

## Treatment adherence in chronic disease

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### Abstract

Research has addressed the problem of poor adherence for the past 4 decades. Much of the research has focused on the prevalence and predictors of adherence, research methodologies, and the development of measures of adherence. To a much lesser extent, attention has been given to intervention studies designed to evaluate strategies to improve adherence to treatment regimens. This article provides an up-to-date review of the literature on medication adherence in chronic disease. © 2001 Elsevier Science Inc. All rights reserved.

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### 1. Introduction

Adherence is the extent to which a person's behavior is consistent with health care recommendations [1]. The problem of poor adherence is significant within the health care arena. As many as 5 to 11% of hospital admissions are due to medication [2,3]. Patients experience repeated hospitalizations as stressful and as contributing to a sense of powerlessness [4], rendering nonadherence both physically and emotionally distressing. The costs of managing the consequences of poor adherence to medication are excessive and have been estimated to be greater than \$100 billion yearly.

Studies reveal low levels of adherence to treatment recommendations across health states, treatments, and ages [5,6]. Indeed, as many as 60% of persons with chronic disorders are poorly adherent to treatment. In a meta-analysis of the literature on medication nonadherence rates in the elderly, it was shown that from 29 to 59% of outpatients do not take medications as prescribed [7]. On average, it has been estimated that only half of those who are prescribed pharmacological therapies take enough doses of the medication to experience a therapeutic effect [8–10]. When persons experience less than therapeutic effects, this may result in prescribed increases in medication dosages or discontinuing a medication because it is believed to be ineffective. This conclusion is often based on the assumption that the patient or subject has taken the medication as prescribed when adherence may be the source of the lack of efficacy. When either acute or chronic conditions are inadequately treated, the

condition may worsen. One example of such outcomes is the case of congestive heart failure, for which treatment failure or inadequate treatment is the most common cause of hospitalization in people over 65 [11,12].

Underdosing may also cause treatment outcomes to vary when the patient is discharged from the hospital to home. Patients in hospitals receive nearly 100% of the prescribed medication regime. Because medications produce an adequate therapeutic response about 90% of the time, patients have favorable odds of experiencing optimal therapeutic outcomes from medications while hospitalized [13,14]. Patients are then discharged at this pinnacle, and often deviate from the medications prescribed [7] as well as other lifestyle recommendations after returning home [12]. Urquhart and Chevalley use the term "average-compliance efficacy" to describe the effect of partial compliance on treatment outcomes [15]. Breakthrough symptoms from self-initiated drug holidays or underdosing include seizures (related to discontinuation of antiepileptics), arrhythmias (antiarrhythmics), fluid retention, and pulmonary retention (diuretics or cardiotonics), to name only a few [15]. As could be expected, nonadherence leads to hospital readmissions from 5 to 40% of the time [2,3,16].

Research has addressed the problem of poor adherence for the past 4 decades. Much of the research has focused on the prevalence and predictors of adherence, research methodologies, and the development of measures of adherence. To a much lesser extent attention has been given to intervention studies designed to evaluate strategies to improve adherence to treatment regimens. Indeed, over the past 4 decades just 19 intervention studies were published, which used a randomized, controlled design with both adherence

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and clinical outcome measured and with a 6-month or longer follow-up period [17]. Approximately one-half of these showed a positive impact on adherence. The limited attention to intervention studies certainly has contributed to the lack of improvement in general adherence rates reported in the literature between the 1970s and the present [18].

One of the factors that had slowed the progress in intervention research was the difficulty in obtaining accurate and specific measures of adherence. Multiple measures of adherence have been used that include self-report, practitioner report, physiological parameters, clinical record review, pill counts [19], and, in the last decade, electronic medication monitors [20]. Within the same study, rates of adherence may vary widely based on the method used to measure adherence. For example, subjects taking a lipid-lowering drug reported their medication adherence via 7-day recall was 97%, pill count indicated it was 94%, and electronic monitors revealed 84% [21]. An examination of the utility of each measure in predicting clinical change indicated that the electronic monitor was the only measure that correlated with cholesterol change in this population. Although there is no universally accepted gold standard for medication adherence measurement, electronic event monitors provide a complete and timely indirect measure, which infers ingestion [15,20]. The addition of improved measures in the past decade shows promise for improving the ability of intervention studies to evaluate adherence improving strategies.

Strategies to improve patient compliance regardless of health issue, theory base, or method yield significant, yet low–moderate effect sizes seldom greater than 0.37 [22]. Multifocused interventions that include cognitive, behavioral, and affective components demonstrate better outcomes than single approaches [22]. It is likely that this is a function of the multiple determinants of poor adherence episodes.

Although adherence has often been approached as a unidimensional construct, evidence has exposed the complexity of this variable. Those factors, which most consistently predict higher levels of adherence, are self-efficacy, initial adherence, regimens where multiple behaviors are required such as taking medications more than once a day, and schedule changes or disruptions [23]. Other complex factors that are observed and require more scientific evaluation include intention, physical and cognitive ability, as well as cost and side effects of medications [8,23,24]. Of particular note, however, is that predictors of adherence appear to vary by method of assessment [25].

