Adherence to Medication Regimens and Recommended Lifestyle Changes in Patients with Cardiovascular Disease

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ABSTRACT

Adherence to medication regimens and recommended lifestyle changes is less than optimal for many disease states. Poor adherence has devastating consequences patients' health, something that has been particularly well studied in patients with cardiovascular disease. Adherence is a complex behavioral process that is strongly influenced by the patient's living environment, beliefs about the disease, concern over medication side effects, effectiveness of treatment, medication costs, cultural factors, behavior of and information from healthcare providers, and healthcare delivery systems. Of the factors that influence adherence, depression is particularly important. Patients with depression are 3 times as likely not to adhere to medical treatment regimens as those without depression. In recognizing that both provider and patient affect adherence, the provider can employ strategies using the A-I-D-S paradigm: Ask, Inform, Discuss, Share. This article offers practical suggestions for implementing this paradigm to identify patients at higher risk of poor adherence and potential barriers to adherence, as well as to reinforce the provider-patient partnership. Future research areas, including the link between depression and adherence, and the possibility that treating depression can improve adherence are discussed.

ologists and internists showed medication use discrepancies in 239 (76%) patients. Of the 545 noted discrepancies, 29% were due to patients not taking a recorded medication and 20% to patients taking different dosages; 51% were taking medications that were not recorded. The discrepancies varied among all classes of drugs, including cardiac and prescription drugs.

Medical professionals are not exemplars of adherent behavior either. A recent study assessed adherence in healthcare providers, assuming that this would represent the “expected upper limit of adherence among the general population.” Only 77% of physicians and nurses surveyed reported adherence to short-term and 84% to long-term medication regimens. Even medical professionals were affected by the complexity of the dosing regimen: a greater number of doses per day was associated with poorer adherence.

Poor adherence or nonadherence has been referred to as “America’s other drug problem” and is just one factor contributing to the “practice-outcome gap” in which clinical guidelines are implemented but the expected benefits in outcome are not realized. Patient factors, provider factors, and system factors all affect adherence. Each of these will be discussed below.

**Effects of Poor Adherence**

Poor adherence has been shown to be a major cause of acute decompensation in patients with chronic heart failure. In a sample of 179 consecutive patients admitted to the hospital with decompensated heart failure, nonadherence to medication regimens was the leading cause of acute decompensation (Table 1).

Three major studies have shown that poor adherence to medication regimens in patients with cardiovascular disease significantly affects mortality. The Coronary Drug Project was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of several lipid-lowering drugs in the therapy of coronary heart disease. No significant difference in the 5-year mortality rate was observed between the 1103 men treated with clofibrate and the 2789 men given placebo (20.0% vs 20.9%, P = 0.55). However, statistically significant differences in mortality were observed based on adherence, in both the treatment group (P < 0.001) and in the placebo group (P < 0.001) (Figure 1). Good adherers (those who took more than 80% of their prescribed capsules — either clofibrate or placebo — during the 5 years of follow-up), had improved mortality rates compared with poor adherers.

The Beta-Blocker Heart Attack Trial evaluated the effect of propranolol on mortality in patients surviving an acute myocardial infarction (MI). The research group also reported data for measures of treatment adherence, clinical severity, and the psychological and social features that may influence post-MI mortality. Poor adherers to study therapy (those who took <75% of the prescribed medication) were 2.6 times more likely to die within 1 year of follow-up than good adherers.

### Table 1. Causes of Acute Decompensation in Chronic Heart Failure

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonadherence</td>
<td>41.9</td>
</tr>
<tr>
<td>Myocardial ischemia</td>
<td>13.4</td>
</tr>
<tr>
<td>Inadequate preadmission treatment</td>
<td>12.3</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>6.1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>6.1</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
<td>5.6</td>
</tr>
<tr>
<td>No cause identified</td>
<td>14.5</td>
</tr>
</tbody>
</table>

Data from Heart 1998;80(5):437-441. With permission from the BMJ Publishing Group.

