and which do not require expensive equipment or highly trained personnel. Pill counts determine how many pills are missing from a container, and this number is compared to the number of pills that should have been taken within a specified time period, resulting in an estimated percentage of adherence. Multiple variables need to be considered in this deceptively simple approach. If patients are required to bring in their pill bottles for counting, missing data will result, particularly from the least adherent patients. Some patients may dump pills to appear adherent. A reliable and valid method for conducting pill counts is to count pills in the individual's home, at unannounced and randomly scheduled visits [9]. An understanding of the home environment can enhance overall adherence assessment. Reactivity to such an assessment can be decreased by longer follow-up periods.

Pill count data can be compromised when participants combine the contents of multiple bottles, throw away empty bottles, or obtain pill samples. To minimize these problems, research participants should be trained on the home-based pill count procedure, and random home visits should occur at short intervals (counting pills every 3–4 weeks). To reduce the burden of random home-based pill counts, Kalichman et al. [23] developed a phone-based pill count procedure shown to correlate with the home-based count for HIV adherence. This approach may be appropriate for psychotropic adherence assessment, but testing in psychiatric samples is needed. In psychiatric populations, home-based pill counts have been found to be moderately to strongly correlated with other measures of adherence [4]. Pill count measures however have not always been found to be related to clinical course. For example, Velligan et al. [24] found little relationship between pill count adherence (or adherence based on electronic monitoring) and psychosis symptoms in a 12-week study of stable outpatients.

Technology-assisted monitoring

There are several types of electronic devices that capture when pill containers are opened and closed to estimate the specific timing of doses, identify patterns of medication use, and calculate adherence rates. Devices used in adherence studies include the MEMS caps, Med-eMonitor, eCaps, and most recently, Medsignals. MEMS and eCaps contain an electronic chip in the bottle cap that records the time and date each time the bottle is opened. Older systems required that the cap be retrieved during an office or home visit, leading to substantial missing data, but newer systems transmit data via phone line. In addition, manual data cleaning is required to eliminate openings that appear unrelated to taking medication (e.g., multiple openings over a brief period or openings to fill the container). If the caps are left off the bottle, data are lost. Helpful features in electronic systems include the ability