

The challenge of patient adherence

Leslie R Martin¹
Summer L Williams²
Kelly B Haskard²
M Robin DiMatteo²

¹Department of Psychology, La Sierra University, CA, USA; ²Department of Psychology, University of California, Riverside, CA, USA

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

Correspondence: Leslie R Martin
Department of Psychology, La Sierra University, 4500 Riverwalk Parkway, Riverside, CA 92515, USA
Tel +1 951 785 2454
Fax +1 951 785 2918
Email lmartin@lasierra.edu

of the literature, along with new empirical advances, highlight the complexities inherent in understanding and effecting 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 59% 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 dispensed 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 pack, 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; Atreya 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 very 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

appointment, and nearly 60% were unable to read and understand a typical informed consent document (Williams et al 1995). Language barriers contributed somewhat to these limitations, but even when patients could understand the language of their medical instructions, many could not comprehend the medical information. Further, older patients in this study had significantly more problems understanding their medical regimens than did younger patients. Other studies confirm these trends and indicate that our current interventions aimed at increasing health literacy to improve patient adherence have, so far, been disturbingly ineffective (Williams et al 1998; Gazmararian et al 1999; Schillinger et al 2003).

Patients' health beliefs are affected by their health literacy, and these beliefs are also contributors to (non)adherence. In a study of asthmatic patients who were given extensive, high-quality information on the use of daily inhaled corticosteroids, only 38% adhered to their medication regimen, whereas the other 62% continued to mistakenly believe that their medication should only be taken when they were symptomatic (Anarella et al 2004). In practice, patients' low health literacy has been linked to ineffective physician-patient communication and, in particular, physicians' failure to assess recall and comprehension of new concepts with their patients (Schillinger et al 2003). Low health literacy has been associated with patient depression (Kalichman 1999) and consequently with the manner in which patients communicate with their doctors. Patient health literacy issues may also be tied to ethnic disparities in screening, such as mammography, probably because of reduced access to and understanding of written cancer prevention materials (Peek and Han 2004).

Another important factor influencing nonadherence is patients' ability to remember the details of the recommendations made to them. Studies have repeatedly shown that forgetting to take (or how to take) medications is a major contributor to nonadherence (Kravitz et al 1993; Cline et al 1999; Brekke et al 2004; Shemesh et al 2004; Zaghoul and Goodfield 2004). Even when information is communicated effectively and comprehension is initially high, much of what is conveyed during the medical visit is forgotten within moments of leaving the doctor's office. One study found that patients forgot 56% of their instructions shortly after leaving the clinic (Ley and Spelman 1965). Optimal verbal communication often does not exist, and the verbal communication between physicians and patients is often

filled with technical terms and "medical jargon" that impedes patients' comprehension and retention of information (Jackson 1992). In the interest of time efficiency, details of the prescribed treatment may not be thoroughly explained and/or rehearsed with patients (Stanton 1987), but such clarification is necessary. Healthcare providers need to explain the specific steps of the regimen, review the most important details, use written instructions, and encourage their patients to ask questions about the regimen for adherence to occur (Becker and Maiman 1980; Carter et al 1982; Wolf 1988; Frank et al 1997).

Not surprisingly, when patients are presented with a very large amount of information, they tend to forget a large proportion of it (Ley 1979; Rost et al 1990). High anxiety also contributes to patients' lower levels of recall, and increases the risk of nonadherence (Ley 1979; Shapiro et al 1992; Montgomery 1999). On the other hand, research suggests that the risk of nonadherence is reduced when patients know their doctors well and are in more familiar, and less anxiety-provoking, physician-patient relationships (Rost et al 1990; Heffer et al 1997). Finally, it has been shown that when patients are more satisfied with their medical visits, they tend to experience better recall of information (Falvo and Tippy 1988). Empathic communication involving a thorough understanding of the patient's perspective, improves adherence. Patients who are informed and affectively motivated are also more likely to adhere to their treatment recommendations (Squier 1990). These findings illustrate the importance of the "psychosocial elements" in the medical encounter and their contribution to improving patient adherence to treatment.

