

Invited Commentary

In Search of a "Magic Pill" for Medication Nonadherence

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In the mid 1970s, David Sackett and colleagues¹ partnered with a group of 250 hypertensive factory workers and their physicians to conduct groundbreaking research on what was then



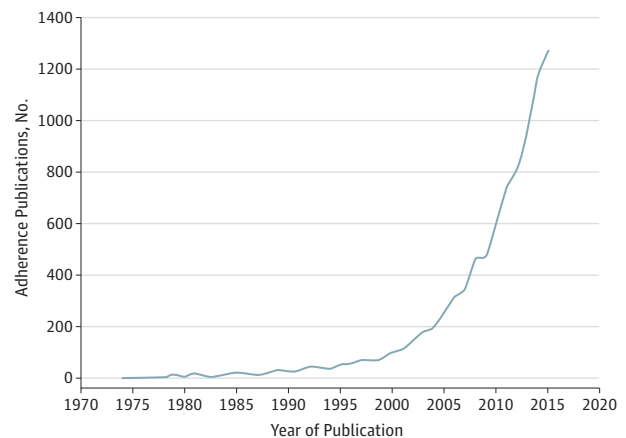
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referred to as *medication compliance*. Using pill counts, the investigators discovered that about half of the workers were taking less than 80% of their blood pressure pills and that the nonadherent workers were less likely to have controlled blood pressure. In the subsequent 40 years, the amount of research dedicated to medication nonadherence increased exponentially (**Figure**). Health economists have identified medication adherence interventions as opportunities for improving health outcomes while reducing health care costs. Stakeholders ranging from the Agency for Healthcare Research and Quality to the World Health Organization issued calls to action for the implementation of strategies to improve medication adherence. Despite this increased attention, the prevalence of medication nonadherence is as high as ever, and up to 50% of patients remain nonadherent to treatments prescribed for chronic health conditions.²

In this issue of *JAMA Internal Medicine*, Choudhry and colleagues³ describe an elegant experiment testing a low-cost, scalable solution to improving medication adherence. Specifically, they compare the effect of providing commercially insured patients who were nonadherent to chronic disease medications with usual care vs with 1 of 3 reminder devices—a standard pillbox, a toggle strip that can indicate whether a daily dose was taken, or a pill cap with a digital timer to indicate the time elapsed since last opening. The authors target forgetfulness, a major reason for nonadherence, and hypothesize that providing reminder devices would improve adherence. Influencing adherence through simple, easy-to-implement, and affordable interventions offers intriguing potential as a public health approach to solving this irascible problem. Unfortunately, the authors found that providing patients with these devices alone was not the answer to nonadherence. None of the 3 devices was superior to usual care at improving refill rates.

The authors are commended for using a pragmatic trial to definitively test the effectiveness of these low-cost reminder devices. Nevertheless, the trial was not without its limitations. First, the authors evaluated the effect of the intervention on refill patterns but were unable to assess its effect on day-to-day adherence behavior; the reminder devices could have improved correct daily dosing (eg, reducing double dosing) without influencing refill rates. Second, the trial excluded elderly patients, who are disproportionately burdened by complex medication regimens and may have had more to gain from an intervention targeting forgetfulness. Third, patients were provided with the devices through an unsolicited mailing, and the extent to which patients actually used

Figure. Forty Years of Medication Adherence Research



Number of publications indexed in PubMed with *medication adherence* or *compliance* in the title or abstract, from 1966 to 2015.

the devices was unknown. It is possible that the devices would have been effective if provided by personal doctors or family members.

Previous studies have sought to implement simple interventions to improve medication adherence. One of the most notable examples, also led by Choudhry, was the MI FREEE (Post-Myocardial Infarction Free Rx Event and Economic Evaluation) study,⁴ a randomized clinical trial that tested the effect of eliminating out-of-pocket expenses for cardiovascular medications among survivors of myocardial infarction. That study found a 4% to 6% improvement in medication adherence. Although the MI FREEE trial did not meet its primary outcome of first major vascular event or revascularization, it was associated with improved secondary outcomes, including lower total health care costs. Other promising simple, scalable solutions, such as synchronizing medication start dates⁵ or automated telephone and mail reminders for filling prescriptions,⁶ have been associated with modest improvements in adherence. In this light, the null findings of the REMIND (Randomized Evaluation to Measure Improvements in Nonadherence From Low-Cost Devices) trial should not dissuade investigators from pursuing simple approaches. For those of us seeking interventions that will have a large, sustained influence on medication adherence, however, other approaches are needed.

Multiple systematic reviews have sought to identify the most effective interventions for improving medication adherence.⁷ Despite differences in methodologies, the conclusions have been consistent: complex, multicomponent, behaviorally oriented interventions are needed to bring about substantial change. Ironically, Sackett and colleagues¹ learned this

lesson back in the 1970s. First, they tested single-component interventions, one that provided chronic disease education and another that increased accessibility to care; neither affected adherence. Next, they tested a labor-intensive intervention that included multiple behavior change techniques such as self-monitoring, feedback, habit formation, social support, and financial incentives. This complex approach led to a more than 20% improvement in adherence, and one-third of intervention patients achieved blood pressure control. Despite confirmation of their importance across 40 years of research, multicomponent patient-oriented adherence interventions are not yet routine parts of the US health care system. The integration of behavioral resources to support medication adherence in clinical practice remains an unfulfilled promise.

So where do we go from here? To make such intensive interventions economical and thus feasible, we first need to improve the detection of nonadherence. Physicians are poor judges of whether their patients are taking their medications. Objective measures, such as pharmacy fill data, drug levels, and electronic monitoring, are needed to accurately identify nonadherence, such as the refill data used by Choudhry et al.³ Innovations in e-prescribing have made it possible to leverage pharmacy fill data such that clinicians can identify nonadherent patients at the point of care. Targeting intensive behavioral adherence interventions at high-risk nonadherent

patients may be an approach to achieving value. Streamlining medications to avoid unnecessary or outdated prescriptions and using once-daily dosing whenever possible can also help to improve adherence. Advances in mobile health and telemonitoring show promise for facilitating behavioral interventions and allowing physicians to tailor these interventions to a patient's individual barriers. It remains to be seen whether such technological innovations can bend the cost curve on multicomponent adherence interventions.

In the meantime, adherence researchers and practicing clinicians need to acknowledge that there is unlikely to be a "magic pill" that will solve medication nonadherence. Routinely inquiring about medication adherence in a nonjudgmental manner remains essential to uncovering nonadherence when objective measures are unavailable. When nonadherence is suspected, clinicians are encouraged to explore the reasons for nonadherence and to incorporate behavior-change techniques from effective, multicomponent interventions into their practice. These techniques may include providing feedback on self-monitoring, enlisting social supports, and recommending use of reminder systems. Partnering with allied health professionals, such as pharmacists or care managers, with expertise in these techniques is recommended when possible. Tackling nonadherence is challenging but not insurmountable, and this work helps inform our strategies.

ARTICLE INFORMATION

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