### Figure 1. Relationship Between Adherence to Clofibrate or to Placebo and Five-Year Mortality

Data from N Engl J Med. 1980;303(18):1038-1041. “Good adherer” designates patients who took 80% or more of protocol prescription during study period.
(mortality 5.4% vs 2.2%, \(P = 0.03\)). Of those taking active drug, the odds ratio (OR) of death for poor adherers to good adherers was 3.1 (\(P = 0.08\)); for those taking placebo, the OR was 2.5 (\(P = 0.10\)).

Irvine et al examined the relationship between adherence and mortality among patients in the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT). The results support the association between good adherence and decreased mortality from sudden cardiac death, total cardiac death, and all-cause mortality (Figures 2A and 2B). Indeed, it even appears that poor adherers to amiodarone were at greater risk of mortality than good adherers to placebo (Figure 3). Clearly, other factors are strongly influencing the outcomes from pharmacotherapy that extend beyond the effects of a particular drug. Irvine et al sought to identify some of those factors and found that involvement in social activities was associated with good adherence and lower mortality. The investigators suggested that good adherence may be a marker for other positive health behaviors, although this remains equivocal based on the results of other studies.

**Patient Factors Affecting Adherence**

Patient factors contributing to poor adherence include a lack of knowledge about the condition or the treatment plan; poor social support; attitudes about the medication, the disease, or their role as the “sick person”; medication side effects; problems with cognition or vision; medication cost; polypharmacy (prescription and over-the-counter medications); the complexity of the dosing regimen; and emotional illness.

Depression is common among medically ill patients and is particularly common among patients with cardiovascular disease. Approximately 15% to 18% of post-MI patients will experience major depression and up to 45% will have significant symptoms of depression soon after the event. Depression is common among medically ill patients and is particularly common among patients with cardiovascular disease. Approximately 15% to 18% of post-MI patients will experience major depression and up to 45% will have significant symptoms of depression soon after the event. Depression is particularly common among patients with cardiovascular disease. Approximately 15% to 18% of post-MI patients will experience major depression and up to 45% will have significant symptoms of depression soon after the event.

Studies have shown that patients with depression are less likely to follow healthcare recommendations. A meta-analysis of 25 studies on patient adherence and depression or anxiety found that depressed patients are 3 times more likely than non-depressed patients to be nonadherent.

Studies have also shown that patients with depression are less likely to follow specific recommendations for reducing cardiac risk during recovery from an MI. In a study of patients admitted to the Johns Hopkins Bayview Medical Center, the presence of depression and/or dysthymia was

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**Figure 2A and B. The Relationship Between Mortality and Adherence in CAMIAT**

A. The Amiodarone Group

- **SCD** (sudden cardiac death)
- **Total CD** (total cardiac death)
- **All-Cause Mortality**

B. The Placebo Group

- **SCD** (sudden cardiac death)
- **Total CD** (total cardiac death)
- **All-Cause Mortality**

Poor adherence over 2 years of study defined as the lower 20th percentile of the pill count distribution. In this study, poor adherence was taking fewer than 66% of pills prescribed. SCD = sudden cardiac death; Total CD = total cardiac death.

determined using the Structured Clinical Interview for DSM-III-R and symptoms of depression were assessed using the Beck Depression Inventory (BDI).\textsuperscript{21-23} The presence of depressive symptoms (ie, BDI score >10) was significantly associated with poor adherence to following a low-fat diet, performing regular exercise, reducing stress, and increasing social support (Figure 4). For those with major depression, dysthymia, or both, significant decreases in adherence were observed for all of those recommendations, as well as for taking their prescription medications and following a diabetic diet (Figure 5). Thus, depression should be considered a risk factor for nonadherence in patients with heart disease.\textsuperscript{12,20}

**Provider Factors Affecting Adherence**

As the Expert Panel on Compliance reported, "The literature on compliance is dominated by reports of patients' noncompliance with prevention and treatment recommendations...There are fewer reports on how the behavior of healthcare professionals and the delivery of medical care contribute to patient compliance with any health behavior. The Expert Panel recognized the importance of a multilevel approach to the compliance challenge: patient, provider, and organization."\textsuperscript{13}

On the part of the healthcare provider, factors contributing to poor patient adherence include the behavior of the practitioner: lecturing or challenging the patient; not assessing adherence; failing to simplify the medication regimen or to provide instruction or education about the drugs or the disease; not querying the patient about side effects or cost issues; or, perhaps most frequently, increasing or changing medications when the patient fails to respond without assessing whether the patient is taking medications as prescribed.