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). Successful

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

al 1995; Lecrubrier 1998; Williams et al 1999; Ballenger et al 2001) despite the potential harm to patients' adherence and health. Even when depression is recognized, it is diagnosed and treated accurately only 30%–40% of the time (Farmer and Griffiths 1992; Kirmayer et al 1993; Rost et al 1994). In the Medical Outcomes Study, 60% of patients with major depression received no medication at all (Wells et al 1994; Sturm et al 1995). Thus, the opportunity to manage major risk factors for nonadherence and for serious patient morbidity and mortality is often missed in primary care.

Why does such a serious risk factor for nonadherence (and other poor healthcare outcomes) so often go unrecognized in the primary care medical interaction? Research suggests that both patients and their physicians contribute jointly to this problem in the medical interaction. Patient factors that prevent recognition of depression in 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 their 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.

References

- Ajzen I. 1985. From intentions to actions: a theory of planned behavior. In Kuhl J, Beckman J (eds). *Action-control: from cognitions to behavior*. Germany: Springer. p 11–39.
- Ajzen I, Fishbein M. 1980. *Understanding attitudes and predicting social behavior*. New Jersey: Prentice Hall.
- Anarella J, Roohan P, Balistreri E, et al. 2004. A survey of Medicaid recipients with asthma: perceptions of self-management, access, and care. *Chest*, 125:1359–67.
- Anatchkova MD, Velicer WF, Prochaska JO. 2005. Replication of subtypes for smoking cessation within the contemplation stage of change. *Addict Behav*, 30:915–27.
- Atreja A, Bellam N, Levy SR. 2005. Strategies to enhance patient adherence: making it simple. *Med Gen Med*, 7(1).
- Ballenger JC, Davidson JR, Lecrubier Y, et al. 2001. Consensus statement on transcultural issues in depression and anxiety from the international consensus group on depression and anxiety. *J Clin Psychiatry*, 62 Suppl 13:47–55.
- Barr RG, Somers SC, Speizer FE, et al. 2002. Patient factors and medication guideline adherence among older women with asthma. *Arch Intern Med*, 162:1761–8.
- Becker MH, Maiman LA. 1980. Strategies for enhancing patient compliance. *J Community Health*, 6:113–35.
- Bedell SE, Jabbar S, Goldberg R, et al. 2000. Discrepancies in the use of medications: their extent and predictors in an outpatient practice. *Arch Intern Med*, 160:2129–34.
- Bensing JM, Keressens JJ, van der Pasch M. 1995. Patient-directed gaze as a tool for discovering and handling psychosocial problems in general practice. *J Nonverbal Behav*, 19:223–42.
- Bieszek N, Patel R, Heaberlin A, et al. 2003. Detection of medication nonadherence through review of pharmacy claims data. *Am J Health Syst Pharm*, 60:360–6.
- Blanchard KA, Morgenstern J, Morgan TJ, et al. 2003. Motivational subtypes and continuous measures of readiness for change: concurrent and predictive validity. *Psychol Addict Behav*, 17:56–65.
- Bowen DJ, Helmes A, Lease E. 2001. Predicting compliance: how are we doing? In Burke LE, Ockene IS (eds). *Compliance in healthcare and research*. Armonk: Futura. p 25–41.
