



NATIONAL QUALITY FORUM

**Improving Use
of Prescription
Medications:
A National
Action Plan**

WORKSHOP
PROCEEDINGS



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of Prescription
Medications:
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Action Plan**

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Kenneth W. Kizer
Editors

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PROCEEDINGS

NATIONAL QUALITY FORUM

Foreword

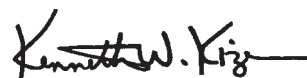
Advances in pharmaceutical science and technology are among the most important triumphs of modern healthcare. For large numbers of patients, modern drug treatments have turned previously fatal diseases into transient acute illnesses or controlled chronic conditions. Other drugs have dramatically improved patients' quality of life. Despite these impressive gains, too many patients are not receiving the benefits of the drugs that have been prescribed for them.

Patients do not use medications as they are prescribed for many reasons. Frequently, patients do not follow drug usage instructions because providers have not clearly communicated the directions. This is particularly true for patients with limited health literacy.

In March 2004, the National Quality Forum (NQF) initiated a project to address the need for a coordinated, national plan to improve consumer use of prescription medications. This project evaluated the major issues implicated in medication non-adherence along with promising practices and measures that could be used as voluntary consensus standards.

The project consisted of three components: a review of the evidence, the development of a framework, and the convening of a multistakeholder workshop in October 2004. This report details the outcome of these activities—an action plan for improving consumer use of prescription medications across the United States, with a focus on those with limited health literacy.

We thank The California Endowment for supporting this project. We also thank the workshop participants and researchers for their generous time commitment and intellectual input.



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Improving Use of Prescription Medications: A National Action Plan

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Improving Use of Prescription Medications: A National Action Plan

Executive Summary

One of the enduring challenges in healthcare today, for both providers and patients, is ensuring that patients follow treatment recommendations once they leave the care setting. Patient non-adherence is a longstanding problem across the healthcare enterprise and is one that raises serious issues for patient health, public health, and healthcare quality. With respect to the use of prescription medications, poor patient adherence—which may occur as a result of cost, side effects, misunderstandings, or other reasons—is especially problematic, given the potential of pharmaceuticals to improve health. In fact, prescription medication non-adherence is a major barrier to fully realizing the benefits of modern medical research and advancements in pharmaceuticals.

Myriad intentional and unintentional factors have been attributed to causing non-adherence, and it can be challenging for healthcare providers to change the motivations of patients who deliberately, or intentionally, choose not to follow recommended treatment regimes. Unintentional causes of poor adherence—such as inadequate provider-patient communication and patient confusion over basic directions—are key leverage points, however, and should be a high priority for improvement.

Given the significant impact of prescription medication adherence on patient safety, equity, effectiveness, efficiency, and other domains of quality, the National Quality Forum (NQF) initiated a project in March 2004 to address the need for a coordinated, national action plan to improve consumer use of prescription medications. The project was not designed to identify specific consensus standards per se; instead, it was an exploratory effort to evaluate the major issues and promising

practices or measures for their potential future use as voluntary consensus standards, with a special emphasis on populations at high risk for unintentional non-adherence, such as persons with limited health literacy, including those with limited English proficiency (LEP).

The project consisted of three major components: a comprehensive evidence review, the development of a framework to define a strategy for the action plan, and the convening of a multistakeholder invitational workshop. The review of the state of the evidence yielded approximately 3,000 relevant articles, underscoring the need for a coordinated effort to evaluate the existing body of work in order to identify priorities for improvement. A framework to outline major issues and define an overall strategy for the action plan was developed based on the input of a small focus group and workshop participants. The invitational workshop was held in October 2004 in Washington, DC, convening a diverse group of experts in quality, performance measurement, prescription medication safety, adherence, health literacy, and minority healthcare quality. The proceedings of this workshop are described in this report, which presents a national action plan for broadly improving consumer use of prescription medications in the United States.

Recommendations

Patients will not be able to benefit fully from medical research and pharmaceutical developments until their use of prescription medications is greatly improved. The coordinated efforts of a broad group of stakeholders, including NQF Members, are critical for enacting the healthcare system reforms that are needed to begin to address the issues involved in medication non-adherence. The solution should begin with the standardization of a set of performance measures that addresses adherence; the standardization of a set of practices that can be used by healthcare providers; and multistakeholder engagement and action to improve adherence. Three major recommendations are offered to create a national action plan for improving consumer use of prescription medications, as follows:

- **Data and measurement.** Identify and implement a standardized set of measures that uses existing data to measure provider performance, drawing on the wealth of information available from pharmacies, pharmacy benefits management organizations, state Medicaid agencies, and other available sources. Promote the sharing of those data with pharmacists, physicians, and other prescribers in order to facilitate the evaluation and improvement of patient adherence.
- **Practices for healthcare providers.** Evaluate and identify a set of practices for improving medication use adherence that healthcare providers at the individual and organization levels can use and that addresses medication use over the continuum of care. The set should include practices that apply to all patients, as well as those that address the additional needs of populations that face challenges in understanding healthcare information, such as those with LEP, limited literacy, and/or cognitive impairments, as well as other vulnerable or high-risk populations. Goals for improvement in a set of provider-focused practices should include facilitating care coordination; improving written information and verbal communication; routinely assessing patient adherence; providing tools patients can use to take charge of their own care; and addressing poor adherence resulting from cost/access issues.
- **Stakeholder engagement.** Engage a broad array of stakeholders, including consumers, pharmacies, provider organizations, purchasers, policymakers, pharmaceutical manufacturers, and information technology vendors, in developing and implementing strategies to improve adherence. Establish a case for each respective stakeholder that emphasizes how improving medication adherence meets its established needs and interests. Implement system-level changes through a combination of policy and purchasing strategies that will support and facilitate action by all involved stakeholders to improve medication adherence.

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Improving Use of Prescription Medications: A National Action Plan

Introduction

One of the enduring challenges for both healthcare providers and patients is ensuring that patients follow treatment recommendations once they leave the care setting. Patient adherence is a longstanding problem across the healthcare enterprise and is one that raises serious issues for patient health, public health, and healthcare quality. With respect to the use of prescription medications, poor patient adherence—which may occur as a result of cost, side effects, misunderstanding, or other reasons—is especially problematic, given the potential of pharmaceuticals to improve patient health. The inappropriate use of prescription drugs can and has resulted in permanent harm, life-threatening situations, and death.¹ In fact, prescription medication non-adherence is a major barrier to fully realizing the benefits of modern medical research and ongoing advancements in the development of pharmaceuticals.

Scope and Impact of the Problem

Twenty-two percent of hospitalizations have been attributed to patient non-adherence.² One study of California Medicaid patients demonstrated that the risk of hospitalization was significantly correlated with medication adherence.³ Poor adherence for prescription medication use is particularly important, given the widespread use of these medications by a large proportion of the population. In 2000, outpatient prescription medicine spending totaled \$102 billion,⁴ comprising about one-tenth of total U.S. healthcare spending and representing the fastest growing type of medical expenditure.⁵ More than 40 percent of Americans take at least one prescription drug, and 16 percent take at

least three. Nearly 90 percent of Medicare beneficiaries report taking prescription medications, and nearly half of those individuals use five or more different medications.⁶

Increasing the effectiveness of interventions to improve adherence could have a far greater impact on population health than any other advancement in medical treatment.⁷ One study found a 76 percent discrepancy rate between what medicines patients were prescribed and what medicines (prescription and non-prescription) they actually took.⁸ As many as 40 percent of seniors are non-adherent,⁶ and a review of nearly 600 studies found general non-adherence rates to be 25 percent, ranging from 12 to 35 percent based on disease.⁹ This non-adherence was estimated to result in 112 million unnecessary visits to healthcare providers and an extra \$300 billion per year in excess spending for healthcare.⁹

Myriad intentional and unintentional factors have been attributed to non-adherence. It is challenging for healthcare providers to change patient motivations involving intentional non-adherence, such as when patients deliberately choose not to follow recommended treatment regimes. Such instances of non-adherence can result from financial issues (e.g., cost/insurance coverage), psychological issues (e.g., perceived need for the medications, unwanted side effects), or other factors. Unintentional causes of poor adherence—such as inadequate provider-patient communication and patient confusion over basic directions—are key leverage points and should be considered high-priority issues for improvement.