**System Factors Affecting Adherence**

Healthcare providers can tailor their practice to enhance patient adherence. The ideal approach and setting for improving adherence is a multidisciplinary team consisting of health educators, nurses, and physicians, each of whom reinforces the importance of adherence and periodically monitors patient adherence to therapy. For the majority of providers who do not have such a team available, focusing efforts by identifying patients at greatest risk for poor adherence can be an effective strategy. Since depression is associated with poor adherence,\textsuperscript{12,20} screening for depression may identify a group that may benefit most from adherence-enhancing initiatives. Assessing depression need not be time consuming, since there are

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**Figure 3. The Relationship Between Mortality and Adherence to Active Drug and Placebo in CAMIAT**

Poor adherence over a 2-year study period, defined as being below the 20th percentile of a pill count distribution. In this study, the 20th percentile cutoff point was taking fewer than 66% of pills prescribed. SCD = sudden cardiac death; CD = cardiac death. Data from Psychosom Med. 1999;61:566-575.\textsuperscript{1}

**Figure 4. Post-MI Depression and Adherence**

The relationship between depression measured by the Beck Depression Inventory (BDI) during the hospitalization for acute MI and self-reported adherence 4 months later. Reprinted with permission from Arch Intern Med. 2000;160(12):1818-1823.\textsuperscript{21}
several short depression screening instruments, including the BDI, that can be completed in a busy office practice setting, even while the patient is in the waiting room. The patient should be instructed to complete the screening instrument when he or she arrives in the office and this should be reviewed by the provider at the time of the patient interview. In this way, patients who are depressed can be identified, both for treatment of their mood disorder and also so that more frequent assessments of adherence to therapy can occur over time.

**Strategies for Improving Adherence: The A-I-D-S Paradigm**

As part of the recognition that both provider and patient affect adherence, the provider can employ strategies using the A-I-D-S paradigm: Ask, Inform, Discuss, Share.

**Ask**

Although asking patients about adherence may not be the best method for addressing the problem, it can open a line of communication and provide an opportunity for expressing empathy not previously established. By acknowledging that adherence may be difficult and by discussing the statistics that bear this out, the practitioner establishes a therapeutic environment in which the patient may feel more comfortable discussing problems with taking medications or following treatment recommendations (Table 2). Asking about adherence problems in an empathic manner (“M any people find that taking medicine on schedule without missing doses is difficult. Is that a problem for you?”) provides an opportunity for patient self-reporting, which has been shown to be a valid measure of adherence compared with objective measures.24

**Inform**

Informing the patient about the treatment plan and the goals of medical therapy is important for increasing adherence. Providers can take the time to inform patients about their medical condition, the type of medications being prescribed and how they work, the intended effects of medical therapy, and possible drug side effects. It is important to let the patient know what to do if a dose is missed or an extra dose is taken by accident, so the patient does not simply “give up.” Techniques for dealing with medication side effects are especially useful for preventing premature discontinuation. This is especially true if a side effect is anticipated, not serious, and likely to be temporary. For example, informing the patient who starts on a beta-blocker for heart failure, “You may be more tired or even slightly more out of breath for the first week or so after you start this medication, but this is likely to pass,” may prevent the patient from stopping this important medication unnecessarily.

