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Self-report measures of medication adherence behavior: recommendations on optimal use

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Abstract

Medication adherence plays an important role in optimizing the outcomes of many treatment and preventive regimens in chronic illness. Self-report is the most common method for assessing adherence behavior in research and clinical care, but there are questions about its validity and precision. The NIH Adherence Network assembled a panel of adherence research experts working across various chronic illnesses to review self-report medication adherence measures and research on their validity. Self-report medication adherence measures vary substantially in their question phrasing, recall periods, and response items. Self-reports tend to overestimate adherence behavior compared with other assessment methods and generally have high specificity but low sensitivity. Most evidence indicates that self-report adherence measures show moderate correspondence to other adherence measures and can significantly predict clinical outcomes. The quality of self-report adherence measures may be enhanced through efforts to use validated scales, assess the proper construct, improve estimation, facilitate recall, reduce social desirability bias, and employ technologic delivery. Self-report medication adherence measures can provide actionable information despite their limitations. They are preferred when speed, efficiency, and low-cost measures are required, as is often the case in clinical care.

Keywords

Adherence, Compliance, Self-management, Medication, Self-report

Implications

Practice: Routine assessment of medication adherence in clinical settings through brief, validated self-report measures can provide actionable information to medical providers about patient nonadherence.

Policy: Clinical guidelines should recommend routine assessment of medication adherence in clinical settings through validated self-report measures, and healthcare policies should support integration of this patient-reported outcome into electronic health records.

Research: The validity of self-report adherence measures may be enhanced through efforts to use validated scales, assess the proper construct, improve estimation, facilitate recall, reduce social desirability bias, and employ technologic delivery; further research to strengthen self-report adherence measures is needed.

Valid measurement of medication adherence plays a crucial role in healthcare and health research. When a patient is not benefiting from a medication regimen, clinicians need sound adherence information to determine whether the medication is ineffective or not being taken as prescribed. Assessing medication adherence during routine clinical care can further ensure that individuals in need of adherence support interventions receive them, ideally before deleterious outcomes occur. In the context of clinical research, proper interpretation of proof-of-concept trials testing new pharmacologic regimens requires valid adherence data, because any null findings may stem from poor adherence rather than a lack of drug efficacy. Research designed to understand and promote medication adherence also requires precise methods of adherence assessment.

Among many approaches to assessing medication adherence, patient self-report measures remain the most common method [1–6]. These measures are defined by asking respondents to characterize their medication adherence behavior. Self-report measures of medication adherence range from simple single-item questions regarding missed doses to complex multi-item assessments that incorporate reasons for nonadherence [7]. The widespread use of self-report adherence measures in clinical care and research reflects their low cost and ease of implementation across a large variety of medication regimens.

There are two primary challenges related to self-report measures of medication adherence. First, there are longstanding concerns about the validity of these

measures due to their vulnerability to social desirability and memory biases that tend to overestimate the degree to which patients execute medication regimens, relative to other assessment methods. Second, there is a paucity of research on how to optimize the validity of self-report adherence measures in clinical care or health research. The myriad of self-report adherence measures that are available in the research literature contain substantial variation in their question phrasing, response scale formats, time intervals for recall, and modes of administration [1, 5, 7, 8]. Few studies have empirically tested the comparative validity of these varied methodologic choices [9], and most self-report adherence measures have only been validated within single areas of chronic illness [7].

This paper reviews the current evidence-base behind self-report measures of medication adherence with an eye toward optimizing their selection and use. The paper was the result of the deliberation of a panel of medication adherence research experts from across the disease spectrum, which was assembled by the NIH Adherence Network–a consortium of science officers working at many different NIH institutes, centers, and offices. The panel met in October 2011 and was charged with reviewing the evidence base for self-report measures across major fields of chronic illness prevention and treatment and making best practice recommendations. The conclusions and recommendations of the panel are reported here, along with key directions for future research to strengthen self-report medication adherence assessments.

DEFINING MEDICATION ADHERENCE BEHAVIOR

Medication adherence has been defined as "the extent to which patients take medications as prescribed by their health care providers" [10]. A scientific consensus group described the primary components of medication adherence as initiation (i.e., starting a recommended medication regimen), implementation (i.e., executing the prescribed dosage schedule), and persistence (i.e., length of time on regimen before discontinuation) [11]. Regimen implementation has been the focus of much research and is commonly defined as the percentage of prescribed medication doses taken over a specific time interval [10].

Adherence behavior is distinct from several other related constructs, such as reasons for nonadherence, patient knowledge or understanding of a medication regimen, perceived adherence barriers or facilitators, adherence self-efficacy, and attitudes or beliefs about medications. These domains may be better conceptualized as antecedents or consequences of medication adherence behavior [12].

IMPACT OF MEDICATION ADHERENCE

Across many chronic medical conditions, adherence has been associated with positive clinical outcomes including improved disease control, reduced symptoms, and decreased complications, hospitalization, and mortality [13–20]. Even modest nonadherence (e.g., 10–20 %) has been linked with clinically significant deteriorations in health outcomes, such as glycemic control, low-density lipoprotein cholesterol levels, and risk for coronary disease [21, 22], as well as failure to achieve health improvements [23], leading to higher healthcare costs [21, 24].