Impact for Populations with Limited Health Literacy

Patients with limited health literacy, including those with limited English proficiency (LEP), are at particularly high risk for unsafe use of prescription medications because of the quality and nature of the written information that is available,^{10,11} and because these patients often do not receive sufficient time or adequate verbal communication from providers. Ensuring adherence for individuals with LEP in particular is of great interest and importance, because they represent a rapidly growing segment of the U.S. population.

Nearly one in five U.S. adults reported speaking a language other than English at home in the 2000 U.S. Census.¹² Moving quickly to implement strategies to improve adherence among individuals with limited health literacy clearly is a high priority.

The U.S. Healthy People 2010 goals also note the need for better communication for patients with limited health literacy in order to avoid the safety problems associated with non-adherence.¹³ Similarly, the National Quality Forum's (NQF's) highest priority for healthcare quality measurement and reporting is to focus on vulnerable populations in order to reduce disparities in health and healthcare.¹⁴

The NQF Project

Urgent action to address medication non-adherence is needed. Patients with limited health literacy represent nearly half of all American adults.¹⁵ These patients are more likely to be non-adherent and to suffer adverse health consequences than those with adequate health literacy. They make more medication/treatment errors,^{16,17} are less able to follow treatments,¹⁸ lack the skills needed to negotiate the healthcare system,¹⁹ and are at higher risk for hospitalization.^{20,21}

To date, numerous initiatives, practices, guidelines, and other strategies designed to improve prescription medication adherence have been developed by healthcare providers, pharmacies, government entities, professional associations, researchers, consumer groups, and others. The lack of coordination and consistency in these approaches, however, has hampered

any significant progress to date. To capitalize on the promising body of existing work, a clear roadmap for action is needed—one that will provide a coordinated, national approach directed at transforming the healthcare delivery system to enable providers to improve prescription medication adherence, particularly as it is related to unintentional patient factors.

Systematic implementation of a comprehensive set of national standards on how to improve medication use could have a substantial impact on a critical issue for the U.S. healthcare system and its consumers.²² Toward that end, NQF initiated a project in March 2004, with support from The California Endowment, to address the need for a coordinated, national action plan to improve consumer use of prescription medications. With the anticipated initiation of the prescription drug benefit component for Medicare beneficiaries (P.L. 108-173) in January 2006, the development of a national action plan for improving prescription medication adherence is more important than ever.

This project was not designed to endorse specific consensus standards per se because of the diffuse nature of the evidence and a current lack of agreement in the field around potential consensus standards that were ready for endorsement through the NQF Consensus Development Process.²³ Instead, the project was an exploratory effort to evaluate the major issues and promising practices or measures for their potential future use as voluntary consensus standards, with a special emphasis on populations at high risk for

unintentional adherence, such as those with limited health literacy, including those with LEP.

Project Components

This project contained three major components:

- **Evidence review.** A comprehensive review of the evidence on improving prescription medication adherence was commissioned, which included a “Call for Practices” to NQF Members and the broader healthcare community in order to solicit information on practices to improve medication adherence (appendix D).
- **Framework development.** An expert group was convened to identify key issues for consideration in developing a preliminary framework that would guide the formation of an action plan to improve prescription medication use. Appendix A includes a list of the focus group members, and appendix C provides the background paper prepared by NQF based on this group’s recommendations.
- **Workshop.** A multistakeholder workshop including experts in medication adherence, patient safety, quality measurement, and related areas was convened to discuss the evidence review and preliminary framework and to recommend a national action plan for broadly improving consumer use of prescription medications. This report includes a synthesis of the workshop discussions and recommendations. Appendix A provides a list of the workshop participants, and appendix B contains the workshop agenda.

NQF is dedicated to improving consumer use of prescription medications broadly across multiple domains of quality for all individuals, but particularly for vulnerable populations with limited health literacy, by implementing the national action plan described in this report. However, this report is just the beginning. The action plan calls on a variety of stakeholders and includes strategies that draw on NQF’s capacity to endorse voluntary consensus standards to drive change and improvement at the system level. Success will require support by and the coordinated efforts of the various stakeholders discussed in the action plan, including NQF Members and other relevant entities that can effect changes in policy and practice.

Review of Evidence-Based Practices

To inform recommendations for the national action plan, NQF commissioned a review of the state of the evidence, which was completed by Kem Krueger, Pharm.D., Ph.D., Bruce Berger, Ph.D., R.Ph., and Bill Felkey, M.S., of the Auburn University Department of Pharmacy Care Systems (appendix D). The purpose of the paper, *Medication Adherence and Persistence*, was to provide a comprehensive review of the body of evidence on practices and strategies to improve the safe, effective, and appropriate use of prescription medications by patients, with a particular focus on practices designed to address the specific needs of patients with limited health literacy. Additionally, NQF issued a public “Call for Practices” to solicit information on the “gray” literature, such as public and

private sector initiatives and recommendations related to medication adherence. The background paper includes a summary of the practices submitted during this process, in addition to the evidence review.

Framework

Medication adherence is a complex issue, as indicated by the diffuseness of the available evidence. In order to provide a comprehensive framework for the workshop discussions on the broad range of issues involved, NQF staff developed the background paper, *A Preliminary Framework for Improving Use of Prescription Medications* (appendix C).

The framework was based on the discussions and recommendations of a small focus group of experts in medication adherence from pharmacy, clinical, academic, and consumer advocacy backgrounds that met in Washington, DC, in July 2004. The focus group outlined the major issues that should be considered in a comprehensive framework for improving prescription medication use on a national level. Participants also discussed the extent of the problem and the state of the field in advancing adherence improvement strategies; key priority areas and leverage points for improvement; special issues for populations at higher risk of poor adherence (such as those with limited literacy and LEP); and general directions for a national action plan, including the potential role of NQF consensus standards. Its recommendations were used by NQF staff to develop the background paper, which provided an overarching framework for workshop discussion.

Workshop

On October 25-26, 2004, NQF convened an invitational workshop in Washington, DC, which included a diverse group of experts in quality, performance measurement, medication safety, adherence, health literacy, and minority healthcare quality. Workshop participants included consumers, public and private purchasers, health plans and pharmacy benefits management (PBM) organizations, providers, community and chain pharmacies, and representatives of the pharmaceutical industry.

As noted above, the primary goal of the workshop was to recommend a national action plan for improving prescription medication use by all consumers, with a special focus on those with limited health literacy. The workshop included an evaluation of NQF's role in implementing and endorsing appropriate consensus standards as part of the action plan. Workshop discussions were framed around the following issues and questions:

- **Evidence.** What is the state of the scientific evidence and existing work in improving medication adherence? What specific initiatives, practices, or strategies emerge as the most promising for use on a national scale?
- **Framework.** How should a national action plan be organized and framed, considering the scope of the problem to be addressed, the level and locus of change, major priority areas for action (including special issues for patients with limited literacy and LEP), and potential mechanisms for change?
- **Practices.** What potential practices could be considered for inclusion in a set of NQF-endorsed™ voluntary consensus standards that could give healthcare providers a standardized set of practices for improving medication adherence? What practices are particularly effective in vulnerable populations, such as those with limited literacy and LEP?
- **Measures.** Which areas of performance could be measured in the pharmacy setting, based on existing data? What specific performance measures would be the most meaningful to prescribers, consumers, purchasers, and others? What measures would be particularly meaningful in vulnerable populations, such as those with limited literacy and LEP?
- **National action plan.** What key recommendations should be included in a national action plan for improving prescription medication use? How can the needs of vulnerable populations, such as those with limited literacy and LEP, be addressed in this plan? Where are the major levers for effecting change? Which stakeholders should be involved in implementing the plan, and what should their roles be? What should NQF's role be?