- Branch WT Jr. 2000. The ethics of caring and medical education. *Acad Med*, 75:127–32.
- Brekke HK, Sunesson A, Axelsen M, et al. 2004. Attitudes and barriers to dietary advice aimed at reducing risk of type 2 diabetes in first-degree relatives of patients with type 2 diabetes. *J Hum Nutr Diet*, 17: 513–21.
- Brody DS, Thompson TL II, Larson DB, et al. 1995. Recognizing and managing depression in primary care. *Gen Hosp Psychiatry*, 17: 93–107.
- Brownell KD, Cohen LR. 1995. Adherence to dietary regimens. 1: an overview of research. *Behav Med*, 20:149–54.
- Burman WJ, Cohn DL, Rietmeijer CA, et al. 1997. Noncompliance with directly observed therapy for tuberculosis. Epidemiology and effect on the outcome of treatment. *Chest*, 111:1168–73.
- Calderón C, Martin LR. 2003. Facilitation of patient involvement in Baja California, México. Presented at the Annual UCLA-PUR Conference; May 2003; Los Angeles, CA, USA.
- Carney PA, Dietrich AJ, Eliassen MS, et al. 1999. Recognizing and managing depression in primary care: a standardized patient study. *J Fam Pract*, 48:965–72.
- Carter WB, Inui TS, Kukull WA, et al. 1982. Outcome-based doctor-patient interaction analysis: I. Identifying effective provider and patient behavior. *Med Care*, 20:550–66.
- Catz SL, Kelly JA, Bogart LM, et al. 2000. Patterns, correlates, and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychol*, 19:124–33.
- Chaitchik S, Kreitler S, Shaked S, et al. 1992. Doctor-patient communication in a cancer ward. *J Cancer Educ*, 7:41–54.
- Cheng TL, Ottolini MC, Baumhaft K, et al. 1997. Strategies to increase adherence with tuberculosis test reading in a high-risk population. *Pediatrics*, 100:210–13.
- Chesney MA. 2000. Factors affecting adherence to antiretroviral therapy. *Clin Infect Dis*, 30 Suppl 2:S171–6.
- Chesney M. 2003. Adherence to HAART regimens. *AIDS Patient Care STDS*, 17:169–77.
- Chesney MA, Morin M, Sherr L. 2000. Adherence to HIV combination therapy. *Soc Sci Med*, 50:1599–605.
- Christensen AJ, Ehlers SL. 2002. Psychological factors in end-stage renal disease: an emerging context for behavioral medicine research. *J Consult Clin Psychol*, 70:712–24.
- Cline CM, Bjorck-Linne AK, Israelsson BY, et al. 1999. Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. *Eur J Heart Fail*, 1:145–9.
- Cooper LA, Roter DL, Johnson RL, et al. 2003. Patient-centered communication, ratings of care, and concordance of patient and physician race. *Ann Intern Med*, 139:907–15.
- Cooper-Patrick L, Gallo JJ, Gonzales JJ, et al. 1999. Race, gender, and partnership in the patient-physician relationship. *J Am Med Assoc*, 282:583–9.
- Coyne JC, Schwenk TL, Fechner-Bates S. 1995. Nondetection of depression by primary care physicians reconsidered. *Gen Hosp Psychiatry*, 17:3–12.
- DiMatteo MR. 1994. Enhancing patient adherence to medical recommendations. *JAMA*, 271:79–83.
- DiMatteo MR. 2004a. Social support and patient adherence to medical treatment: a meta-analysis. *Health Psychol*, 23:207–18.
- DiMatteo MR. 2004b. Evidence-based strategies to foster adherence and improve patient outcomes. *JAAPA*, 17:18–21.
- DiMatteo MR. 2004c. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*, 42:200–9.

