The challenge of patient adherence

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Abstract: Quality healthcare outcomes depend upon patients’ adherence to recommended treatment regimens. Patient nonadherence can be a pervasive threat to health and wellbeing and carry an appreciable economic burden as well. In some disease conditions, more than 40% of patients sustain significant risks by misunderstanding, forgetting, or ignoring healthcare advice. While no single intervention strategy can improve the adherence of all patients, decades of research studies agree that successful attempts to improve patient adherence depend upon a set of key factors. These include realistic assessment of patients’ knowledge and understanding of the regimen, clear and effective communication between health professionals and their patients, and the nurturance of trust in the therapeutic relationship. Patients must be given the opportunity to tell the story of their unique illness experiences. Knowing the patient as a person allows the health professional to understand elements that are crucial to the patient’s adherence: beliefs, attitudes, subjective norms, cultural context, social supports, and emotional health challenges, particularly depression. Physician–patient partnerships are essential when choosing amongst various therapeutic options to maximize adherence. Mutual collaboration fosters greater patient satisfaction, reduces the risks of nonadherence, and improves patients’ healthcare outcomes.

Keywords: patient adherence, health outcomes, physician–patient relationship

Introduction
For most medical conditions, correct diagnosis and effective medical treatment are essential to a patient’s survival and quality of life. A significant barrier to effective medical treatment, however, is the patient’s failure to follow the recommendations of his or her physician or other healthcare provider. Patient nonadherence (sometimes called noncompliance) can take many forms; the advice given to patients by their healthcare professionals to cure or control disease is too often misunderstood, carried out incorrectly, forgotten, or even completely ignored. Nonadherence carries a huge economic burden. Yearly expenditures for the consequences of nonadherence have been estimated to be in the hundreds of billions of US dollars (DiMatteo 2004b). Estimates of hospitalization costs due to medication nonadherence are as high as $13.35 billion annually in the US alone (Sullivan et al 1990). In addition to the most obvious direct costs, nonadherence is also a risk factor for a variety of subsequent poor health outcomes, including as many as 125 000 deaths each year (Smith 1989; Burman et al 1997; Christensen and Ehlers 2002; Kane et al 2003).

The corpus of literature on patient adherence is large, and there are many conceptual models that attempt to integrate a large number of complex factors that affect adherence (Bowen et al 2001). To manage the size and complexity of the empirical findings of this massive research enterprise, reliance on meta-analytic work is necessary to provide the building blocks for data-driven models of patient adherence. Currently, ongoing meta-analytic studies at the University of California, Riverside, USA, are beginning to identify a number of stable and consistent factors that affect patient adherence (DiMatteo 2004a, 2004c; DiMatteo et al 2000, 2002). Syntheses
of the literature, along with new empirical advances, highlight the complexities inherent in understanding and affecting changes in patient adherence and suggest solutions to common problems in medication management. Much that has been learned from recent research on the communication between healthcare providers and their patients can lessen the economic burden of nonadherence and improve healthcare processes and outcomes for patients.

Overview

Research during the past several decades indicates that, depending upon their conditions and the complexity of the regimens required, as many as 40% of patients fail to adhere to treatment recommendations (DiMatteo and DiNicola 1982; DiMatteo 1994, 2004a, 2004c; Lin et al 1995; Rizzo and Simons 1997; Dunbar-Jacob et al 2000; Laederach-Hofmann and Bunzel 2000; Haddad et al 2004; Haynes et al 2004). When preventive or treatment regimens are very complex and/or require lifestyle changes and the modification of existing habits, nonadherence can be as high as 70% (Dishman 1982, 1994; Brownell and Cohen 1995; Katz et al 1998; Chesney 2000; Li et al 2000). Although patients with HIV/AIDS may be highly motivated to adhere, their medication regimens are particularly complex, often involving multiple drug “cocktails” (Catz et al 2000; Heckman et al 2004).