Evidence on How to Improve the Use of Prescription Medications

The evidence base for practices to improve medication adherence is immense. A systematic search of the published literature from 1994 through 2004 identified nearly 12,000 articles for preliminary review, from which approximately 3,000 articles were selected for a detailed review for the background paper. The sheer volume of the literature alone underscores the diffuse nature of the field and the need for a coordinated action plan to capitalize on this massive body of research. Dr. Krueger and colleagues synthesized the most relevant interventions that have been studied to improve medication adherence and/or persistence problems; described barriers to medication adherence and persistence; and identified other interventions that can be used by practitioners and organizations to address barriers to medication adherence and/or persistence problems in practice.

The reviewed articles were sorted into several different types or categories of interventions for improving adherence: theory-based, disease-based, dosage simplifications, reminders, discharge, one time, and self-care. In defining intervention categories, it was noted that no single approach is adequate to ensure patient adherence and that a combination of approaches is likely to be the most effective given the complex set of barriers and issues associated with patient non-adherence. Based on the evidence review, Dr. Krueger highlighted several issues to inform workshop discussion about the state of the science in medication use adherence.

Standardized Approaches

A pressing need exists for greater agreement around a standardized set of methods for improving adherence. No single approach is enough to ensure patient compliance, and current methods are often complex and do not produce consistent improvements. New ways of thinking and more comprehensive approaches are needed.

Provider Role

To improve adherence, providers must develop supporting and trusting relationships with patients, which requires assessing a patient's understanding of the illness and treatment; communicating treatment benefits; assessing patient readiness to carry out the treatment plan; and discussing any barriers or obstacles to adherence that a patient may have. Any attempts to improve adherence must involve the patient in the process of making decisions and setting treatment goals. Because patients with diverse racial and ethnic backgrounds, including those with LEP, often report lower levels of trust, satisfaction, and communication in healthcare, providers must take extra measures to improve quality for these populations.

Patient Role

Individual factors among patients also have an impact on adherence, with major barriers being cognitive impairment; level of social support; LEP; ability to obtain and pay for medications; complexity of treatment; quality of the clinical setting and continuity of care; and severe side effects. A number of these factors disproportionately affect racial and ethnic minorities, including

many with LEP. Patients with LEP, compared with fluent English speakers, have less access to healthcare services; lower satisfaction with the quality of care; lower adherence; poorer health outcomes; and longer hospital stays. Specific interventions should be targeted to address the higher risks faced by these patients.

Short-Term Adherence

Compliance with short-term therapy can fall off rapidly. Patients must be properly educated about how long a medicine needs to be used, its intended effects, and what benefits and side effects to expect.

Long-Term Adherence

For long-term therapies, persistence in using prescribed medications is critical. To improve long-term adherence, the benefits of the therapy must be clear; barriers must be discussed and strategies for overcoming them determined; regimens need to be tailored to patients' daily routines; follow-up care should be provided; and patient compliance/improvements should be rewarded.

Measures

Measures of adherence often are correlated with one another, but they rarely produce the same estimate of adherence. The advantages and disadvantages of any adherence measure should be kept in mind when it is being used.

Workshop Discussion on Evidence

Workshop participants generally agreed that the evidence base for effective strategies to improve prescription medication adherence was strong—both in the peer-reviewed and in the “gray” literature. Participants identified a number of additional strategies based on qualitative research and policy guidance for improving adherence, including work done by organizations such as the American Medical Association and the National Consumers League. They noted, however, that the diffuse nature of the literature and the lack of focused efforts to implement such strategies have precluded noticeable improvements. The complexity of the issues demonstrated in the evidence review was another major reason for the lack of progress in this area.

Workshop participants discussed the wide range of barriers to adherence demonstrated in the literature, and they drew a clear distinction between patients who were non-adherent for unintentional reasons (e.g., low literacy, LEP, cognitive ability) and those who were non-adherent for intentional reasons (e.g., cultural differences, self-motivation, trust, cost, and access for both insured and uninsured populations). Participants noted that because the types of interventions needed to address non-adherence for each of these groups differ, strategies must be tailored appropriately. They also agreed that unintentional reasons for adherence were a high priority in the action plan, particularly given the pressing need to reduce disparities in healthcare quality and health outcomes for racial and ethnic minority populations.

Framework for Improving the Use of Prescription Medications

Based on their diverse range of experiences in medication adherence-related issues, workshop participants expanded on the proposed framework developed by NQF (appendix C) and agreed on a number of general parameters that should define how a national action plan to improve medication use should be framed. The potential scope of issues under consideration was extremely broad, but workshop participants were asked to focus on the highest priorities for improvement.

Level of Change

Improvement can occur at the level of systems, providers/organizations (including pharmacies, pharmacists, hospitals, outpatient practices, physicians, physician assistants), and patients. To drive change at each of these levels, respective environmental, inter-relational, and individual factors must be considered. Workshop participants discussed how interventions at each level could impact adherence broadly and acknowledged that a large number of individuals interact with patients in the process of medication prescribing and use. They noted that compared with other healthcare providers, pharmacists interact more frequently with the public, making the pharmacy setting a key area for intervention. For long-term, widespread improvement, however, workshop participants called for broad, system-level changes that would, in turn, support provider/organization- and patient-level efforts to improve medication use.

Priority Areas for Improvement

The specific priority areas around which to frame a set of standards can be categorized in many ways, such as by the NQF-endorsed priorities for healthcare quality measurement and reporting;²⁴ cross-cutting conditions/features; condition-specific priorities; high-risk, high-volume, high-cost, and problem-prone areas; high-risk demographic populations; continuum of care (e.g., prevention, treatment,

and rehabilitation); and/or major healthcare delivery settings. Workshop participants outlined the major priority areas, as follows:

- **Specific conditions.** Patients with chronic diseases and comorbidities represent those for whom the cost of avoided hospitalizations would result in the greatest savings. This group includes persons with diabetes, asthma, cardiovascular disease, and/or hypertension. Those with substance abuse and/or behavioral health issues also were identified as high-priority groups for medication use adherence.
- **Patient risk factors/barriers to adherence.** Patients with major risk factors or other barriers to adherence are likely targets for improvement interventions. These patients include those with limited health literacy, including LEP, or cognitive impairments; those in assisted living situations; those with financial restraints (e.g., low income, under- and uninsured, homeless); and children.
- **Settings of care.** Medication adherence must be improved across the continuum of care. Pharmacies, inpatient and outpatient providers, health plans, and PBM organizations are important settings of care for intervention.

Criteria for Evaluating Potential Consensus Standards

Other NQF-endorsed consensus standards have evaluated potential consensus standards against a comprehensive set of criteria that broadly includes the issues of importance, scientific acceptability, usability, and feasibility. Whether this approach is suitable for medication adherence-related consensus standards will require further review, based on the nature of the proposed consensus standard. Workshop participants generally agreed that this set of criteria was useful and may be appropriate for identifying the best consensus standards for assessing the quality of safe medication use.