- DiMatteo MR, DiNicola DD. 1982. Achieving patient compliance. Elmsford: Pergamon.
- DiMatteo MR, Giordani PJ, Lepper HS, et al. 2002. Patient adherence and medical treatment outcomes: a meta-analysis. *Med Care*, 40:794–811.
- DiMatteo MR, Lepper HS, Croghan TW. 2000. Depression is a risk factor for noncompliance with medical treatment: a meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med*, 160:2101–7.
- DiMatteo MR, Reiter RC, Gambone JG. 1994. Enhancing medication adherence through communication and informed collaborative choice. *Health Commun*, 6:253–65.
- Dishman RK. 1982. Compliance/adherence in health-related exercise. *Health Psychol*, 1:237–67.
- Dishman RK. 1994. The measurement conundrum in exercise adherence research. *Med Sci Sports Exerc*, 26:1382–90.
- Docherty JP. 1997. Barriers to the diagnosis of depression in primary care. *J Clin Psychiatry*, 58 Suppl 1:5–10.
- Dunbar-Jacob J, Erlen JA, Schlenk EA, et al. 2000. Adherence in chronic disease. *Annu Rev Nurs Res*, 18:48–90.
- Eidlitz-Markus T, Zeharia A, Baum G, et al. 2003. Use of the urine color test to monitor compliance with isoniazid treatment of latent tuberculosis infection. *Chest*, 123:736–9.
- Eisen SA, Miller DK, Woodward RS, et al. 1990. The effect of prescribed daily dose frequency on patient medication compliance. *Arch Intern Med*, 150:1881–4.
- Elliott WJ, Maddy R, Toto R, et al. 2000. Hypertension in patients with diabetes. Overcoming barriers to effective control. *Postgrad Med*, 107:29–32.
- Elwyn G, Edwards A, Britten N. 2003. “Doing prescribing”: how might clinicians work differently for better, safer care. *Qual Saf Health Care*, 12 Suppl 1:i33–6.
- Falvo D, Tippy P. 1988. Communicating information to patients. Patient satisfaction and adherence as associated with resident skill. *J Fam Pract*, 26:643–7.
- Farmer AE, Griffiths H. 1992. Labeling and illness in primary care: comparing factors influencing general practitioners’ and psychiatrists’ decisions regarding patient referral to mental illness services. *Psychol Med*, 22:717–23.
- Farmer KC. 1999. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther*, 21:1074–90.
- Frank JC, Hirsch SH, Chernoff J, et al. 1997. Determinants of patient adherence to consultative comprehensive geriatric assessment recommendations. *J Gerontol A Biol Sci Med Sci*, 52:M44–51.
- Frankel RM. 1995. Emotion and the physician-patient relationship. *Motiv Emot*, 19:163–73.
- Frasure-Smith N, Lespérance F. 2005. Depression and coronary heart disease: complex synergism of mind, body, and environment. *Am Psychol Soc*, 14:39–43.
- Gazmararian JA, Baker DW, Williams MV, et al. 1999. Health literacy among Medicare enrollees in a managed care organization. *JAMA*, 281:545–51.
- Graham NM. 1998. Studies of antiretroviral therapy in the Multicenter AIDS Cohort Study. *J Acquir Immune Defic Syndr Hum Retroviro*, 17:S9–12.
- Graveley EA, Oseasohn CS. 1991. Multiple drug regimens: medication compliance among veterans 65 years and older. *Res Nurs Health*, 14:51–8.
- Greenberg PE, Stiglin LE, Finkelstein SN, et al. 1993. The economic burden of depression in 1990. *J Clin Psychiatry*, 54:405–18.
- Greenfield SF, Borkan J, Yodfat Y. 1987. Health beliefs and hypertension: a case-control study in a Moroccan Jewish community in Israel. *Cult Med Psychiatry*, 11:79–95.
- Haddad M, Inch C, Glazier RH, et al. 2000. Patient support and education for promoting adherence to highly active antiretroviral therapy for HIV/AIDS. *Cochrane Database Syst Rev*, 3.
- Haidet P, Paterniti DA. 2003. “Building” a history rather than “taking” one: a perspective on information sharing during the medical interview. *Arch Intern Med*, 163:1134–40.