Overall demographic factors do not seem to predict adherence reliably. Age, however, when examined in the older adult group is a demographic attribute shown to predict levels of adherence [26–29]. Adherence has been found to be particularly problematic for the old-old or those over 75 [23,28]. The age differences in medication adherence are believed to be mediated by cognitive changes [28]. The young-old, or those 60–70 years old, demonstrate the highest levels of adherence, whereas the adherence levels of those over 75 are the lowest [23,28]. This age group, as well as their

“young-old” counterparts, have a number of critical factors associated with cognitive problems, which may influence medication taking. The risk factors for cognitive impairments in those over 65 years of age are (1) the aging neurological system and cognitive changes related to aging; (2) The existence of one or multiple chronic illnesses, which may impact cognition; (3) this age group also is prescribed multiple prescription medications as well as (4) the related higher than normal incidence of side effects, including cognitive side effects, of medication. Thus, when addressing the older adult population, attention to age category may be important.

Adherence is not only a complex variable with multiple determinants, it is a continuous variable. Hence, once a method of measurement is chosen, a *level* of acceptable adherence must be defined. The convention has been to define good adherence as carrying out 80% of the recommended behaviors [20,30]. Medication adherence is reflected in the number of pills taken per day/week/month as well as the pattern of dosing within a day. For example, prescribed a twice-daily dose of an antihypertensive medication, a person may take two doses per day consistently each day, reflecting the definition of “good adherence.” However, the dosing pattern may be stable or erratic, 1 day taken in the morning and the evening, another day close together such as at supper and bedtime, and yet another day take both together at one time. Individuals may skip doses or entire days of medication. Multiple patterns of poor adherence are seen, often within the same individual. An example of electronically monitored “poor adherence” has been placed in Figure 1.

Why do individuals miss dosing events? The most common reason given by patients for missing medication is “forgetting” [31,32]. A second reason includes symptom management, that is, more medication than prescribed may be taken in the face of increased symptoms while less medication may be taken in the presence of side effects or lack of symptoms. Schedule disruptions form a third reason for missed dosing events. This includes such factors as travel, dining out, interruptions, and so on. Once patients have made a decision to adopt a regimen, the poor adherence problems appear to be pragmatic ones rather than motivational.

## 2. Implications for future research

As a fifth decade of research on patient adherence commences, a number of issues remain in need of attention. Clearly, more effort needs to be expended on intervention studies. Given the identification of various patterns of missed events and the pragmatic reasons for many of these events, examining intervention strategies targeted to specific problems may be a worthwhile venture. Further exploration of these reasons for missed dosing events would be useful in designing intervention strategies. The major costs of poor adherence also suggest that intervention strategies should be evaluated for their cost-effectiveness. Little attention has also been given to the impact of adherence improvement on clinical outcomes. Beyond the study of adher-

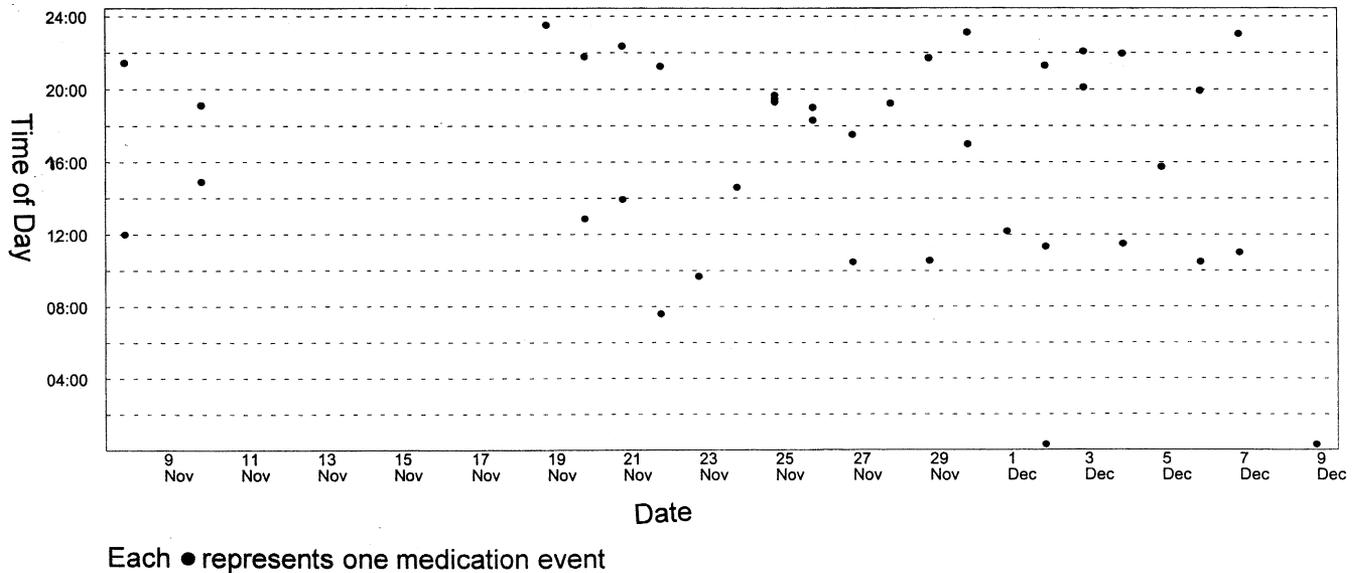


Fig. 1. Daily pattern of medication adherence.

ence interventions is the need to further examine the predictors of adherence within the context of measurement. Accurately capturing predictors may be useful in targeting subgroups for adherence attention. Thus, while 4 decades of research have been in place, there is considerable to be learned about adherence in chronic disorders. The newer technologies for assessment provide the opportunity for a more finely grained analysis of adherence behavior and for the evaluation of adherence intervention strategies.

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