Organizing Framework

A comprehensive framework is needed to provide an overall structure and approach for improving safe medication use. It must take into consideration the major levels and leverage points for change, priority areas, and criteria for evaluating

potential standards. Workshop participants considered a number of proposed approaches to organizing and framing these concepts, including whether priority actions should be defined by categories such as barriers to adherence; major risk factors for non-adherence; the World Health Organization model (i.e., based upon the healthcare team, condition, characteristics of therapies, and patient-related factors); high-risk populations; high-priority conditions/diseases; specific medications; or steps across the pathway of care. Appendix C provides additional detail about these various frameworks.

Workshop participants supported an organizing framework that would promote coordination of care across the healthcare system, noting that at least one group of providers—either pharmacists or physicians—needs to be held accountable for maintaining comprehensive patient medication histories. Given the complex interactions between patients, physicians, prescribers, health plans, and other stakeholders, one of the most daunting challenges involved in improving medication use and healthcare quality in general is addressing the decentralized nature of patient medical records; improving documentation in this area was identified a critical step toward achieving coordinated care.

Mechanisms for Change

There are two major pathways for improving healthcare quality: through change and quality improvement, and through selection and accountability (as applied, for example, in public reporting and pay

for performance).²⁵ Specific strategies for improving adherence can occur at the patient, provider, organization, or system level, and at each level the effectiveness of various mechanisms—interventions, policies, guidelines, practices, and/or measures—in promoting change must be considered.

The key drivers of change identified by workshop participants utilized both pathways for improving quality. Change and quality improvement could be achieved by establishing a business case for improving medication adherence; disseminating a coordinated set of proven methods and best practices; and implementing standardized measures that providers could use to monitor patient adherence, such as prescription refill rates. Using the accountability pathway, adherence could be enhanced by reimbursing providers based on performance; providing report cards to consumers; issuing a national call for action to engage and educate consumers about the importance of proper medication use; and using a celebrity figure or other spokesperson to garner public attention.

A National Action Plan to Improve Safe Medication Use

Based on the review of evidence, general agreement among participants around the key parameters required for a comprehensive framework, and other input from workshop participants, recommendations were developed to serve as the core of a national action plan for safe medication use. These recommendations identify

high-priority areas for action that can and should be acted on by a variety of health-care stakeholders in order to contribute to more equitable, safe, effective, timely, patient-centered, and efficient use of prescription medications. Specifically, policy-makers and healthcare professionals can improve medication use by implementing changes in the following three areas:

- data and measurement;
- practices for healthcare providers; and
- stakeholder engagement.

Safety in medication use is a broad concept with implications across the healthcare system, and many other areas will need to be addressed to support improvement. For example, although these recommendations rely heavily on safe and appropriate prescribing of prescription medications by physicians and other providers, it should be noted that this does not always occur. Enhancing consumers' ability to take charge of their own safety and health through proper prescription medication use, however, is an important first step toward improving the quality of healthcare overall.

Data and Measurement

It was widely agreed by workshop participants that there is a wealth of existing data pertaining to prescription medication use that could provide the information needed to monitor and improve patient adherence, particularly for the insured population. Electronic data that are routinely entered for billing and reimbursement by private health plans/PBM organizations, pharmacies, and state Medicaid agencies hold

great potential for use in performance measurement, although issues such as compliance with Health Insurance Portability and Accountability Act of 1996 requirements, problems involving the interoperability of different data collection systems, and private ownership of the data are challenges that must be considered before a standardized set of measures can be implemented effectively.

Potential Measures. Workshop participants recommended a variety of potential performance measures that could be implemented in the pharmacy or provider setting to improve adherence, based on data that currently exist or on fields that could be added readily to existing systems. These measures could provide information useful to internal quality improvement interventions and could inform consumers about the best sources for care. Potential issues that could be measured and reported include the following: patient adherence (e.g., as defined by refill rates, refill timeliness, and other dimensions); provision of verbal counseling by physicians, pharmacists, and/or other providers; and availability of translated drug inserts and labels for medication usage (although further testing and development are needed to determine how the measures should be defined and the data collected in order to ensure that the results are scientifically acceptable and useful).

Challenges to Standardized Measurement. No gold standard or professional agreement exists for defining and measuring patient adherence. In addition, a vast literature documents the various advantages and disadvantages involved with different

adherence measures, such as patient self-report, in-office pill counts, and electronically monitored pill bottles. Patient self-reported adherence rates, for example, have been shown to differ substantially from rates estimated from prescription refill data; one study found that while 91 percent of patients reported being adherent, actual adherence ranged from 70 percent to 83 percent, based on the condition.²⁶ Electronic forms of adherence measurement, such as specially designed pill bottles, however, are more expensive and may be viewed by some patients as overly intrusive. Furthermore, the ideal level of adherence is unknown, particularly considering that patients may have prescriptions from several different physicians, with no coordination of care, and considering the wide variations in provider prescribing patterns. As noted earlier, the challenges of collecting and sharing data between PBM organizations, pharmacies, physicians, and others also must be considered.

Clearly, measures related to patient adherence and provider processes to improve adherence are not sufficient by themselves to improve patient health. A broader set of measures of patient-centered care that also addresses care coordination, medication management, and other related issues is needed. However, using existing pharmacy claims data to measure and report on patient refill rates and related indicators could be a powerful and relatively simple way to move forward in the short term.

Recommendation: Identify and implement a standardized set of measures that uses existing data to measure provider performance, drawing on the wealth of information available from pharmacies, PBM organizations, state Medicaid agencies, and other available sources. Promote the sharing of those data with pharmacists, physicians, and other prescribers in order to facilitate the evaluation and improvement of patient adherence.

Practices for Healthcare Providers

Prescribing, dispensing, and using medications involves many interactions, and workshop participants noted that the number of potential points of intervention exceeds what is

practical to measure. Thus, in addition to a set of standardized performance measures, a single, coordinated set of practices to improve consumer use of prescription medications would be an extremely useful tool for healthcare providers. Participants emphasized that the practices should benefit all patients, but also focus on the additional needs of populations at higher risk of non-adherence resulting from communication challenges and those for whom the consequences of non-adherence could be severe.

A comprehensive set of practices should combine approaches that could be used by individual healthcare providers, including pharmacists, physicians, and other prescribers, as well as strategies that could be implemented broadly across healthcare organizations, such as pharmacies, hospitals, and physician groups. Workshop participants explored a number of possible practices for use by these entities (table 1) and also considered what specific practices would be particularly useful for vulnerable populations. The practices recommended by workshop participants focused primarily on improving unintentional non-adherence for reasons related to communication and health literacy issues. However, a multitude of other factors, such as patient self-motivation, behavioral and psychological issues, personal preferences, and cultural values that impact adherence also would need to be addressed within a comprehensive set of practices.

Although a number of steps must be taken before a coordinated set of practices can be implemented, there is no shortage of work that has already been done related to medication adherence that would support such an effort. The evidence base documenting the many potential healthcare provider practices that could be used to improve adherence is immense. Medication adherence initiatives have been attempted by many stakeholder groups, and “experiential evidence” from real-world situations may provide valuable insights that cannot be captured well in the controlled studies typically published in the peer-reviewed scientific literature.