- Hall JA, Roter DL, Milburn MA, et al. 1996. Patients’ health as a predictor of physician and patient behavior in medical visits. A synthesis of four studies. *Med Care*, 34:1205–18.
- Hamilton GA. 2003. Measuring adherence in a hypertension clinical trial. *Eur J Cardiovasc Nurs*, 2:219–28.
- Hamilton GA, Toberts SJ, Johnson JM, et al. 1993. Increasing adherence in patients with primary hypertension: an intervention. *Health Values*, 17:3–11.
- Hannover W, Thyrian JR, Hapke U, et al. 2002. The readiness to change questionnaire in subjects with hazardous alcohol consumption, alcohol misuse and dependence in a general population survey. *Alcohol Alcohol*, 37:362–9.
- Harrison CJ. 1995. Rational selection of antimicrobials for pediatric upper respiratory infections. *Pediatr Infect Dis J*, 14:S121–9.
- Haug MR, Lavin B. 1981. Practitioner or patient—whom’s in charge? *J Health Soc Behav*, 22:212–29.
- Haynes RB, McDonald H, Garg AX, et al. 2002. Interventions for helping patients to follow prescriptions for medications. *Cochrane Database Syst Rev*, 4.
- Hays RD, DiMatteo MR. 1987. Key issues and suggestions, sources of information, focus of measures, and nature of response options. *J Compliance Health Care*, 2:37–53.
- Heckman BD, Catz SL, Heckman TG, et al. 2004. Adherence to antiretroviral therapy in rural persons living with HIV disease in the United States. *AIDS Care*, 16:219–30.
- Heffer RW, Worchel-Prevatt F, Rae WA, et al. 1997. The effects of oral versus written instructions on parents’ recall and satisfaction after pediatric appointments. *J Dev Behav Pediatr*, 18:377–82.
- Higgins ES. 1994. A review of unrecognized mental illness in primary care. Prevalence, natural history, and efforts to change the course. *Arch Fam Med*, 3:908–17.
- Hinkin CH, Castellon SA, Durvasula RS, et al. 2002. Medication adherence among HIV+ adults: effects of cognitive dysfunction and regimen complexity. *Neurology*, 59:1944–50.
- Hogbin B, Fallowfield L. 1989. Getting it taped: the ‘bad news’ consultation with cancer patients. *Br J Hosp Med*, 41:330–3.
- Irvine J, Baker B, Smith J, et al. 1999. Poor adherence to placebo or amiodarone therapy predicts mortality: results from the CAMIAT study. *Psychosom Med*, 61:566–75.
- Ismail K, Winkley K, Rabe-Hesketh S. 2004. Systematic review and meta-analysis of randomised controlled trials of psychological interventions to improve glycaemic control in patients with type 2 diabetes. *Lancet*, 363:1589–97.
- Jackson LD. 1992. Information complexity and medical communication: the effects of technical language and amount of information in a medical message. *Health Commun*, 4:197–210.
- Jahng KH, Martin LR, Golin CE, et al. 2005. Preferences for medical collaboration: patient-physician congruence and patient outcomes. *Patient Educ Couns*, 57:308–14.
- Johnson JA, Bootman JL. 1995. Drug-related morbidity and mortality. A cost-of-illness model. *Arch Intern Med*, 155:1949–56.
- Joshi N, Milfred D. 1995. The use and misuse of new antibiotics: a perspective. *Arch Intern Med*, 155:569–77.
- Kadam UT, Croft P, McLeod J, et al. 2001. A qualitative study of patients’ views on anxiety and depression. *Br J Gen Pract*, 51:375–80.
- Kalichman SC, Ramachandran B, Catz S. 1999. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. *J Gen Int Med*, 5:267–73.
- Kane S, Huo D, Aikens J, et al. 2003. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *Am J Med*, 114:39–43.
- Katz DL, Brunner RL, St Jeor ST, et al. 1998. Dietary fat consumption in a cohort of American adults, 1985–1991: covariates, secular trends, and compliance with guidelines. *Am J Health Promot*, 12:382–90.