Inadequate adherence to medications is unfortunately widespread across ages, health conditions, and medication regimens [10, 25–27]. DiMatteo's [27] seminal review of over 500 adherence studies spanning multiple chronic conditions and medication classes reported an average medication nonadherence rate of 24.8 %. Other large studies crossing multiple chronic conditions and drug classes report nonadherence rates around 40–60 % [25, 28, 29], suggesting that approximately one of every two prescription doses are missed. Medication adherence tends to decline over time [30, 31] and discontinuation (nonpersistence) is common [13].

ADVANTAGES AND DISADVANTAGES OF SELF-REPORT ADHERENCE MEASURES

Every method of assessing medication adherence presents advantages and disadvantages [32], and there is no agreement on a single gold standard approach [1, 33–35]. Self-report measures present some specialized advantages and uses for medication adherence assessment. Key advantages include low-cost, noninvasiveness, minimal patient burden, ease of administration, and flexibility in timing and mode of administration. Self-report medication adherence measures are almost certainly the most practical method of measuring adherence in the context of clinical care and can provide information to providers about nonadherence prior to development of adverse clinical outcomes [1, 10, 36–39]. In addition to providing estimates of medication dose-taking behavior, self-reports can uniquely provide information about adherence determinants such as understanding of the medication regimen, reasons for nonadherence, attitudes and beliefs toward medicines, and other psychosocial factors. In clinical research settings, self-reports are frequently one component of triangulation strategies that combine multiple forms of adherence measurement [40], such as using self-report adherence measures to refine adherence data from electronic drug monitors (EDM) [32].

Self-report measures of adherence have several potential disadvantages as well. These include the contestable assumptions that medication adherence behavior can be accurately recalled or reported without deference to social desirability concerns that encourage over-reporting (for a review, see [9]). Social desirability and memory biases can lead to ceiling effects in self-report scales where an unrealistic majority of respondents indicate perfect adherence [41]. In contrast to EDM data, self-report measures seldom provide time-stamped data for adherence behavior, which limits precision when assessing timing or patterns of dose-taking.

AVAILABLE SELF-REPORT ADHERENCE MEASURES

Numerous self-report medication adherence measures have been developed and reported in health research

on chronic illness to date. Examples of some of the more commonly used measures include the Morisky scale [42] and variations of the adult AIDS Clinical Trials Group (ACTG) adherence assessment [43]. Three primary components of most self-report measures are the question stem, recall period, and response options [44]. These three elements are operationalized differently across various adherence measures. Many of the most common measures employ count- or estimation-based recall [35]. Count-based measures ask respondents to report the number of medication doses missed or taken in a certain interval, whereas estimation measures ask respondents to characterize their overall degree of regimen execution in terms of ratings or visual analog scales. The number of items on self-report adherence measures varies from single-item questions to more elaborate multi-item scales [1, 5, 45]. The number of items often reflects the degree to which the measure is seeking to capture a variety of adherence-related factors, such as reasons for nonadherence.

A set of commonly-used self-report medication adherence measures with available validation data is provided in Appendix. To identify these measures, the terms "adherence," "compliance," "self-report," and "measure" were used in combination to search the electronic database PUBMED. The criteria used for study inclusion in this review were: (a) research report regarding one or more retrospective self-report measures of medication adherence behavior; (b) published in English in the last 30 years; and (c) reporting validation data relative to clinical outcomes and/or other adherence measures in one or more areas of chronic illness. Despite these search efforts, it is possible that additional studies meeting these criteria were missed.

The wide variety of self-report adherence measures is striking. The characteristics of these measures vary substantially in terms of single or multiple items, response options, and specified recall period (if any). Measures may focus on the extent of medication adherence and/or other considerations (e.g., reasons for nonadherence). A few measures have been validated in multiple chronic illness areas, but most have been validated in only one. The validity data reported for each measure also varies in strength and scope, which invites a broader look at the validity of this measurement approach as a whole.

VALIDITY OF MEDICATION ADHERENCE SELF-REPORTS

Considerable research has sought to evaluate the validity and sensitivity/specificity of self-report measures. The criterion validity of adherence measures is established through comparison with clinical outcomes and biological endpoints likely affected by adherence [32]. Convergent validity has been tested through comparison of self-report measures to other medication adherence measures, such as EDM and pharmacy refill measures [32].

Criterion validity–Research generally shows low-to-moderate correspondence between self-report adherence measures and clinical outcomes, and estimates are highly variable by chronic disease area and measure [46]. Two syntheses of research conducted with adult HIV/AIDS patients offer strong evidence that self-report medication adherence measures can significantly and meaningfully predict clinical outcomes [5, 47]. Across pooled studies containing over 15,000 HIV patients, Nieuwkerk and Oort [47] determined that those who self-report nonadherence (at any cutoff level) were 2.31 times more likely to have clinically detectable HIV viral load than those who self-report high adherence. Simoni and colleagues [5] examined 77 studies and found statistically significant correlations between self-report adherence rates and viral load in 84 % of assessment intervals, with correlation coefficients ranging from 0.30 to 0.60. The consistent correspondence of self-report adherence to HIV viral load led Simoni et al. to conclude that "even brief self-report measures of antiretroviral adherence can be robust" (p. 227). Recent meta-analyses further support the criterion validity of self-report adherence measures in HIV/AIDS when used with pediatric, child, and adolescent patients and their caregivers [48, 49].