Table 1 – Potential Provider Practices for Improving Adherence

GOAL	RELEVANT PRACTICES
<p>Facilitate care coordination by improving the exchange of information. Quality and patient safety could be greatly enhanced by coordinating the care process, particularly with respect to how information about patient medication use is shared among providers and patients.</p>	<ul style="list-style-type: none"> ■ Encourage all patients to maintain comprehensive personal medication records and share them with healthcare providers. ■ Integrate personal medication records into electronic medical records. ■ Ask patients to bring all their current medications to physician office visits. ■ Share pharmacy/payer data on refill rates and other adherence-related indicators with prescribers in order to facilitate their ability to track and coordinate patient medication use.
<p>Improve written prescription medication information. Revising the various forms of written information and instructions about prescription medications would lead to better informed patients and particularly would benefit those with limited literacy and English language barriers.</p>	<ul style="list-style-type: none"> ■ Revise prescription medication labels, drug inserts, and related patient educational information to simplify the reading level. ■ Offer all written prescription medication information in foreign languages and large print. ■ Improve the style, content, and format of prescription drug inserts and other patient education material to present the key information about usage and safety up front in order to make it more reader friendly. ■ Use standardized, universal symbols developed by a national body on prescription medication labels.
<p>Improve verbal communication about prescription medication use. Pharmacists see patients five times more often than any other healthcare provider and are a key leverage point for improvement;²⁷ clinicians can inform patients about the importance of using medications as prescribed to address their health condition. Proper communication by all of these providers across the continuum of care is critical to improving consumer use of prescription medication, and special communication strategies must be used to address the needs of populations with limited health literacy.</p>	<ul style="list-style-type: none"> ■ Increase the quality, appropriateness, and timeliness of patient education, following well-established guidelines for patient counseling on proper medication use. ■ Educate patients on the importance of the medications for their condition, in addition to how to properly use the medications. ■ Assess patient understanding about how and why to use their prescribed medications using active communication methods such as “teach back” (as described in NQF’s Safe Practice 10^{28,29,30}), or by using a structured question and answer program, instead of using passive methods, such as the common “yes/no” check box to assess patients’ desire for counseling in pharmacies. ■ Improve the design of pharmacies to provide an appropriate location for confidential patient counseling. ■ Educate providers on the extent of limited health literacy and on the health and patient safety implications with respect to medication use. Also, educate providers on how to communicate clearly with all patients, particularly in a way that meets the needs of those with limited health literacy. ■ Provide language assistance options for counseling for patients with limited English proficiency, such as telephone interpretation services and pharmacy staff with medical interpreter training.
<p>Routinely assess patient adherence as a standard “vital sign.” Although providers routinely ask patients what medications they are using, more detailed and equally important information about how patients use those medications often is not asked.</p>	<ul style="list-style-type: none"> ■ Improve providers’ standard patient history and physical examination processes by adding medication adherence as a “vital sign” to be routinely assessed at each healthcare encounter. ■ Educate providers about the importance of patient adherence, and identify effective strategies that providers can use to assess patient adherence.

Table 1 – Potential Provider Practices for Improving Adherence (continued)

GOAL	RELEVANT PRACTICES
Provide tools patients can use to take charge of their own care. Simple and effective patient adherence aids are available that could be economical and powerful ways to improve the use of medications as prescribed.	<ul style="list-style-type: none"> ■ “Prescribe” and distribute pill boxes to all patients with medications where such adherence aids are helpful. ■ Integrate electronic reminder systems into pharmacy systems, and implement a standard process for reminding patients to refill medications.
Address poor adherence resulting from cost/access issues. Providers must be more cognizant of how cost and access affect patient adherence. This could particularly benefit patients with no or inadequate insurance coverage for prescription medications.	<ul style="list-style-type: none"> ■ Educate providers on the costs of common medications and the need to be sensitive to how cost affects adherence. ■ Integrate medication cost information into information technology tools, such as physicians’ personal digital assistants (PDAs). ■ Discuss medication cost with patients as part of a shared decisionmaking approach to prescribing an optimal treatment plan that the patient will follow.

Recommendation: Evaluate and identify a set of practices for improving medication use adherence that health-care providers at the individual and organization levels can use and that addresses medication use over the continuum of care. The set should include practices that apply to all patients and those that address the additional needs of populations that face challenges in understanding healthcare information, such as those with LEP, limited literacy, and/or cognitive impairments, as well as other vulnerable or high-risk populations. Goals for improvement in a set of provider-focused practices should include facilitating care coordination; improving written information and verbal communication; routinely assessing patient adherence; providing tools patients can use to take charge of their own care; and addressing poor adherence resulting from cost/access issues.

Stakeholder Engagement

A coordinated effort of all stakeholders is needed to successfully achieve system-level change and improvement in medication adherence. Workshop participants explored the individual roles and inter-relationships of the many relevant stakeholders, including those involved in aspects of manufacturing, distributing, prescribing, dispensing, managing, financing, and using medications. They developed recommendations pertaining to how these various entities should be engaged in implementing the national action plan at the individual, organization, and system levels. The relevant stakeholders were identified as:

- consumers;
- pharmacies;
- providers;
- purchasers;
- policymakers;
- pharmaceutical manufacturers; and
- information technology (IT) vendors.

Traditionally, many groups have overlooked the issue of medication adherence, despite its central role in patient safety, health outcomes, and efficiency. An essential precursor to achieving multistakeholder engagement is ensuring that the recommended actions are based on the needs and interests of each respective stakeholder—that is, the case must be made in such a way that each stakeholder understands how it will benefit from engaging in such actions. Payers, for example, need to hear a business case that demonstrates how efforts to improve medication adherence will improve overall efficiency and costs. Likewise, the case for consumer-directed actions must be based on patient motivations for using prescription medications appropriately. The recommended actions for stakeholder engagement are described in the following sections.

Consumers. Although unintentional reasons for non-adherence were a primary focus of the workshop discussion, because of the interest in the communication challenges that are experienced by populations with limited health literacy, much of the literature involving adherence relates to intentional reasons for non-adherence, including psychosocial factors, personal preferences, cultural attitudes, and financial constraints. Improved communication by healthcare providers could benefit many patients who are unintentionally non-adherent, but healthcare consumers and the public in general can be empowered to play a role as well. Those who wish to engage the public and improve consumer self-care in medication adherence must consider the many factors that cause non-adherence, both unintentional and intentional. They also must tailor messages appropriately to reach diverse populations.

Participants' recommendations for engaging consumers included involving public health promotion entities, the media, and a celebrity or other high-profile spokesperson in national and regional educational campaigns and a "call for action" to the public. Using direct-to-consumer prescription medication advertising as an opportunity to raise awareness about the health and safety reasons for adherence (or, perhaps more convincing, about the potential implications of non-adherence) also was discussed. Participants emphasized that the messages used must be meaningful and comprehensible

to a variety of audiences, particularly with respect to cultural and linguistic appropriateness.

Pharmacies. Potential practices to improve adherence that could be used in the pharmacy setting by individual pharmacists and pharmacies are described in table 1. The additional time and resources needed to engage in many of these recommended practices may result in an immediate and short-term burden on pharmacies; however, one of the benefits of improved patient understanding about the importance of using medications properly is higher refill rates, which translates to more business and improved outcomes.

Pharmacies that offer additional services to patients to address their communication needs may also have a competitive advantage, which is particularly important given the range of options available today to consumers filling prescriptions (e.g., health system, community, chain, and Internet-based pharmacy). Many pharmacies already utilize marketing strategies that appeal to customers' interest in safety (e.g., computer-based medication interaction checking), and pharmacies should be encouraged to compete in providing similar services that improve the clarity of written and verbal information for patients, such as simpler, reader-friendly, multilingual labels and drug information.

Providers. Potential practices that could be used in the healthcare delivery setting by individual prescribers and other providers are described in table 1. As with pharmacies, however, the initial adoption and use of these practices may be burdensome, or at least viewed as such.