Studies exploring simple versus complex dosing schedules have found that adherence falls off appreciably when regimens become more complicated and affect patients’ lifestyles (Chesney 2003). For example, the number of medications to be taken per day can have a significant influence, with adherence rates dropping to as low as 20% among patients who must take thirteen or more pills each day (Graveley and Oseasohn 1991). In one study of patients with hypertension, adherence to a thrice-daily medication regimen was only 50% compared with about 84% for a once-daily regimen (Eisen et al 1990). In another study of patients with severe persistent asthma, only 32% adhered to a regimen that included multiple components such as inhaled and systemic corticosteroids and long-acting bronchodilators (Barr et al 2002).

Adherence to recommendations involving lifestyle changes such as exercise frequently poses significant difficulties for patients. For example, those with chronic illnesses in the Medical Outcomes Study had average adherence rates to exercise regimens of only 19% (Kravitz et al 1993). In another study involving a physical therapy exercise regimen, only 35% of patients adhered fully; 76% followed their prescribed regimen partly but not wholly (Sluijs et al 1993). Such programs, of course, tend to be more successful in supervised rather than home-based programs (McKelvie et al 2002).

The health consequences of nonadherence can be quite severe. Nonadherence compromises patient outcomes in many different ways but is most obvious when patients fail to take medications that likely would cure or at least effectively manage their illnesses (Miller 1997; Chesney et al 2000; Weir et al 2000). For HIV patients who are not at least 90%–95% adherent, viral replication and consequent disease progression may result (Catz et al 2000; Hinkin et al 2002). For patients suffering from or those at risk of coronary heart disease, nonadherence to medication treatments can jeopardize survival (McDermott 1997). Among diabetic patients, adherence to medication for controlling hypertension is essential to preventing mortality from diabetes and myocardial infarction (Elliott et al 2000). Further, aside from direct biomedical benefits, studies show that health may depend partly upon the act of adhering to a regimen. Some research suggests that adherence, even to a placebo, is itself beneficial to health outcomes (McDermott 1997; Irvine et al 1999).

The clinical picture in a patient’s treatment can also be confused by nonadherence with patients’ risk profiles increased as a result. When physicians erroneously assume that their patients have taken prescribed medication(s), they may make inappropriate medication and/or dosage changes, which can then result in further complications and suboptimal health outcomes. Thus, not only do nonadherent patients fail to benefit from effective medication, they also risk being harmed by less than ideal medication and dosage choices (Joshi and Milfred 1995; Salzman 1995; Bedell et al 2000). Relatedly, the risk of new illness may increase in the context of nonadherence, such as when antibiotic-resistant bacterial infections develop because patients have not taken their full, prescribed doses of antibiotics (Harrison 1995; Lutfey et al 1996; Graham 1998; Rao 1998; Raviglione et al 2001). Thus, it is clear that nonadherence often results in a combination of wasted medical care dollars (Johnson and Bootman 1995; Rizzo and Simons 1997; DiMatteo 2004b), wasted time and energy for patients and healthcare providers alike (DiMatteo et al 1994), and frustration and dissatisfaction for all interactants.

Research on patient adherence

The research literature on patient adherence is extensive. Over the past 50 years, there have been 32,550 adherence-
related citations in PubMed and 10 087 in PsychLit. Of these citations, more than 2000 represent empirical research articles that involved the assessment of medical patients’ adherence to a variety of physician-prescribed regimens (medication, diet, exercise, lifestyle changes, etc).