- Katz J. 1984. The silent world of doctor and patient. New York: Free Pr.
- Kirmayer LJ, Robbins JM, Dworkind M, et al. 1993. Somatization and the recognition of depression and anxiety in primary care. *Am J Psychiatry*, 150:734–41.
- Kravitz RL, Hays RD, Sherbourne CD, et al. 1993. Recall of recommendations and adherence to advice among patients with chronic medical conditions. *Arch Intern Med*, 153:1869–78.
- Laederach-Hofmann K, Bunzel B. 2000. Noncompliance in organ transplant recipients: a literature review. *Gen Hosp Psychiatry*, 22: 412–24.
- Leclercq Y. 1998. Is depression under-recognised and undertreated? *Int Clin Psychopharmacol*, 13 Suppl 5:S3–6.
- Ley P. 1979. The use and improvement of written communication in mental health care and promotion. *Psych Health Med*, 18:245–55.
- Ley P, Spelman MS. 1965. Communications in an out-patient setting. *Br J Soc Clin Psychol*, 4:114–16.
- Li BD, Brown WA, Ampil FL, et al. 2000. Patient compliance is critical for equivalent clinical outcomes for breast cancer treated by breast-conservation therapy. *Ann Surg*, 231:883–9.
- Lin EHB, Von Korff M, Katon W, et al. 1995. The role of the primary care physician in patients' adherence to antidepressant therapy. *Med Care*, 33:67–74.
- Lutfey M, Della-Latta P, Kapur V, et al. 1996. Independent origin of monorifampin-resistant mycobacterium tuberculosis in patients with AIDS. *Am J Respir Crit Care Med*, 153:837–40.
- Macharia WM, Leon G, Rowe BH, et al. 1992. An overview of interventions to improve compliance with appointment keeping for medical services. *JAMA*, 267:1813–17.
- Martin LR, DiMatteo MR, Lepper HS. 2001. Facilitation of patient involvement in care: development and validation of a scale. *Behav Med*, 27:111–20.
- Martin LR, Jahng KH, Golin CE, et al. 2003. Physician facilitation of patient involvement in care: correspondence between patient and observer reports. *Behav Med*, 28:159–64.
- McCusker J, Bigelow C, Frost R, et al. 1994. The relationship of HIV status and HIV risky behaviour with readiness for treatment. *Drug Alcohol Depend*, 34:129–38.
- McDermott MM, Schmitt B, Wallner E. 1997. Impact of medication nonadherence on coronary heart disease outcomes. A critical review. *Arch Intern Med*, 157:1921–9.
- McDonald HP, Garg AX, Haynes RB. 2002. Interventions to enhance patient adherence to medication prescriptions: scientific review. *JAMA*, 288:2868–79.
- McKelvie RS, Teo KK, Roberts R, et al. 2002. Effects of exercise training in patients with heart failure: the exercise rehabilitation trial (exert). *Am Heart J*, 144:23–30.
- Milgrom H, Bender B, Ackerson L, et al. 1996. Noncompliance and treatment failure in children with asthma. *J Allergy Clin Immunol*, 98:1051–7.
- Miller NH. 1997. Compliance with treatment regimens in chronic asymptomatic diseases. *Am J Med*, 102:43–9.
- Mishler EA. 1984. The discourse of medicine: dialectics of medical interviews. Norwood: Ablex.
- Montgomery C, Lydon A, Lloyd K. 1999. Psychological distress among cancer patients and informed consent. *J Psychosom Res*, 46:241–5.
- Murray CJ, Lopez AD. 1997. Global mortality, disability, and the contribution of risk factors: global burden of disease study. *Lancet*, 349:1436–42.
- Myers RE, Chodak GW, Wolf TA, et al. 1999. Adherence by African American men to prostate cancer education and early detection. *Cancer*, 86:88–104.
- O'Malley AS, Forrest CB, Mandelblatt J. 2002. Adherence of low-income women to cancer screening recommendations. *J Gen Intern Med*, 17:144–54.
- Ong LM, de Haes JC, Hoos AM, et al. 1995. Doctor-patient communication: a review of the literature. *Soc Sci Med*, 40:903–18.