The criterion validity of self-report medication adherence measures in chronic illnesses other than HIV/AIDS has mostly been lower or more variable. For example, hypertension studies report associations between blood pressure and various self-report measures of antihypertensive medication adherence that range from very weak [50] to a modest yet statistically significant relationship [51, 52]. In type 2 diabetes, few studies have tested the relationship between glycemic control and self-report of medication adherence [2]. Although some diabetes research supports the validity of self-report measures [19, 53], a review of diabetes treatment adherence studies found that just 42.9 % (6 of 14) of studies that used self-report measures found a statistically significant relationship with HbA1c levels [18].

Variable correspondence between self-report adherence and clinical outcomes across chronic conditions may reflect variation in the strength of the adherence-outcomes relationship across different illnesses. In type 2 diabetes adherence research, Gonzalez and colleagues [53] noted that modest relationships between self-report measures and clinical outcomes may partially reflect a modest effect of medication (even when regularly taken) on clinical outcomes. Most evidence shows that medication adherence plays an important role in glycemic control, but many other factors can affect glycemic control besides medication-taking (e.g., diet, exercise, extent of insulin deficiency, and adequacy of the prescribed regimen), so comparisons of self-report medication adherence measures to the clinical outcome of HbA1c levels should show a modest relationship at best. Expectations regarding the ability of self-report measures to predict clinical outcomes should be set accordingly [2, 53].

Simultaneous comparison of multiple adherence measurement approaches with clinical outcomes is helpful for judging their comparative validity. Research

Table 1 | Ten ways to improve the validity of self-report measures

1. Do not reinvent the wheel; choose a self-report adherence measure with validation data for your target population whenever possible.
2. Define the adherence construct of interest (i.e., extent of adherence vs. reasons for nonadherence) and select a measure containing items matched to that need.
3. Administer adherence measures through computer surveys rather than face-to-face data collection to reduce social desirability concerns and improve data quality.
4. In research contexts, staff members who collect adherence data should be separate from staff members who deliver adherence support or adherence interventions.
5. Introduce the self-report adherence measure with a statement which normalizes nonadherence to help address social desirability concerns.
6. Use a question response format that asks respondents to estimate their overall adherence behavior. Response items that characterize adherence in ordinal terms (e.g., anchored Likert ratings scale) or quantitative continua (e.g., estimated percent of doses taken) may help reduce ceiling effects.
7. Use a self-report adherence measure that specifies a recall period for adherence behavior. A recall period of the last 30 days may reduce ceiling effects relative to shorter intervals. Populations characterized by cognitive impairment may require other approaches (e.g., daily text message or interactive voice response surveys).
8. Consider dichotomization of self-report adherence measures at the 100 % mark to recognize their tendency for over-reporting relative to other adherence measures.
9. Add a social desirability measure to complement analysis of self-report adherence data.
10. Research publications should include clear descriptions of any self-report adherence measure, its administration method, and descriptive data resulting from the measure (e.g., mean, median, standard deviation) to help further the science.

typically indicates that self-report measures have weaker or less consistent relations with clinical outcomes relative to other measures of adherence [18, 51, 54]. A review of type 2 diabetes research found that significant relationships between medication adherence and glycemic control occurred more frequently in studies measuring adherence via prescription refill rather than various self-report measures [18]. A review of type 1 diabetes research found that the relation between adherence to diabetes management behaviors and glycemic control in type 1 diabetes showed no overall differences when using either self-reports or blood glucose meter downloads, but studies using self-report measures showed significant heterogeneity in their effect size estimates, whereas meters showed little variability [19]. In HIV research, Arnsten and colleagues [54] concluded that both self-reports and EDM devices show strong correspondence to HIV viral load, but EDMs were more sensitive for detecting nonadherence than self-report. These reports indicate that self-report measures contain value for predicting clinical outcomes, but this value may be limited relative to more precise yet resource-intensive electronic instruments.

Convergent validity–Syntheses of chronic illness research have generally demonstrated moderate relationships between self-report medication adherence measures and other adherence assessments. In a review of 41 medication adherence studies, Shi and colleagues [55] determined that a majority of studies (68 %) report correlations between self-report and EDM adherence measures that are either high (27 %), moderate (29 %), or low yet statistically significant (12 %). A related meta-analysis estimated that the pooled correlation coefficient between self-report and electronically monitored adherence was 0.45 (95 % CI, 0.34–0.56) [56]. Moderate correlations between self-report and electronic monitoring reflect the performance of both adherence measures, and as such, may reflect limitations in self-reports as well as logistic challenges in EDM [57].