In this research, as in clinical practice, adherence is measured in a variety of ways including pill counts; self-reports or patient diaries; physician reports; reports by others (such as the patient’s spouse); electronic measures (eg, metered dose inhalers or electronic recordings of dispensing eye drops); blood or urine assays; medical record/chart and pharmacy records; and biologic markers (Farmer 1999). These various methods are used in the context of a vast array of disease conditions both chronic and acute. Assessment methods differ in their degree of subjectivity and sophistication, ranging from simple self-reports to more technologically-oriented tools such as the Medication Event Monitoring System (MEMS)™ – an innovative method for measuring adherence in which a hidden microchip mechanism records the time and date that a patient opens a pill box, removes a pill from a packet, actuates an inhaler, or dispenses an eye drop (Farmer 1999). With technologies such as these, every removed dose of medication sends an electronic signal to the physician with the date and time the bottle was opened (Eisen et al 1990), providing a very reliable indicator of medication access (despite the remaining possibility that the dose was removed but not actually taken as prescribed). Direct observation of a patient taking medication is another, albeit more energy-intensive, method for assessing adherence (Volmink et al 2000). In the treatment of latent tuberculosis infection, for example, measurement of adherence to isoniazid (INH) can be direct, using an assessment of INH metabolites in patients’ urine (Perry et al 2002; Eidlitz-Markus et al 2003). Pharmacy records represent another resource for measuring adherence. Recent studies have analyzed pharmacy claims databases involving large numbers of patient records and indicating such data as when the medication was obtained and whether prescriptions were refilled on schedule (Tai-Seale et al 2000; Bieszk et al 2003).

Understanding adherence requires a multi-method approach to give a clear and accurate picture of whether and how medical recommendations are being followed. Adherence needs to be measured using multiple tools. For example, adherence to antidepressant medication might be assessed by pill count, patient self-report, and MEMS (Thompson et al 2000; Hamilton 2003). The combination and reconciling of various assessment techniques can be quite valuable, as individual measures of adherence have been shown to differ from one another by as much as 37% (Milgrom et al 1996).

Just as studies of adherence vary greatly in the way they measure the construct, they also range widely in scope and application. Some studies focus on variations in rates of nonadherence (DiMatteo 2004c), some on particular types of nonadherence and their associations with patient outcomes (DiMatteo 2002), others on the correlates of adherence (DiMatteo 2000, 2004a), and still others on the ways clinicians can improve adherence rates for their patients (Roter et al 1998; Atreja et al 2005). Meta-analytic techniques are now being used as well (Macharia et al 1992; DiMatteo et al 2000, 2002; McDonald et al 2002; Peterson 2003; Ismail 2004). Their goal is to synthesize and summarize what we currently know about adherence and to develop data-driven models for understanding the phenomenon and initiating interventions. Such an approach requires careful organization and assessment of the research findings on adherence, seeking evidence for convergence, and stability in research findings. It is clear from the research to date that as we compile and analyze the empirical evidence on patient adherence, we approach an enhanced understanding of this complex and important issue. In this article, we review some of the most robust findings on patient adherence, identifying what we currently know about how to manage and reduce its associated clinical risks in the context of medical practice, as well as what we have yet to determine.

Factors that affect adherence
Cognitive factors
It goes without saying, perhaps, that patients must understand what they are supposed to do before they can follow medical recommendations. Thus, patients’ health literacy is central to their ability to adhere. According to Healthy People 2010, health literacy involves the “degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions” (US DHHS 2000, p 20). Studies show that the risk of nonadherence is high when patients cannot read and understand basic written medical instructions. Misunderstanding of this type is not as uncommon as one might imagine. One large study of over 2500 patients found that nearly one third had marginal or inadequate health literacy. Of these, 42% misunderstood directions for taking medications on an empty stomach, 25% misunderstood the scheduling of their next
Communication between physicians and patients is often disturbingly ineffective. Optimal verbal communication make it possible for patients and physicians to work together to help patients follow mutually agreed-upon recommendations (Jahng et al 2005). Cohesive partnerships and effective interpersonal communication make it possible for patients and physicians to work together to help patients follow mutually agreed-upon recommendations (Jahng et al 2005).

**Interpersonal factors**

The interpersonal dynamics of the physician–patient relationship play an important role in determining a variety of patient outcomes including patient adherence to their treatment recommendations. Patients who feel that their physicians communicate well with them and actively encourage them to be involved in their own care tend to be more motivated to adhere (Frankel 1995; Safran et al 1998; Martin et al 2001; O’Malley et al 2002). Additionally, when physicians and patients agree on how involved patients should be in their care, adherence is improved (Jahng et al 2005). Cohesive partnerships and effective interpersonal communication make it possible for patients and physicians to work together to help patients follow mutually agreed-upon recommendations (Jahng et al 2005).
communication between physicians and patients promotes greater patient satisfaction with medical care, which in turn fosters higher levels of adherence.

