

Advancing the Science of Adherence Measurement: Implications for the Clinician

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The article by Patel et al.¹ sheds new light on an old topic and advances the science of measuring nonadherence. Treatment nonadherence continues to be a significant barrier to asthma control and contributes to costly asthma exacerbations. Remarkably, fewer than one-half of patients with a new inhaled corticosteroid prescription refill again in the year after an initial fill. Patients who do not altogether abandon therapy take on average fewer than one-half of the prescribed number of doses.²⁻⁴ Nonadherence with asthma therapy has significant consequences and is associated with adverse asthma outcomes. In a retrospective cohort study that used administrative database assessments of adherence in >50,000 adults with asthma, decreased adherence to inhaled corticosteroids was correlated with increased hospitalizations, days of oral steroid use, and emergency department visits,⁵ in turn contributing significantly to increased asthma health care expenditures.⁶

Improving patients' asthma self-management and adherence depends first on having adequate tools to monitor adherence. In many cases, attempts to measure adherence have been remarkably inaccurate. For example, diary cards and other forms of measuring adherence by self-report, the staple of clinical trial adherence measurement for many years, have been repeatedly found to greatly exaggerate adherence. In the Childhood Asthma Management Program, an 8-center trial of asthma treatments, objectively measured adherence dropped from approximately 70% to 50% over 4 years, yet children and their parents continued to report adherence of >80% for the duration of the trial.⁷ Clearly, it is easier to report the behavior one wishes others to see than the behavior that actually occurs. Misrepresentation of trial adherence may have the unfortunate consequence of leading to incorrect understanding of drug effectiveness, side effects, or optimal dosing.⁸

Other means of measuring adherence exist, and each has strengths and weaknesses. Adherence questionnaires are used widely, yet at best they correlate moderately with objective measures of adherence and lack the specificity of measurement to provide a concise quantitative measure of percentage of adherence.⁹ Physician estimates of adherence may be delivered with confidence but in

fact are often incorrect.¹⁰ Bioassays were the primary means of measuring adherence when theophylline was the treatment of choice for asthma, but they are impractical for measurement of inhaled medications.¹¹ Adherence assessment through pharmacy databases is emerging as the predominant measurement strategy in research and, more recently, has been adopted as a Healthcare Effectiveness Data and Information Set (HEDIS) measure of quality of care within health care systems.¹² With few exceptions, patients who do not continue to fill medications are not using them. Refill data can be converted to days of medication, which in turn provides a continuous adherence measure. However, such data provide reliable adherence estimates only over a period of 12 months or more. Careful calculation is required to determine that the investigator does not underestimate adherence by failing to account for medication filled shortly before the measurement window begins, overestimate adherence in patients who obtain a multiple-month medication supply that is never consumed, or fail to consider other sources of the prescribed medication obtained by the patient, including sampling or purchasing outside the health care system.¹³

Medication adherence measurement through microchip-equipped electronic devices provides another objective means of assessment. The first nebulizer chronologs, used in the Lung Health Study 30 years ago, shattered common perceptions about adherence in clinical trials and revealed intentional deception on the part of some study participants.¹⁴ Clearly, these devices possess distinct advantages over other adherence measures by offering precise documentation of medication use, a capacity to measure daily use and patterns of behavior over time, and the potential to establish adherence-mediated dose-response relations.¹¹ However, electronic devices are not without limitations. Specifically, they can be prone to failure and error, and they can overestimate adherence. For these reasons, it is essential that the accuracy, reliability, and validity of any marketed adherence measurement device be adequately established through peer-reviewed research. Although the initial emergence of electronic measures was greeted with the assumption that they provide correct measurement, a study of their reliability and accuracy revealed failures in 42% of metered dose inhaler chronologs.¹⁵ Worse yet, these devices did not simply stop working, a situation in which at least the investigator would recognize device failure. They also had "seizures" that generated bursts of erroneous recordings that delivered inaccurate data.¹⁵ Another report found that some medications could short-circuit the chronologs and consequently cause them to fail.¹⁶ A subsequent set of studies of the accuracy of the Doser CT, a less sophisticated and less expensive alternative to the chronology device, found them to be reasonably reliable and appropriate for clinical research although overrecording and underrecording of inhaler use was still documented.^{17,18} In short, more complex technology does not assure more accuracy.