Research on the convergent validity of self-report adherence measures shows clear evidence that they tend to overestimate the extent of regimen execution relative to other adherence assessments [32, 46]. In an examination of 57 studies across many chronic illnesses, Garber and colleagues [8] found high concordance between self-report and other adherence assessments in 43 % of comparisons. Among comparisons that were not highly concordant, self-reports produced higher estimates of adherence than other assessment methods 92 % of the time (45 out of 49 comparisons). A meta-analysis showed the estimated degree of regimen execution is approximately 15 % higher by self-report when compared with EDM devices [56], which is consonant with estimates in other reviews and syntheses [5, 35, 56, 58].

Sensitivity and specificity–Because of potential over-reporting, self-report adherence measures are considered to have good specificity (i.e., positive predictive value) and weak sensitivity (i.e., negative predictive value) for detecting poor adherence [5, 32, 46]. Stated simply, self-reports of nonadherence can be trusted; self-reports of adherence less so. Osterberg and Blaschke [10] explained that "a patient who admits to poor adherence is generally being candid."

A review of self-report measures found that only 12 of 43 scales reported sensitivity and specificity data [7]. Sensitivity and specificity may be infrequently calculated because it requires comparison with a "gold-standard" clinical outcome or adherence measure, as well as establishment of an appropriate cut-off for determining nonadherence–and there is lack of

consensus on neither point. In light of the strong tendency for over-reporting with self-report adherence, it has been recommended that any dichotomization occur at the 100 % mark (i.e., perfect vs. imperfect self-report adherence) [5, 58].

RECOMMENDATIONS FOR OPTIMIZING THE VALIDITY OF SELF-REPORT MEASURES

Although self-report measures can show valid correspondence to health outcomes and other adherence assessment methods, the limitations of this assessment approach are evident in its routine overestimation of adherence. Evidence-based steps to strengthen the validity and precision of self-report measures are discussed below and further summarized in Table 1.

Use a validated self-report measure where possible–Failure to use standardized and validated self-report measures is a common problem in much of health research and clinical practice [1, 35]. A review of 41 studies of the agreement between adherence self-report measures and EDM devices identified 19 publications that failed to name or describe the particular self-report measure used in the study; these studies showed significantly lower correspondence between self-report and electronically monitored adherence when compared with studies that used named, standardized self-report measures [55]. With many validated self-report scales available for clinical or research use, there are sound options from which to choose (see Appendix). It is recommended that researchers and clinicians select a self-report measure that has prior validation data within the relevant chronic illness area and preferably one that has demonstrated both concurrent and criterion validity [35]. To help improve available information on measures, adherence-related publications should include a clear description of any self-report measure and its administration method, along with descriptive data resulting from the measure (e.g., mean, median, standard deviation) [9, 35].

Define the adherence construct you want to assess–It is important to define the specific construct of interest when conducting medication adherence assessments and to select an appropriately corresponding measure [7, 52, 59, 60]. Voils and colleagues [12, 52, 61] have argued that self-report adherence measures often conflate two distinct constructs–the extent of nonadherence and reasons for nonadherence–and this conflation may be one factor that has limited the psychometric properties and validity of many existing self-report measures. For example, many commonly used self-report measures of medication adherence in hypertension [62–66] are wholly or partially composed of items concerning reasons for missed doses (e.g., due to forgetfulness, side effects, attitudes toward medicines). Voils and colleagues maintained that reasons for nonadherence represent a conceptually distinct antecedent to adherence behavior, and that different measurement models and validation methods are appropriate for each.

When selecting validated self-report measures, researchers and clinicians should consider if they wish to assess extent of medication adherence, reasons for nonadherence, or both–and a scale matched to the particular clinical or research need should be selected. Voils' group has developed two self-report adherence measures for use in hypertension research or clinical care that provide discrete assessment of the extent of medication adherence (3 items) and reasons for nonadherence (21 items), and the scales have shown promising psychometric properties and convergent and critierion validity [52]. Since many chronic conditions involve multiple forms of health behavior (e.g., medication dose-taking, dietary guidelines, exercise, prescription refills), researchers and clinicians should additionally be clear about the specific adherence behavior that they seek to assess when selecting an adherence measure [60, 67].

Optimize response options and recall periods to reduce ceiling effects–Research is yielding new insights into optimal response options and recall periods for self-report measures of medication adherence. Wilson and colleagues have argued that individuals completing self-report scales typically make estimates of their adherence behavior rather than conscientiously remembering and counting doses taken or missed [9]. Self-report measures that ask participants to make global estimates of their adherence behavior instead of reporting doses missed or doses taken may therefore be helpful. A series of HIV studies [44, 68–70] have determined that self-report measures with rating scales as response options (e.g., "In the last 30 days, how good a job did you do at taking HIV medicines in the way you were supposed to? Never, rarely, sometimes, usually, almost always, always") yield greater variability and reduced ceiling effects (i.e., reports of perfect adherence) than measures asking about a specific number of missed doses. Similar findings have emerged in hypertension studies, although Gonzales and colleagues [53] found the best performance when asking for an estimate of the percentage of doses taken, rather than rating adherence on a Likert-type scale. This evidence suggests that self-report measures that ask for global estimates of adherence may be preferable.