To change provider behavior and encourage the use of practices such as "teach back" and assessment of adherence as a "vital sign," which may be viewed as time-consuming tasks, providers must be made aware of the evidence that documents the broad implications of poor adherence on their primary goal: improving patient health and ensuring safety. As noted, patient non-adherence is a frequent cause of hospitalization and also contributes to patient safety events that may be life threatening. Other data that could be used to convince providers about the importance of improved adherence include those related to short-term successes from chronic

disease interventions that focus on medication management. For example, one potential model for demonstrating the immediate, tangible outcomes that can result from medication adherence is provided by the Asheville (North Carolina) Project's demonstrated success in diabetes care.²⁷ Educational efforts are needed that span multiple points of provider training and practice, including medical education, continuing education, and other organizational education and quality improvement efforts.

Purchasers. Organizations that act as purchasers/payers of prescription medications, including health plans, PBM organizations, employers, and federal and state entities (e.g., Medicare and Medicaid), could have a significant impact on safe medication use. Workshop participants representing both public and private healthcare purchaser organizations noted that medication adherence issues are generally not high priority for purchasers, and many purchasers are unaware of how improving adherence impacts them. They commented that value-based purchasing was a priority, however, and that measuring and reporting information that could drive value-based purchasing was needed to engage purchasers. Specifically, participants noted that in order for the issue of medication adherence to resonate with purchasers, a return on investment must be apparent and the business case must be clear. Designing programs that specifically target patients with chronic diseases and/or comorbidities, for whom adherence interventions could have the most immediate and noticeable impact, was noted as one

way to accomplish this, as the Asheville Project demonstrated.

It may seem counterintuitive that encouraging consumers to use more prescription medications (e.g., for those cases in which poor adherence stems from underuse of recommended medications) actually benefits organizations that pay for healthcare. Studies have shown, however, that the longer-term costs of medication non-compliance are far greater than the short-term costs of fully compliant medication usage, particularly given the relationship between poor adherence and higher hospitalization. One study of California Medicaid patients found that direct healthcare costs were significantly higher for patients with bipolar disorder who underused prescribed medications.³¹ A separate study also found that California Medicaid patients who under- or overused antipsychotic medications had higher hospitalization costs than those who used them as often as prescribed.³² Similarly, another study recently demonstrated that for patients with diabetes and hypercholesterolemia, those who had higher levels of medication adherence, and therefore higher medication costs, had lower overall medical costs related to their disease.³³ Purchasers should be educated on these findings and the successes that have resulted from related efforts in order to demonstrate the impact of improved adherence on cost.

Workshop participants viewed purchaser engagement as an especially critical link because purchaser actions to address adherence through strategies such as pay for performance are needed to drive

change by many other stakeholders. Pay for performance is increasingly being used to align provider performance and reimbursement. Pay-for-performance efforts have been initiated by many health plans across the nation, by the Centers for Medicare and Medicaid Services, and by private purchaser coalitions. The Integrated Healthcare Association leads one of the most comprehensive pay-for-performance initiatives in the nation, encompassing health plans, 7 million commercial health maintenance organization enrollees, 215 physician groups, and 45,000 physicians in California.

Pay for performance is an important mechanism that can be used to drive provider change by, for example, reimbursing providers for providing pill boxes and for using other practices listed in table 1 and by monitoring and rewarding provider performance on adherence-related measures such as refill rates. Linking provider practices and quality improvement interventions designed to improve patient adherence and self-management to financial incentives and rewards is a powerful way to encourage providers to improve care, particularly if the reimbursement structures are designed to lend additional weight to practices and performance measures that address the needs of patients with limited health literacy.

Policymakers. Workshop participants commented that an evaluation is needed of existing state and federal regulations that may affect the ability of other stakeholders in the healthcare system to improve adherence. Such an undertaking could identify opportunities for tort reform

and broader legislative changes that would improve the ability of the healthcare system to provide quality care in this area. Workshop participants commented, for example, that state laws vary on whether pharmacists must document whether patients received or refused counseling. In those states where documentation already is required, there is an opportunity to revise existing laws to expand the degree and nature of effort that pharmacies must make to offer counseling to patients, such as by describing how pharmacies can ensure that the needs of patients with limited health literacy are addressed.

On the federal level, the Voluntary Prescription Drug Benefit Program (Part D) of the Medicare Modernization Act of 2003, which introduces the first prescription drug benefit into the Medicare program, is scheduled to take effect in January 2006.³⁴ Initiatives are ongoing to educate Medicare beneficiaries about their options for receiving prescription drug benefits, and these broad public awareness and enrollment efforts are a prime opportunity to reach a high-priority group of healthcare consumers with respect to appropriate medication usage, given the high use of prescription drugs by this population.

Workshop participants noted that the Food and Drug Administration (FDA) also must play a central role in a national action plan to improve medication adherence by evaluating and proposing revisions to its regulations and associated guidance that could improve medication adherence. Much FDA work already has been done to improve written drug information, but medication non-adherence and patient

safety mishaps caused by the complexity of written information clearly still occur. Additional work is needed to identify how FDA regulations can address these issues more effectively.

Pharmaceutical Manufacturers. Packaging inserts and other forms of written information developed by drug manufacturers are a prime area for improving communication to populations with limited health literacy. Currently, information provided by pharmaceutical manufacturers is written at reading levels that are far too high even for individuals with adequate levels of health literacy, and the information generally is not widely available in non-English languages. Internet-based information often is available to supplement inserts, but it may not be accessible to many of the most vulnerable populations for unintentional non-adherence—i.e., those with limited health literacy are likely to have lower levels of computer literacy as well.

Workshop participants called on pharmaceutical manufacturers to revise packaging inserts and other written information to be more usable for all health consumers, especially those with limited and inadequate health literacy. Revisions should focus not only on the content and reading level of the information, which should be at or below the fifth-grade reading level, but also the presentation style and format (providing critical consumer information up front was recommended); the languages in which information is available also should be expanded. Given the rapidly increasing racial, ethnic, and language diversity of the U.S. population, pharmaceutical manufacturers would be well served by providing information that appeals to these audiences and that encourages individuals to refill medications as prescribed.

IT Vendors. Information technology was commonly cited by workshop participants as a critical tool for effectively implementing the recommended measures and practices, given its vital role in facilitating data exchange between pharmacies, physicians, and other data collection entities. As noted, a great deal of electronic data exist that could greatly inform healthcare providers about their patients' needs with respect to medication use; the missing link is the sharing of that information between PBM organizations, pharmacies, and other entities that track prescription fill/refill data with

healthcare providers, who could use the information to follow up with patients and better manage their medication use. Nonetheless, even if the data ownership and privacy issues for PBM organizations and other relevant entities are resolved, IT systems must be interoperable in order to allow such data to be seamlessly shared. Standardization in the IT industry is an issue that extends well beyond medication adherence issues to healthcare quality and patient safety in general. Such standardization is much needed in order to fully realize the potential of IT to dramatically improve U.S. healthcare quality.

Recommendation: Engage a broad array of stakeholders, including consumers, pharmacies, provider organizations, purchasers, policymakers, pharmaceutical manufacturers, and IT vendors, in developing and implementing strategies to improve adherence. Establish a case for each respective stakeholder that emphasizes how improving medication adherence meets its established needs and interests. Implement system-level changes through a combination of policy and purchasing strategies that will support and facilitate action by all involved stakeholders to improve medication adherence.