Patients’ trust in their physicians is essential to their emotional disclosure and is therefore a crucial component of the patient–physician relationship. Patients must believe that their physician is someone who can understand their unique experience of being a patient, and someone who can provide them with reliable and honest advice (Branch 2000). Trusting relationships between physicians and patients can greatly affect patient outcomes. For example, it has been shown that physicians who promote trust in the therapeutic relationship, who have effective communication and “bedside manner”, and who express compassion for their patients succeed in fostering cooperation and patient adherence with a variety of preventive and treatment recommendations (O’Malley et al 2002). Adherence rates have been found to be nearly 3 times higher in primary care relationships characterized by very high levels of trust coupled with physicians’ knowledge of the patient as a whole person. In fact, patients’ trust in their physician has been found to far exceed many other variables when it comes to promoting patients’ satisfaction with their care (Safran et al 1998).

**Patient involvement and participatory decision making**

Studies have found that both patient satisfaction and patient adherence are enhanced by patients’ involvement and participation in their care (Martin et al 2001, 2003). The behavior of physicians and patients tends to be reciprocal when they strive toward partnership. Patients who want to be more involved tend to ask more questions and display more confidence, and physicians who are willing to sustain collaborative relationships with their patients tend to act in ways that prompt their patients to be involved and active (Street et al 2003). Research has also shown that patients who participate in discussions of behavioral strategies with their doctor are more likely to adhere to antidepressant medication (Lin et al 1995). Physician–patient partnership and social support from health professionals, as well as from members of the patient’s social network, are essential to patients’ adherence to recommended treatments (DiMatteo et al 1994; DiMatteo 2004a, 2004c).

This reciprocity and mutuality between patients and their physicians is sometimes termed *concordance* and is key to greater patient involvement in decision making. When health professional–patient relationships are concordant, patients understand the costs and benefits of their recommended regimens, and through a process of negotiation with their physicians they arrive at a better understanding of treatment. When physicians and patients work together and strive for mutual agreement, they both achieve higher levels of satisfaction with the treatment encounter (Elwyn et al 2003). This reciprocal exchange of information is vital to the decision making process that actively involves the patient (eg, Ong et al 1995). Patients tend to be more satisfied with such exchanges and take more responsibility for and adhere better to treatment choices that are made jointly. Even when dealing with a serious illness such as cancer, most patients have been found to desire all possible information regarding their condition and treatment, even if that information is initially emotionally disturbing to them (Hogbin and Fallowfield 1989; Chaitchik et al 1992). The health professional’s willingness to enter this discussion and process of negotiation with patients is critical to subsequent outcomes.

**Patients’ attitudes**

Patients’ understanding of their recommendations and good physician–patient relationships are, of course, not sufficient to eliminate the risk of nonadherence. Patients’ attitudes, beliefs, and group norms all influence adherence in meaningful and sometimes complex ways. Various cognitive and behavioral models, such as the Theory of Reasoned Action (Ajzen and Fishbein 1980), the Theory of Planned Behavior (Ajzen 1985), and the Transtheoretical Model of Change (Prochaska and DiClemente 1984) demonstrate that people’s intentions to carry out a behavior, such as to follow medication treatment, are the immediate precursors to the behavior itself. In other words, *intending* to adhere, whether this is labeled an intention, a readiness, or a stage of change, is essential to following treatment advice (McCusker et al 1994; Prochaska and Velicer 1997; Willey et al 2000; Hannover et al 2002; Blanchard et al 2003; Anatchkova et al 2005). Intentions, in turn, depend upon what people think and believe, what attitudes they hold, and how other people influence them. Thus, if patients hold beliefs that are incongruent with what their physicians prescribe for them, or if their family or social group members hold divergent views about their illnesses and treatments, patients may have difficulty even forming a willingness or intention to adhere (Greenfield et al 1987; Myers et al 1999; Soliday and Hoeksel 2000; Straughan and Seow 2000). The social
environment and the social support available to patients also affect their willingness to adhere, especially when dealing with such conditions as depression, anxiety, HIV, and other illnesses that carry a potential stigma (Roter and Hall 1992; Bensing et al 1995; Kadam et al 2001; Sirey et al 2001).