Self-report adherence measures which specify a time frame for recall of adherence behavior are helpful when conducting longitudinal assessments that examine adherence trends over time [1, 5, 12]. Determining the optimal recall period requires balancing shorter intervals (to improve recall/estimation) with longer intervals (to increase the representativeness of the sampled time period and capture cases of infrequent nonadherence). Studies comparing self-report measures with different recall time frames have determined that 30-day recall intervals reduce ceiling effects relative to shorter intervals [44, 68, 69, 71]. A single-item rating of medication adherence over the last 30 days has been validated against viral load in large HIV patient samples and showed the smallest ceiling effect relative to other self-report measures [44, 68, 69]. Cognitive testing of adherence items indicates that the phrase "30 days" is preferable to "the last month" because

the latter can be misunderstood as reflecting the calendar month [70].

Although these findings suggest that estimated adherence over 30-day periods may be optimal, this approach could present concerns when working with populations characterized by significant cognitive impairment or memory problems, such as persons with severe mental illness or dementia. Basic approaches to assist recall include use of medication lists and pill diagrams, as well as anchoring recall to salient events through a timeline follow-back method [5, 9]. Assessment of self-reported medication adherence among cognitively compromised populations may additionally benefit from more specialized techniques such as the conduct of daily or periodic ecologic assessments via text message or interactive voice response surveys regarding medication adherence over the last 24 h [72]. For groups characterized by severe cognitive impairment and memory deficits, the use of adherence measures other than self-report (e.g., pill counts, EDM, or drug levels) may be preferred.

Address social desirability concerns–Efforts to reduce social desirability concerns among individuals completing self-report adherence measures should help to improve their validity. Nieuwkerk et al. [71] used a social desirability scale to stratify a large sample of Dutch HIV patients into those reporting lower vs. higher social desirability concerns. The team found that the relationship between self-report medication adherence and viral load was statistically significant for patients indicating low social desirability concerns, but not for those indicating high social desirability concerns.

Several techniques may help address social desirability concerns. Regardless of the assessment modality or setting, it is usually beneficial to introduce adherence items with a statement which normalizes nonadherence by acknowledging the widespread nature of nonadherence and/or the difficulty of always taking all medications [5, 10, 32, 35]. Providers should approach adherence questions with patients in a nonjudgmental manner. A research staff member who interviews a patient to obtain self-report adherence data should not be the same person who is delivering an adherence counseling intervention to that research participant. Another important approach is to avoid administration of self-report adherence measures through face-to-face interviews in favor of utilizing computer or paper-based self-administration of questionnaires. Finally, a validated measure of social desirability could be included in research studies to provide a means of statistically adjusting adherence estimates for each participant's individual level of social desirability, thus potentially minimizing its effect upon associations between adherence and outcomes.

Consider computer administration–Computer technology has the potential to improve accuracy of self-report by reducing biases caused by social desirability, interviewer characteristics, and questionnaire structure. Studies in many domains have demonstrated that computer administration of sensitive questions has been shown to increase reporting levels of sensitive behaviors, particularly in comparison with interviewer-based administration [73, 74] as patients prefer and are more willing to disclose sensitive information to a computer rather than an interviewer [74–87]. Direct computer entry further enhances the quality of data by not allowing double or ambiguous answers [88], and it is often associated with a lower rate of unanswered questions than paper forms [80, 82, 85, 88, 89] because patients must provide a valid response to a question and/or press the "next" button to move on.

Besides computer administration, several other alternatives to interviewer-based collection of adherence information are available. These include paper questionnaires, diaries, interactive voice response (IVR) calls, and text messaging. When reviewing the validity of self-report adherence measures, Garber and colleagues [8] determined that questionnaire or diary measures were superior to in-person interviews in terms of their correspondence to objective adherence measures like EDM and pharmacy refill measures [8]. Although little research is available regarding use of IVR for adherence measurement in comparison with other assessment modalities, some research has been conducted on the use of IVR to increase adherence, with mixed results [90–92]. The viability of interactive text-messaging for monitoring medication adherence remains unclear. This method appears to overestimate adherence when compared with MEMS or laboratory-based measures of symptom status and functioning [93, 94]. One study found text message reminders to be feasible and acceptable, however, response rates to requests about adherence were low (48 %) [95]. More research is needed on the use of these modalities for adherence measurement and intervention.

Technology is not a panacea for self-report validity concerns. For example, randomization of children with asthma and their caregivers to either audio computer-assisted self-interviewing (ACASI), face-to-face interviews, or paper questionnaire versions of a self-report adherence measure made no appreciable difference in adherence estimates compared with electronic adherence data from metered-dose inhalers, and each modality represented an overestimate compared with objectively monitored adherence [96]. Most evidence nonetheless indicates that computer administration of self-report adherence measures should improve their validity.

CONTEXTUAL CONSIDERATIONS IN SELF-REPORT ADHERENCE MEASURES

The contributions that self-report medication adherence measures can make to health research and practice vary according to the context and purpose of their use. What is chosen for screening in clinical care will likely be different from what is chosen for assessment in a clinical trial with adherence as a primary outcome variable. Below some specialized applications and

recommendations for self-report measures in different contexts are considered.