NQF's Role in the National Action Plan

As a public-private partnership of more than 270 Member organizations representing consumers, purchasers, research and quality improvement organizations, and health professionals, providers, and plans, NQF is uniquely positioned to implement and call on others to implement the

recommended action plan. Workshop participants recommended that the following actions be undertaken by NQF:

- identify and obtain consensus on a standard set of performance measures to improve medication adherence that includes a consideration of data collection and implementation issues;
- identify and obtain consensus on a standard set of practices for healthcare providers to improve medication adherence that also establishes a case that can be made to healthcare providers regarding why they should engage in the practices;
- collaborate with other organizations that have engaged in medication adherence initiatives to build on their existing work;
- increase awareness and interest in medication adherence among NQF Members and others in order to garner broad support and commitment on the part of these organizations to implement the national action plan in their respective capacities; and
- call on federal and state policymakers to explore regulatory and other options that will encourage and facilitate systemwide improvements in medication adherence.

NQF has endorsed a focus on vulnerable populations in order to reduce disparities in health and healthcare as its highest priority across all national priorities for healthcare quality measurement and reporting²⁴ and is committed to improving quality for all patients. Endorsing performance measures and practices to improve safe medication use is an NQF-endorsed priority.

Conclusion

Despite its fundamental role in shaping patients' health outcomes, safe medication use, especially for patients with LEP and limited health literacy, is a much-neglected area in major quality improvement and health policy initiatives. Patients will continue to be limited in their ability to benefit fully from the wealth of medical research and pharmaceutical developments that are emerging today until their ability to safely use medications is greatly improved; those with communication and other challenges are particularly disadvantaged. The solution to this ongoing problem should begin with the standardization of data collection and reporting for a set of performance measures that addresses adherence; the standardization of a set of practices that can be used by healthcare providers to improve consumer use of prescription medications; and multistakeholder engagement and action at all levels.

Healthcare stakeholders face increasing pressure to improve efficiency and maximize the use of limited resources to improve health, and they must address multiple quality problems in order to meet this challenge. Improvements in medication use could generate substantial progress towards addressing the widespread quality problems in healthcare, and the coordinated efforts of a broad group of stakeholders is needed to enact these reforms. Additional work will be needed to implement the national action plan, but the recommendations from this workshop constitute an important first step by identifying a set of priority actions that could markedly improve patient safety, equity, efficiency, and other domains of quality for consumer use of prescription medications.

Acknowledgments

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References

1. U.S. Pharmacopeia, Center for the Advancement of Patient Safety (CAPS). *Examining Medication Errors That Occur in the Patient's Home*. USP Patient Safety CAPSLink; March 2004.
2. Einarson TR. Drug-related hospital admissions (review). *Ann Pharmacother*. 1993;27(7-8):832-840.
3. Weiden PJ, Kozma C, Grogg A, et al. Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. *Psychiatr Serv*. 2004;55(8):886-891.
4. Stagnitti MN. Trends in outpatient prescription drug utilization and expenditures – 1997-2000: statistical brief #1. Rockville, MD: Agency for Healthcare Research and Quality (AHRQ); July 2003.
5. National Center for Health Statistics. *Health, United States, 2004*. HHS Publication No. 2004-1232. Hyattsville, MD: Department of Health and Human Services (DHHS); 2004.
6. Safran DG, Neuman P, Schoen C, et al. Prescription drug coverage and seniors: findings from a 2003 national survey. *Health Affairs Web Exclusive*; April 19, 2005. Available at www.healthaffairs.org. Last accessed July 7, 2005.
7. Haynes RB, Montague P, Oliver T, et al. *Interventions for Helping Patients Follow Prescriptions for Medications*. The Cochrane Library (Oxford); 2001.
8. Bedell SE, Jabbour S, Goldberg R, et al. Discrepancies in the use of medications. *Arch Int Med*. 2000;160(14):2129-2134.
9. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004;42(3):200-209.
10. Wilson FL, Racine E, Tekieli V, et al. Literacy, readability, and cultural barriers: critical factors to consider when educating older African Americans about anticoagulation therapy. *J Clin Nurs*. 2003;12(2):275-282.
11. Estrada CA, Hryniewica MM, Higgs VB, et al. Anticoagulant patient information material is written at high readability levels. *Stroke*. 2000;31(12):2966-2970.
12. U.S. Census Bureau. Census 2000, Summary File 3, Tables P19, PCT13, and PCT14. Available at www.census.gov/population/www/cen2000/phc-t20.html. Last accessed June 28, 2005.
13. DHHS. *Healthy People 2010: Understanding and Improving Health*, 2nd ed. Ch.17: Medical Product Safety. Washington, DC: U.S. Government Printing Office; November 2000. Available at www.healthypeople.gov/Document/HTML/Volume2/17Medical.htm. Last accessed July 7, 2005.
14. National Quality Forum (NQF). *National Priorities for Healthcare Quality Measurement and Reporting: A Consensus Report*. Washington, DC: NQF; 2005.
15. Institute of Medicine. *Health Literacy: A Prescription to End Confusion*. Washington, DC: National Academies Press; 2004.

16. Williams MV, Baker DW, Honig EG, et al. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest*. 1998;114(4):1008-1015.
17. Baker DW, Parker RM, Williams MV, et al. The healthcare experience of patients with low literacy. *Arch Fam Med*. 1996;5(6):329-334.
18. Doak CC, Doak LG, Root JH. The literacy problem. In: *Teaching Patients With Low Literacy Skills*, 2nd ed. Philadelphia: J.B. Lippincott Co; 1996, 1-9.
19. Weiss BD, ed. *20 Common Problems in Primary Care*. New York: McGraw Hill; 1999, 468-481.
20. Baker DW, Gazmararian JA, Williams MV, et al. Functional health literacy and the risk of hospital admission among Medicare managed care enrollees. *Am J Public Health*. 2002;92(8):1278-1283.
21. Baker DW, Parker RM, Williams MV, et al. Health literacy and the risk of hospital admission. *J Gen Intern Med*. 1998;13(12):791-798.
22. International Conference on Improving Use of Medicines. *Policies and Programmes to Improve Use of Medicines: Recommendations from ICIUM 2004*. Available at www.icium.org. Last accessed July 7, 2005.
23. NQF. Consensus Development Process version 1.7. August 19, 2004.
24. NQF. *National Priorities for Healthcare Quality Measurement and Reporting: A Consensus Report*. Washington, DC: NQF; 2004.
25. NQF. *A National Framework for Healthcare Quality Measurement and Reporting: A Consensus Report*. Washington, DC: NQF; 2002.
26. Cook CL, Wade WE, Martin BC, et al. Concordance among three self-reported measures of medication adherence and pharmacy refill records. *J Am Pharm Assoc*. 2005;45(2):151-159.
27. Bunting B. Asheville Project update: results continue to exceed ADA goals. *North Carolina Pharmacist*; Jan/Feb 2000. Available at www.ncpharmacists.org. Last accessed May 27, 2005.
28. NQF. *Safe Practices for Better Healthcare: A Consensus Report*. Washington, DC: NQF; 2003.
29. AHRQ. *Evidence Report/Technology Assessment No. 43, Making Health Care Safer: A Critical Analysis of Patient Safety Practices*. Ch. 48. AHRQ Publication No. 01-E058; 2001.
30. NQF. *Improving Patient Safety through Informed Consent in Populations with Limited Health Literacy: An Implementation Report*. Washington, DC: NQF; 2005.
31. Li J, McCombs JS, Stimmel GL. Cost of treating bipolar disorder in the California Medicaid (Medi-Cal) program. *J Affect Disord*. 2002;71(1-3):131-139.
32. Gilmer TP, Dolder CR, Lacro JP, et al. Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry*. 2004;161(4):692-299.
33. Sokol MC, McGuigan KA, Verbrugge RR, et al. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care*. 2005;43(6):521-530.
34. Centers for Medicaid and Medicare Services. *Medicare Modernization Act 2003, Part D*. Available at www.cms.hhs.gov/mmu/HR1/PL108-173summary.asp#tlpartD. Last accessed July 7, 2005.