Cultural variations
Of course, the best way for physicians to facilitate their patients’ involvement in care varies across cultures (Calderón and Martin 2003). Preliminary results from our ongoing studies with several ethnic groups in Indonesia demonstrate that interventions aimed at increasing adherence require a multifaceted approach and sophisticated understanding of the complexity of issues involved. Guidelines for improving patient adherence must be tailored to the cultural backgrounds of the individual patients. Although some research has shown positive correlates and outcomes of partnerships when patients and physicians are of the same ethnic background (Cooper-Patrick et al 1999; Saha et al 1999; Cooper et al 2003) other studies have failed to demonstrate this effect and suggest that matching physicians and patients according to their ethnicity is not necessary (eg, Jahng et al 2005). Certainly constructs such as ethnicity, age, and gender are not unimportant, but they interact in very complex ways and may not be as important as communication factors. Recent evidence suggests that physician–patient congruence on their preferences for patient involvement in care is more important than congruence on demographic variables such as ethnicity, age, or gender (Jahng et al 2005). This study evaluated each of these demographic characteristics and found that congruence in preferences for patient involvement was the only significant predictor of self-reported patient adherence, accounting for approximately one fourth of the variance; similarity in age or being of the same ethnicity or gender were unrelated to adherence. These findings illustrate the importance of discussing the physician–patient partnership and together negotiating the patient’s role, and suggest that communication (both verbal and nonverbal), partnership and participation, behavior modification strategies, and the prompts and reminders that encourage adherence should be developed uniquely for each individual patient.

In addition to attitudes and sociocultural norms, patients’ perceptions of their physicians are also very good predictors of patients’ intentions to adhere. In a study we are currently conducting in conjunction with the Bayer Institute for Health Care Communication, our preliminary findings suggest that (in a US sample) patients’ intentions to adhere to their recommended treatments are significantly correlated with having choices regarding medical treatments; having the opportunity to discuss their care with their physicians; having their preferences taken into account; and having a doctor who communicates well (all significant at p < 0.001). In addition, preliminary data confirm and extend previous research showing that the amount of trust patients have in their physicians is a strong predictor of whether they plan to carry out treatment recommendations.

Depression
In meta-analytic work, findings suggest that one of the strongest predictors of patient nonadherence to medical treatment is patient depression (DiMatteo et al 2000). The risk of patient nonadherence is 27% higher if a medical patient is depressed than if he or she is not (it is 30% higher if that patient has end-stage renal disease). Depression has long been known to predict poor health outcomes, a fact that may be explained partly by the adherence problems caused by depression. Depressed patients experience pessimism, cognitive impairments, and withdrawal from social support, all of which can diminish both the willingness and ability to follow treatment regimens.

Depression is a prevalent and powerful factor in health and illness, and one that cannot be ignored. It is associated with impairment equal to or greater than that of chronic recurrent disorders such as diabetes, hypertension, arthritis, and emphysema (Wells et al 1988, 1989). Depression is currently the most prevalent mental illness and a cause of immense disability in industrialized countries. Major depression is second only to coronary heart disease in functional limitations and serious role impairment (Murray and Lopez 1997; Frasure-Smith and Lespérance 2005). Depression has been cited as the most common clinical problem that primary care physicians are called upon to diagnose and treat. In a given year, in primary care settings, up to 20% of adults present with depression (and often comorbid anxiety) (Greenburg et al 1993; Kirmayer et al 1993).

Psychological disorders are often comorbid with chronic illnesses, increasing their associated morbidity and mortality rates (Brody et al 1995; Waldron 1999; Frasure-Smith and Lespérance 2005). These conditions, however, often go untreated (Young et al 2001). Primary care physicians fail to diagnose as many as 50%–70% of persons who present with current depressive disorder (Higgins 1994; Coyne et
primary care include lack of awareness and understanding of depression symptoms, complaints of physical symptoms that take precedence or confuse the clinical picture, and failure to admit to psychological symptoms because they fear a stigma of mental illness (Docherty 1997). Patients may be reluctant to talk about non-medical matters because they expect physician disinterest or the risk of embarrassment, or because of anxiety about the possible significance of their psychological symptoms (Roter and Hall 1992).