In clinical trials and research–The large number of patients and complex protocols used in many clinical trials create a need for low-cost, low-burden adherence measures. Adherence assessment may be needed at several junctures during clinical trials. At screening, measures may be needed to assess risk of nonadherence prior to randomization to allow exclusion of participants likely to have problems adhering to the protocol. At baseline, adherence assessment will allow early identification of potential problems so that study resources can be devoted to improving adherence and retention for those likely to have problems adhering. Throughout any trial, monitoring adherence can aid in determining proper drug dosages and identifying low adherence so that staff can intervene to address problems as they develop.

Self-report adherence measures are readily integrated into clinical research visits and represent a low burden assessment approach that may be more acceptable to patients than alternatives. Unique types of self-report measures may be needed at different junctures within a clinical trial. For example, single-item measures including Visual Analogue Scales (VAS) can be useful as brief adherence screens at medication management visits [97–99]. Self-report measures that can indicate reasons for nonadherence such as the Morisky adherence measure [42, 63] may be administered at baseline and during selected visits to ascertain adherence barriers to inform interventions to address and improve these challenges. If it is feasible to implement self-report measures through technologic approaches such as ACASI, this may also benefit the validity of the adherence assessments in clinical research.

In medication adherence research–Self-report measures may be disadvantageous when used as the primary outcome in clinical trials testing counseling and behavioral interventions to improve medication adherence, because intervention participants may be disproportionately influenced to self-report faithful adherence relative to comparison arm participants. The evidence for this is mixed, however. A study combining data from multiple randomized trials of HIV treatment adherence interventions found no moderation by arm of the association between self-report medication adherence and other estimates of the intervention's effects, including biological outcomes and EDM data [100]. Further research is needed to determine whether self-report can be a valid indicator of adherence intervention effects. Until then, randomized controlled trials of adherence interventions would benefit from a more objective method of adherence assessment as the primary study outcome (e.g., EDM devices, prescription refill measures, or multiple measures with complementary properties, such as self-report and adherence biomarkers). Use of multiple measures in adherence research can triangulate intervention effects [34, 72] and advance measurement science through comparisons with one another.

In health care settings–Medication adherence is not consistently and reliably assessed as a part of routine primary and specialty healthcare. Although many clinicians believe they can accurately estimate patient adherence, research shows that clinician estimates of patient adherence are often inaccurate [101–105]. Brief, validated self-report measures of adherence therefore have an important role to play in clinical practice, and some clinical guidelines recommend routine assessment of adherence by validated self-report measures [106].

The ideal adherence assessment for clinical care involves single-item or other short self-report or measures that can be administered by the clinician, support staff, or electronic systems prior to or during the office visit. Clinician inquiries about patient adherence could help strengthen the patient-clinician alliance by conveying respect and interest in the patient's point of view. Computer-assisted methods may enable patients to report potentially "sensitive" issues in privacy, possibly leading to greater disclosure of nonadherence and barriers to adherence. Direct integration of data from computer-based self-report measures into electronic medical records further allows results to be immediately available for use by providers to improve care, and it decreases staff burden through elimination of a data entry step that could otherwise result in delays, costs, and errors.

In recent years, electronic collection of patient-reported outcomes such as medication adherence has become more feasible with reduced costs, development of touch-screens, and more common use of computers in everyday life (e.g., bank ATM, grocery store cashier, etc.). Electronic data collection such as ACASI is less expensive than interviews [107] but associated with greater start-up costs than paper-based assessment. Despite the larger start-up costs, touch screen-based electronic collection of self-report data has been found to be less expensive per assessment in clinical settings doing six or more assessments per day [108], and continued reductions in the prices of touch-screen computers have made electronic collection even more economical over time. Touch-screen data entry eliminates the need for typing and avoids using mouse-based data entry systems that have not been universally successful [109–111]. An example of routine computer-assisted collection of self-report adherence from patients in clinical settings is provided by Feldman and colleagues [112]. More than 2300 HIV-infected patients completed touch-screen tablet-based computer assessments of a single self-rating scale item (SRSI) for medication adherence during routine clinic visits. The measure was significantly correlated with other self-report adherence items and inversely correlated with known predictors of medication nonadherence, such as illicit substance use and depression,

indicating validity of the SRSI for measuring adherence. The SRSI also predicted $CD4^+$ cell count and viral load as well or better than other adherence items, indicating good criterion validity. Findings suggest that the SRSI may be an effective, brief way to routinely measure self-report adherence in clinical settings with minimal workflow disruption and patient burden.

CONCLUSION AND PRIORITIES FOR FUTURE RESEARCH

This review indicates that self-report measures are imperfect, in that they tend to overestimate adherence compared with other assessment approaches. Self-reports of imperfect adherence can be trusted, however, and rigorously developed and well-validated self-report measures show expected relationships with both clinical outcomes and other forms of adherence assessment. A number of steps can be undertaken to strengthen the validity and precision of self-report measures of medication adherence (see Table 1). These include using well-validated scales, defining the specific adherence construct of interest, using optimized question response formats and recall periods, taking steps to address social desirability concerns, and avoiding interview-based assessments. The growing ease with which self-report measures may be administered through computer- or technology-assisted approaches also brings fresh opportunities for improved administration.