- Peek ME, Han JH. 2004. Disparities in screening mammography. Current status, interventions and implications. *J Gen Intern Med*, 19:184–94.
- Perry S, Hovell MF, Blumberg E, et al. 2002. Urine testing to monitor adherence to preventive therapy. *J Clin Epidemiol*, 55:235–8.
- Peterson AM, Takiya L, Finley R. 2003. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health Syst Pharm*, 60:657–65.
- Prochaska JO, DiClemente CC. 1984. The transtheoretical approach: crossing traditional boundaries of therapy. Chicago: Dow Jones/Irwin.
- Prochaska JO, Velicer WF. 1997. The transtheoretical model of health behavior change. *Am J Health Promot*, 12:38–48.
- Rao GG. 1998. Risk factors for the spread of antibiotic-resistant bacteria. *Drugs*, 55:323–30.
- Raviglione MC, Gupta R, Dye CM, et al. 2001. The burden of drug-resistant tuberculosis and mechanisms for its control. *Ann NY Acad Sci*, 953: 88–97.
- Rizzo JA, Simons WR. 1997. Variations in compliance among hypertensive patients by drug class: implications for health care costs. *Clin Ther*, 19:1446–57.
- Rost K, Roter D, Bertakis K, et al. 1990. Physician-patient familiarity and patient recall of medication changes. The collaborative study group of the SGIM task force on the doctor and patient. *Fam Med*, 22: 453–7.
- Rost K, Smith R, Matthews DB, et al. 1994. The deliberate misdiagnosis of major depression in primary care. *Arch Fam Med*, 3:333–7.
- Roter DL, Hall JA. 1992. Doctors talking with patients, patients talking with doctors: improving communication in medical visits. Westport: Auburn House.
- Roter DL, Hall JA, Merisca R, et al. 1998. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care*, 36: 1138–61.
- Roter D. 2000. The enduring and evolving nature of the patient-physician relationship. *Patient Educ Couns*, 39:5–15.
- Safran DG, Taira DA, Rogers WH, et al. 1998. Linking primary care performance to outcomes of care. *J Fam Pract*, 47:213–20.
- Saha S, Komaromy M, Koepsell TD, et al. 1999. Patient-physician racial concordance and the perceived quality and use of health care. *Arch Intern Med*, 159:997–1004.
- Salzman C. 1995. Medication compliance in the elderly. *J Clin Psychiatry*, 56 Suppl 1:18–22.
- Schillinger D, Grumbach K, Piette J, et al. 2002. Association of health literacy with diabetes outcomes. *JAMA*, 288:475–82.
- Schillinger D, Piette J, Grumbach K, et al. 2003. Closing the loop: physician communication with diabetic patients who have low health literacy. *Arch Intern Med*, 163:83–90.
- Shapiro DE, Boggs SR, Melamed BG, et al. 1992. The effect of varied physician affect on recall, anxiety, and perceptions in women at risk for breast cancer: an analogue study. *Health Psychol*, 11:61–6.
- Shemesh E, Shneider BL, Savitzky JK, et al. 2004. Medication adherence in pediatric and adolescent liver transplant recipients. *Pediatrics*, 113:825–32.
- Sirey JA, Bruce ML, Alexopoulos GS, et al. 2001. Stigma as a barrier to recovery: perceived stigma and patient-rated severity of illness as predictors of antidepressant drug adherence. *Psychiatr Serv*, 52: 1615–20.
- Sluijs EM, Kok GJ, van der Zee J. 1993. Correlates of exercise compliance in physical therapy. *Phys Ther*, 73:771–82.
- Smith DL. 1989. Compliance packaging: a patient education tool. *Am Pharm*, NS29:42–5, 49–53.
- Smith RC, Hoppe RB. 1991. The patient's story: integrating the patient- and physician-centered approaches to interviewing. *Ann Intern Med*, 115:470–7.
- Soliday E, Hoeksel R. 2000. Health beliefs and pediatric emergency department after-care adherence. *Ann Behav Med*, 22:299–306.