Physician factors can also interfere with the recognition of depression in primary care settings. These include lack of knowledge about the disease, lack of training in the management of depression, reluctance to inquire about patients’ emotional states, and limited time available for patients (Docherty 1997; Carney et al 1999). Indeed, patients’ health status can influence the degree of interest and responsiveness they receive. Physicians have been found to convey greater negativity toward physically or mentally less healthy patients and to act more positively toward healthier ones (Hall et al 1996).

Despite many barriers to recognition and treatment, depression continues to play a central role in nonadherence. Appreciation of the importance of patients’ mental health in the care of their acute and chronic medical conditions can help to reduce the risks of nonadherence and contribute to more positive health outcomes (Ballenger et al 2001). New and developing models of depression management in primary care show great promise for improving patient commitment to and ultimately the success of medical treatments.

**Improving patient adherence**

The first step toward improving patient adherence involves accurately assessing whether or not patients have followed the treatments recommended to them. The precise estimation of patient adherence is not easy, and a full understanding of whether and why any given patient chooses and is able to adhere is often elusive. Physicians are typically not well informed about their patients’ adherence, and reliance upon their own intuition or upon attempts to “catch” their patients in nonadherence can be quite problematic. Patients tend to be truthful in their adherence reports only when they feel free to admit adherence difficulties without the risk of criticism and in the context of true partnership with their physicians (Haug and Lavin 1981; Hays and DiMatteo 1987). The accurate assessment of adherence depends, to a large degree, on the development of a trusting and accepting relationship between the patient and the healthcare team. Adherence assessments that are simple (presenting as little burden to the respondent as possible) and nonthreatening will also likely yield the most honest and accurate responses.

Realistic assessment of patients’ knowledge and understanding of the regimen, and their belief in it, will enable a more effective targeting of the potential for adherence problems. Many of the factors necessary to carry out such assessment are the very elements that foster communication and partnership in the medical visit. Patients need to be given the opportunity to tell their story (Mishler 1984; Smith and Hoppe 1991; Roter and Hall 1992; Roter 2000; Haidet and Paterniti 2003) and to present their point of view to the physician. From this, much information about patients’ beliefs, attitudes, subjective norms, cultural contexts, social supports, and emotional health challenges (particularly depression) can be learned. These elements are central to the establishment of adherence intentions, and must be explored and discussed in the therapeutic relationship. Perfect agreement will not always be reached, and in fact may not be desirable. Some degree of conflict between the views of physician and patient may be necessary if truly adult collaboration is to take place and a variety of therapeutic options, and ways to adhere to them, jointly considered (Katz 1984; Wolf 1988). The acknowledgment of differences is an important part of building respectful and trusting relationships between physicians and their patients.

No single intervention strategy can improve the adherence of all patients (Hamilton et al 1993; Cheng et al 1997; Roter et al 1998). Success depends upon tailoring
interventions to the unique characteristics of patients, disease conditions, and treatment regimens (McDonald et al. 2002). For example, some patients may be unable to maintain a complicated regimen without a strong system of social support and many prompts to remind them of what needs to be done. Other patients may have problems keeping appointments because they do not have access to reliable transportation or because family emergencies arise. Still others may find that side effects of medications are prohibitive or they may simply be unmotivated. The healthcare provider must be attuned to the individual, picking up on subtle hints (verbal and nonverbal) that the patient may express. A flexible mindset in which the physician thinks creatively about treatment options is always an asset. The physician–patient partnership itself, however, remains at the core of all successful attempts to improve adherence behaviors. Participation, engagement, collaboration, negotiation, and sometimes compromise enhance opportunities for optimal therapy in which patients take responsibility for their part of the adherence equation. These partnerships foster greater patient satisfaction, improved patient adherence, and ultimately optimal healthcare outcomes.

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