**Discuss**

Potential barriers to adherence should be openly discussed, including extension of social support, which may enhance adherence and improve mild symptoms of depression that may adversely affect adherence.25 The provider should inquire whether the cost of medications is a barrier to adherence. If this is identified, the provider should make certain to prescribe the least costly, but still effective, medical regimen possible. Providers should always strive to eliminate unnecessary medications; this is even more important when cost or complexity of a medical regimen is a barrier to adherence. Other potential barriers to adherence, including the patient’s attitudes about medications in general or about a particular medicine, should also be addressed. The patient’s expectations and his or her perceived ability to make changes to improve health outcomes should be assessed and used to

![Figure 5. Post-MI Depression/Dysthymia and Adherence](image-url)

The relationship between depression and/or dysthymia, as determined by the Structured Clinical Interview for DSM-III-R administered during the hospitalization for acute MI and self-reported adherence 4 months later. Reprinted with permission from Arch Intern Med. 2000;160(12):1818-1823.21
motivate behavioral change. Motivational interviewing is a technique for negotiating behavior change that was originally developed for the treatment of addiction. Although a discussion of motivational interviewing is beyond the scope of this paper, the provider can try to motivate change by asking the patient what impact poor adherence would have on his or her illness and on his or her life. After assessing the patient's beliefs, the provider can try to improve adherence by specifically discussing potential negative consequences of poor adherence and the likely benefits of good adherence for that particular patient.

SHARE

Since provider and patient factors affect adherence, the treatment plan should be shared by both parties. The provider should strive to provide information in a therapeutic relationship that is nonthreatening and equitable, rather than in a relationship that more resembles that of a parent and a child. Nothing better communicates empathy and understanding of how hard it is to take medications properly than working with the patient to develop the simplest medical regimen possible that does not jeopardize efficacy. The provider should encourage adherence by working with the patient to establish clear treatment goals and to provide ongoing education and answers to questions by using educational materials (e.g., websites, audiotapes, printed materials, videos, and workshops). Two websites that provide useful information to patients about cardiovascular diseases are www.americanheart.org and http://familydoctor.org. Standard messages that may improve adherence are outlined in Table 3.

FUTURE DIRECTIONS

Much remains to be learned about the factors influencing adherence. In particular, additional work should focus on whether treating depression improves adherence. Since successful treatment of depression is itself dependent on patient adherence, this may be a difficult issue to study. It has been demonstrated that increasing the intensity and frequency of visits with a primary care physician and a psychiatrist during the first few weeks of treatment for depression, and continuing to monitor treatment adherence, increases adherence to antidepressant therapy. It is possible that this approach, or a similar one, may improve adherence to other medications and treatment recommendations as well.

As noted, several studies show that adherence to placebo is as related to mortality as adherence to active drug. It is therefore clear that there is something about the “adherent phenotype” per se that is associated with good outcome. Studying patients who are good adherers to determine the characteristics of this phenotype may therefore be useful in identifying novel therapies for various medical conditions.

CONCLUSION

Significant evidence supports inclusion of depression as a risk factor for nonadherence or poor adherence among patients with cardiovascular disease. The negative outcomes associated with poor adherence to placebo is as related to mortality as adherence to active drug. It is therefore clear that there is something about the “adherent phenotype” per se that is associated with good outcome. Studying patients who are good adherers to determine the characteristics of this phenotype may therefore be useful in identifying novel therapies for various medical conditions.

Table 2. Issues to Explore with Patients for Optimal Adherence

| Explore patient’s feelings about being on prescribed medications |
| Discuss difficulties that might have arisen taking medications as prescribed |
| Focus on helping the patient to understand his/her disease |
| Discuss ways in which the disease has negatively impacted the patient’s life |
| Aid the patient in understanding the risks of skipping doses of the medication |
| Focus on helping the patient accept his/her disease |
| Discuss how the medication has changed the patient’s life |
| Inquire if the patient is taking the medication as instructed |

Adapted from Neuropsychopharmacol. 2001;24(2):192-197.

Table 3. Standard Message to Improve Adherence

| • Take medications as prescribed. |
| • You will not always notice that you feel better when you take your medication. Some medications are intended to help you live longer, but may not necessarily make you feel better. |
| • Continue to take medications, even if you are feeling better. |
| • Don’t stop taking medications without checking with me or another healthcare provider. |
| • If you have any questions about your treatment, please call me. |
adherence warrant efforts by providers to identify patients at greatest risk of poor adherence, and to use the A-I-D-S paradigm to create an alliance with the patient in a therapeutic relationship that facilitates communication about this issue.

REFERENCES


24. Walsh JC, Mandalia S, Gazzard BG. Responses to 1 month self report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS. 2002;16(2):269-277.