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No funding was received for this work.

Conflicts of interest: B. G. Bender declares that he has no relevant conflicts.

Received for publication October 17, 2012; accepted for publication October 18, 2012.

Cite this article as: Bender BG. Advancing the science of adherence measurement: Implications for the clinician. *J Allergy Clin Immunol: In Practice* 2013;1:92-3. <http://dx.doi.org/10.1016/j.jaip.2012.10.007>.

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J Allergy Clin Immunol: In Practice 2013;1:92-3.
2213-2198/\$36.00

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<http://dx.doi.org/10.1016/j.jaip.2012.10.007>

The study by Patel and colleagues has advanced this research into electronic devices, reporting on the second of 2 studies designed to establish the accuracy of the SmartInhaler Tracker, an inhaled medication—tracking device developed and tested in New Zealand. In the first study, 22 monitors were tested in a laboratory study wherein study staff repeatedly activated the devices, finding that 2 monitors failed and the remaining monitors were 99.7% accurate in recording actuations.¹⁹ The present investigation was designed to test the “real-world” reliability of the Tracker by placing each of 2642 Trackers in the hands of 303 patients with asthma as they took their asthma medication for 24 weeks. A remarkable list of data-checking procedures were used, including 11 prestudy device checks, 10 within-study device checks, and 7 within-study data checks. Altogether, 127 devices (4.8%) failed and another 93 (3.5%) were lost by participants. Of the recovered and functioning Trackers, 98% produced data. This study establishes a new standard for researching the performance properties of a commercially available electronic adherence measurement by testing a large number of devices in the hands of patients for an extended period of time.

The question remains as to how and when such devices should be used. Although the authors suggest utility in both research and clinical practice, this presumption is more convincing for the former than the latter. Given a long and troubling history of developing medication guidelines on the basis of studies with flawed adherence data susceptible to inaccurate conclusions about dosing effectiveness and side effect risks, it is compelling to require maximum accuracy in adherence measurement in ongoing and future clinical trials. In fact, electronic monitors have now been used in many trials. In clinical practice, however, the case for using devices such as the Tracker is less compelling. Four reasons can be identified. (1) These devices are expensive, ranging from \$150 to \$200 each with additional costs for software and docking equipment necessary for data downloading. No evidence exists that many patients, insurers, or health care providers are willing to absorb this cost. (2) Time is required from patients and office personnel to initialize and test each device and to download data to a computer. Few practices are likely to be willing to commit resources to this set of tasks. (3) No clear guideline indicates exactly how and when the devices should be tested in clinical practice; certainly a 28-point testing procedure is beyond the reach of even the most motivated clinical practice group. (4) It will likely be difficult to convince patients that they should be willing to be inconvenienced by the necessity of dealing with this new piece of equipment, the purpose of which is to police their use of the prescribed medication.

However, medication refill data, where available to the provider, is likely to be more easily adopted in clinical practice. In Kaiser Permanente, the nation's largest health maintenance organization, patients overdue in filling their inhaled corticosteroid medication were contacted with a computerized, interactive voice recognition system that prompted them to refill and use their medication, resulting in a small but significant increase in adherence over 12 months.²⁰ This intervention was automated and did not require more time from health care providers. Kaiser Permanente has also adopted into clinical practice the strategy of contacting patients whose asthma medication ratio (the number of controller medications dispensed during the previous year

divided by the total number asthma medications dispensed) has fallen below 50%.²¹ As health care moves further toward electronic health records shared between organizations or within health maintenance organizations or accountable care organizations, such adherence monitoring is likely to facilitate increasingly effective interventions to improve asthma management and to reduce exacerbations.

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