- Squier RW. 1990. A model of empathic understanding and adherence to treatment regimens in practitioner-patient relationships. *Soc Sci Med*, 30:325-39.
- Stanton AL. 1987. Determinants of adherence to medical regimens by hypertensive patients. *J Behav Med*, 10:377-95.
- Straughan PT, Seow A. 2000. Attitudes as barriers in breast screening: a prospective study among Singapore women. *Soc Sci Med*, 51:1695-703.
- Street RL Jr, Krupat E, Bell RA, et al. 2003. Beliefs about control in the physician-patient relationship: effect on communication in medical encounters. *J Gen Intern Med*, 18:609-16.
- Sturm R, Jackson CA, Meredith LS, et al. 1995. Mental health care utilization in prepaid and fee-for-service plans among depressed patients in the medical outcomes study. *Health Serv Res*, 30:319-40.
- Sullivan S, Kreling DH, Hazlet TK. 1990. Noncompliance with medication regimens and subsequent hospitalizations: a literature analysis and cost of hospitalization estimate. *J Res Pharmaco Econ*, 2:19-33.
- Tai-Seale M, Croghan TW, Obenchain R. 2000. Determinants of antidepressant treatment compliance: implications for policy. *Med Care Res Rev*, 57:491-512.
- Thompson C, Peveler RC, Stephenson D, et al. 2000. Compliance with antidepressant medication in the treatment of major depressive disorder in primary care: a randomized comparison of fluoxetine and a tricyclic antidepressant. *Am J Psychiatry*, 157:338-43.
- [US DHHS] US Department of Health and Human Services. 2000. Healthy People 2010, understanding and improving health: objective for improving health [online]. 2nd ed. Accessed 16 Jun 2005. URL: <http://www.healthypeople.gov/document/pdf/Volume1/11HealthCom.pdf>.
- Volmink J, Matchaba P, Garner P. 2000. Directly observed therapy and treatment adherence. *Lancet*, 355:1345-50.
- Waldron T. 1999. 'Low-grade' depression. Primary care physicians need a crash course in detection and treatment. *Behav Health Tomorrow*, 8:32-5.
- Weir MR, Maibach EW, Bakris GL, et al. 2000. Implications of a health lifestyle and medication analysis for improving hypertension control. *Arch Intern Med*, 160:481-90.
- Wells KB, Golding JM, Burnam MA. 1988. Psychiatric disorder in a sample of the general population with and without chronic medical conditions. *Am J Psychiatry*, 145:976-81.
- Wells KB, Katon W, Rogers B, et al. 1994. Use of minor tranquilizers and antidepressant medications by depressed outpatients: results from the medical outcomes study. *Am J Psychiatry*, 151:694-700.
- Wells KB, Stewart A, Hays RD, et al. 1989. The functioning and well-being of depressed patients. Results from the medical outcomes study. *JAMA*, 262:914-19.
- Willey C, Redding C, Stafford J, et al. 2000. Stages of change for adherence with medication regimens for chronic disease: development and validation of a measure. *Clin Ther*, 22: 858-71.
- Williams JW Jr, Rost K, Dietrich AJ, et al. 1999. Primary care physicians' approach to depressive disorders. Effects of physician specialty and practice structure. *Arch Fam Med*, 8:58-67.
- Williams MV, Baker DW, Parker RM, et al. 1998. Relationship of functional health literacy to patients' knowledge of their chronic disease. A study of patients with hypertension and diabetes. *Arch Intern Med*, 158:166-72.
- Williams MV, Parker RM, Baker DW, et al. 1995. Inadequate functional health literacy among patients at two public hospitals. *JAMA*, 274:1677-82.
- Wolf SM. 1988. Conflict between doctor and patient. *Law Med Health Care*, 16:197-203.
- Young AS, Klap R, Sherbourne CD, et al. 2001. The quality of care for depressive and anxiety disorders in the United States. *Arch Gen Psychiatry*, 58:55-61.
- Zaghloul SS, Goodfield MJ. 2004. Objective assessment of compliance with psoriasis treatment. *Arch Dermatol*, 140:408-14.