The rigorous development and testing of self-report measures of adherence should be a research priority. While numerous self-report measures are available, there is a relative dearth of measures that have been rigorously tested for convergent or criterion validity, internal consistency, and test-retest reliability. Few measures have been systematically developed for populations with self-report challenges such as impaired cognitive functioning. Research is also needed to better understand how to best assess adherence among patients taking multiple medications, particularly because many individuals have two or more chronic conditions.

Future efforts to develop self-report measures of adherence behavior would benefit from approaches such as item response theory to improve efficient and accurate assessment, as well as cognitive testing to ensure sound item understanding and comprehension [9, 70]. It is important to test the criterion validity of self-report measures through comparisons with biomarkers or clinical treatment outcomes, but caution should be used because many factors may affect this relationship, and the impact of any recent adherence behavior on biologic outcomes may lag [5, 9]. When comparisons with clinical outcomes are made, it may be helpful to test self-report alongside other adherence assessment methods, to gauge their comparative strength and concurrent/criterion validity. One example is provided by Dunbar-Jacob and colleagues [51] who examined how multiple self-report and EDM measures corresponded to cholesterol levels in a trial testing cholesterol-reducing medication strategies.

Research on self-report adherence measures is also needed to inform evidence-based strategies to further mitigate ceiling effects and social desirability concerns. Studies should build on the promising directions noted here regarding 30-day recall intervals and global adherence estimates by further testing optimized self-report question phrasing, recall periods, and response item formats. There is also a need for continued research on brief measures of medication adherence for use as a patient-reported outcome in routine clinical care, and for integration into electronic health records. Administration of self-report measures through innovative methods such as IVR and text messaging is another important direction for future research. There may be utility to text messaging or smart phone applications that allow an individual to report when they have taken their dose, or IVR applications that allow a patient to remotely record whether their medication has been taken for the day. In addition to the promise of being simple to use, these eHealth options can provide a wealth of data to better understand patterns and predictors of adherence. These applications may be particularly useful for groups with cognitive impairment who may be less accurate at reporting about behavior over longer periods of time.

Understanding and addressing adherence problems are important keys to improving health care delivery. Given the longstanding ubiquity of self-report medication adherence measures in research and practice, further research to improve and optimize these measures should provide benefits to health care and health research more generally.

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Appendix

Table 2 | Selected Adherence Self-Report Measures in Chronic Disease Reporting Validity Data

Domain	Self-Report Measure	Item Count	Recall Period	Validity Data
Asthma	Four Item Questionnaire for Asthma Inhaler Adherence [113]	4 items	Not specified	Correlation with controller compliance ratio=.348; Correlation with pharmacy claims data=.382; Cronbach alpha=.86.
	Pediatric Inhaler Adherence Questionnaire [112]	6 items	Not specified	Correlation=.42 with canister weight change, sensitivity 50-75 %.
Hemophilia	Hemophilia Regimen Treatment Adherence Scale [114]	24 items	Not specified	Cronbach alpha=.94, test-retest=.77 (m=28 days), self-reported adherence correlated with self-reported infusions.
HIV/AIDS	AIDS Clinical Trials Group (*ACTG*) *Adherence* Questionnaire [43, 115]	1-5	Past 3 days; past 4 days; Past 2 days and past Saturday; Past week; Past month	Scores of studies demonstrating statistically significant correlations with HIV viral load.
	Community Programs for Clinical Research on AIDS (CPCRA) Antiretroviral Medication Self-Report (3 or 7 day adherence version) [31]	Global 3 or 7 day recall for use of medication; also includes a checklist with 10 possible reasons for missed antiretroviral doses	Past 3 days; Past 7 days	Predicts virologic suppression (OR, 3.41; 95 % CI, 2.29–5.06; $p<.001$); dose–response relationship with CD4+ cell count ($p<.001$); adherence was significantly associated with undetectable viral load, change in viral load, and change in CD4+ cell counts during a 12-month period.
	Self-Rating Scale Item (SRSI) [68, 69]	1 item	Last 30 days	Significantly predictive of HIV viral load and immunologic outcome (CD4 count); superior to other self-report measures when predicting viral load or MEMS adherence.
	Self-Reported Adherence (SERAD) Questionnaire [116]	Three components (second part includes a 13-item section on reasons for nonadherence)	Past week/month/3 months	Relatively high agreement with other adherence measures (75 % with electronic monitoring and 71 % with pill count).
	Self-Reported Questionnaire Assessing Adherence to Antiretroviral Medication [117]	9 main questions	Past day, Penultimate day, past week, past month	Sensitivity, 71 %; specificity, 72 %; correct classification, 72 %; odds ratio, 6.15.
	Simplified Medication Adherence Questionnaire (SMAQ) [37]	6 items	Past day; Past week; past weekend; days over past 3 months	Cronbach's α=.75, and good inter-observer agreement (88.2 %); SMAQ showed 72 % sensitivity, 91 % specificity and a likelihood ratio of 7.94 in identifying non-adherent patients as compared to the MEMS.
	Visual Analog Scale (VAS) [94, 95, 118]	1 item (patients mark a linear scale to indicate percent adherence)	1 month	Significant associations with unannounced pill counts and HIV viral load (r=0.76 and −0.49); significantly correlated with the ACTG adherence questionnaire (r=0.59, $p<$ 0.0001).
Hypertension	Brief Adherence Self-Report Questionnaire (ASRQ) [119, 120]	6 items	Not specified	Sensitivity 46 % & specificity 66 % with MEMS cap timing adherence.
	Hill-Bone Compliance to high blood pressure therapy scale [62]	14 items (three subscales for reduced sodium, appointment keeping, and medication taking)	Not specified	Cronbach's α=0.74 and 0.84 in two samples, and mean inter-item correlations were 0.18 and 0.28.
	Voils Measure of Extent and Reasons for Medication Non-Adherence [52]	3 items on extent of non-adherence and 21 items on reasons for non-adherence	Last 7 days	Extent items significantly predicted systolic and diastolic blood pressure and showed Cronbach's α=.81 over 21 days.

Immuno-suppression	Frazier Noncompliance Inventory (FNI) [121, 122]	11 items	Not specified	Association between measure and self-rating of adherence & pill counts.
	Immunosuppressive Adherence Scale (ITAS) [123]	5 items	Not specified	Cronbach's α=.81, positive correlations with refill record and serum immunosuppression levels.
	Medication Therapy Adherence Scale (ITAS-M) [124]	4 items	3 months	Modified ITAS; designed to address all medications.
Mental health	Brief Adherence Rating Scale (BARS) [125]	4 items	Number of days over past month	Cronbach's α=.92 and test–retest reliabilities ranged from r=0.46 to 0.86; Spearman correlations between MEMS and the BARS for each month of 6-month trial were moderate (0.42–0.59); BARS showed good sensitivity (73 %) and specificity (71 %) in identifying non-adherent outpatients.
	Tablets Routine Questionnaire (TRQ) [126]	2 general questions regarding any difficulties taking or coping with medications followed by 4 questions regarding approximate number of missed doses in the past week and past month	Past Week/Month	Adherence scores significantly related (r=.24, p<.04) to lithium levels; partial adherence score (missing 30 % or more of prescribed mood stabilizers) over past week has relatively good specificity (100 % and 87 %) for nonadherence in the past 2 years and past week, respectively; partial adherence score (missing 30 % or more of medications) over past week has somewhat lower sensitivity (65 % and 84 %) for nonadherence in the past 2 year and past week, respectively.
Multiple Sclerosis	Multiple Sclerosis Treatment Adherence Questionnaire (MS_TAQ) [127]	30 items (in three subscales: Barriers, Side Effects, and Coping Strategies)	28 days	Correlated with adherence self-report.
Osteoporosis	Adherence Evaluation of Osteoporosis Treatment (ADEOS-12) [128]	12 items	Not specified	Scores between 16 and 20 predict treatment discontinuation.
Rheumatology	Compliance-Questionnaire-Rheumatology (CQR) [129]	19 items	Not specified	Sensitivity=98 %, specificity=67 %; Kappa=.78; sensitivity=62 % and specificity=95 % with MEMS.
General Use	Adherence Estimator [130]	3 items	Not specified	Sensitivity 88 %, specificity 59 % with self-reported adherence.
	Adherence to Refills and Medication Scale (ARMS) [131]	12 items	Not specified	Cronbach's α=.81; correlation with Morisky=.65 and .3 with refill measure; low scores associated with controlled diastolic blood pressure.
	Brief Medication Questionnaire (BMQ) [66]	9 items	Past week	Sensitivity=80 % & specificity 100 % repeat non- adherence vs no nonadherence with MEMS; r=.67 dose omissions past week & r=.89 past month.
	Medical Outcomes Study (MOS) [132]	5 items	Past 4 weeks	In a variety of chronic conditions, 2-year test-retest reliability=.32-.66; internal consistency=.81.
	Medication Adherence Scale (MAS) [133]	32 items (subscales on knowledge, attitudes and barriers)	Not specified	Cronbach's α=.85 (3 factors - .75 knowledge, .attitude .75, barriers .94), MEMS correlation with factors knowledge NS; attitudes .3, barriers .31.
	Medication Management Instrument for Deficiencies in the Elderly (MedMalDE) [134]	20 items	Not specified	Test-retest reliability .93 (interval not specified); cronbach's alpha=.71; interrater reliability=.73; sensitivity .68; specificity .83.
	Medical Adherence Measure [135]	Semi-structured interview	1 week	Correlated with MEMS r=.40, associated with kidney transplant rejection r=.62.
	Morisky Adherence Questionnaire 4 item (MAQ) [64]	4 items	Not specified	Point biserial correlation=.43 score and .58 at 6 & 42 months; coefficient of determination=R^2=.33; sensitivity=.81; specificity=.44.
	Morisky Adherence Questionnaire 8 item (MAQ) [42]	8 items	Not specified	Cronbach's α=.83; significant association with blood pressure control (p<.05); estimated sensitivity 93 % and specificity 53 %.

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