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Appendix A

Focus Group, Workshop Participants, and Project Staff

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Appendix B

Agenda—Workshop on Improving Use of Prescription Medications

WASHINGTON, DC

MONDAY, OCTOBER 25, 2004

- 9:00 AM Welcome and Introductions**
Ira S. Ockene, MD (Co-Chair), Director, Preventive Cardiology and Associate Director, Cardiovascular Medicine, University of Massachusetts Medical School
Eleanor M. Vogt, RPh, PhD (Co-Chair), Presidential Scholar/Visiting Professor, School of Pharmacy, University of California-San Francisco
Robyn Y. Nishimi, PhD, NQF Chief Operating Officer
- 9:15 AM Project Background and Overview**
Helen W. Wu, MSc, NQF Program Director
- 9:30 AM Overview of Background Paper, *Medication Adherence and Persistence***
Kem P. Krueger, PharmD, PhD, Associate Professor of Pharmacy Care Systems, Auburn University
- 9:50 AM Discussion**
- 10:30 AM Break**
- 10:45 AM Overview, *A Preliminary Framework for Improving Use of Prescription Medications***
Helen W. Wu, MSc
- 11:00 AM Discussion: General Issues in Identifying a Framework for Improving Use of Prescription Medications**
- 11:50 AM NQF Member and Public Comment**
- NOON Lunch**

- 1:00 PM** **Small Group Break-Out Discussions: Specific Issues in Identifying a Framework for Improving Use of Prescription Medications**
- 1:45 PM** **Small Group Reports**
- 2:00 PM** **Break**
- 2:15 PM** **Discussion: Recommendations for an Action Plan to Improve Use of Prescription Medications—Key Leverage Points and Stakeholders Within the Framework**
- 3:30 PM** **NQF Member and Public Comment**
- 3:45 PM** **Next Steps**
- 4:00 PM** **Adjourn Day 1**

TUESDAY, OCTOBER 26, 2004

- 8:30 AM** **Welcome and Summary of Day 1**
Eleanor M. Vogt, RPh, PhD (Co-Chair)
Ira S. Ockene, MD (Co-Chair)
- 8:45 AM** **Overview of the Proposed Action Plan**
Helen W. Wu, MSc
- 9:00 AM** **Member Council Perspectives on Members' and Councils' Roles in the Action Plan**
Rita M. Gallagher, PhD, RN, Health Professional, Provider and Health Plan Council
Christopher Queram, Purchaser Council
Mary Jo Payne, Consumer Council
Clare Bradley, MD, MPH, Research and Quality Improvement Council
- 9:20 AM** **Discussion: NQF and Other Stakeholders' Roles in the Action Plan**
- 10:15 AM** **Break**
- 10:30 AM** **Discussion: Identifying National Voluntary Consensus Standards for Improving Use of Prescription Medications**
- 11:45 AM** **NQF Member Comment**
- NOON** **Lunch**
- 1:00 PM** **Identifying National Voluntary Consensus Standards for Improving Use of Prescription Medications (continued)**
- 2:30 PM** **NQF Member Comment**
- 2:45 PM** **Summary of Recommendations and Next Steps**
- 3:00 PM** **Adjourn**

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Appendix C

NQF Background Paper: A Preliminary Framework for Improving Use of Prescription Medications

Prescription medicines are an indispensable component of medical care. In 2001, approximately 1.3 billion prescription drugs were provided or prescribed during nearly two-thirds of physician office visits,¹ and outpatient prescription medicine expenditures in the United States totaled \$102 billion in 2000.² Overall, nearly 2.5 billion prescriptions were filled at pharmacies in the United States in 1998, at a cost of approximately \$92 billion.³ An issue of both national and global importance,⁴ increasing the effectiveness of interventions to improve medication adherence could have a far greater impact on population health than any other advancement in medical treatment.⁵

However, poor consumer adherence to provider recommendations for prescription medication use is both common and costly. Appropriate use of medications is critical to improving health outcomes, and inappropriate use—which is common—can lead to disabling and/or fatal consequences. One study found a 76 percent discrepancy rate between what medicines patients were prescribed and what medicines (prescription and non-prescription) they actually took.⁶ In another study, patient non-adherence and unintentional inappropriate use of medications were the reasons for up to 22 percent of hospitalizations.⁷ Errors in medication use in patients' homes have resulted in permanent harm, life-threatening situations, and death.⁸

A variety of factors contribute to patient non-adherence, which generally occurs when patients misunderstand, forget, or choose not to follow medication usage instructions for a number of possible reasons. Poor adherence that is caused by inadequate communication with patients on the part of healthcare providers, however, provides a prime opportunity for system improvement.

Communication and knowledge deficits have been cited as the most common reasons for errors in patient medication use at home.⁸ In 2000, one national telephone survey found that 76 percent of consumers were not given basic information about risks and instructions for prescription medication use at the doctor's office, and 88 percent of consumers failed to receive that information at pharmacies.⁹ Clearly, a large opportunity exists for healthcare providers to improve their communication with patients in order to increase adherence.

Adherence in certain populations, such as patients with limited health literacy and/or limited English proficiency (LEP), is especially problematic because of the quality and nature of the written information that is available, as well as basic verbal communication challenges. Flores et al. documented that during communication with pediatric patients, interpreters made numerous errors, and 77 percent of those errors had potential clinical consequences (e.g., omitting information about the dose, frequency, and duration of antibiotics).¹⁰ Andrulis et al. found that 27 percent of patients who needed but did not get an interpreter failed to understand instructions

for taking their medications, compared with 2 percent of those who got an interpreter or who did not need one.¹¹ With Hispanic/Latino populations, which have many members who may not speak English fluently, now comprising the largest U.S. racial/ethnic minority group, addressing the needs of populations with LEP has become increasingly important.

Patients with limited health literacy are less likely to appropriately use their medications, chiefly because of difficulty in understanding verbal or written instructions and patient educational materials, which often are written at reading levels that are too high for the majority of the population.^{12,13} Research has shown that patients with low literacy make more medication or treatment errors,^{14,15} are less able to follow treatments,¹⁶ lack the skills needed to negotiate the healthcare system,^{17,18} and are at higher risk for hospitalization than those who have adequate literacy skills.¹⁹

Individuals with limited health literacy are not only at greater risk for adverse health consequences, but they comprise a large segment of the population. About 90 million (47 percent) of all Americans have difficulty understanding health information and are at a severe disadvantage in interacting with the healthcare system: approximately 40 to 44 million people function at the lowest level of literacy, while approximately 50 million people are at the second-lowest literacy level and are likely to have difficulty with tasks such as understanding children's medication dosage charts.²⁰ Moreover, it has been well

documented that regardless of literacy level, any person may have difficulty with healthcare terms and phrases, because individuals' functional health literacy may be much worse than their general literacy (a result of the complex design and terminology of the healthcare system).^{20,21}

Medication Safety Quality Improvement Initiatives and Research

Over the past two decades, a number of promising initiatives, practices, and other strategies for improving patient medication adherence have been developed—including community hospital- and pharmacy-based education initiatives; industry, government, and healthcare provider association action plans, guides, and recommendations; and clinical studies of specific interventions in limited settings. Despite attempts by many groups to address safe prescription medication use, the lack of standardization and consistency in approaches has hampered any large-scale progress. Systematic implementation of a comprehensive set of national policies could dramatically improve medication use.²²

However, no clear, single approach for improving appropriate medication use exists. Nonetheless, a substantial effort has been made to develop and test strategies to improve appropriate patient medication use in various settings, and this scattered, but rich, body of work holds great potential for improving patient outcomes. What is needed to capitalize on the promising work done to date is a clear roadmap for action based on the state of the evidence in

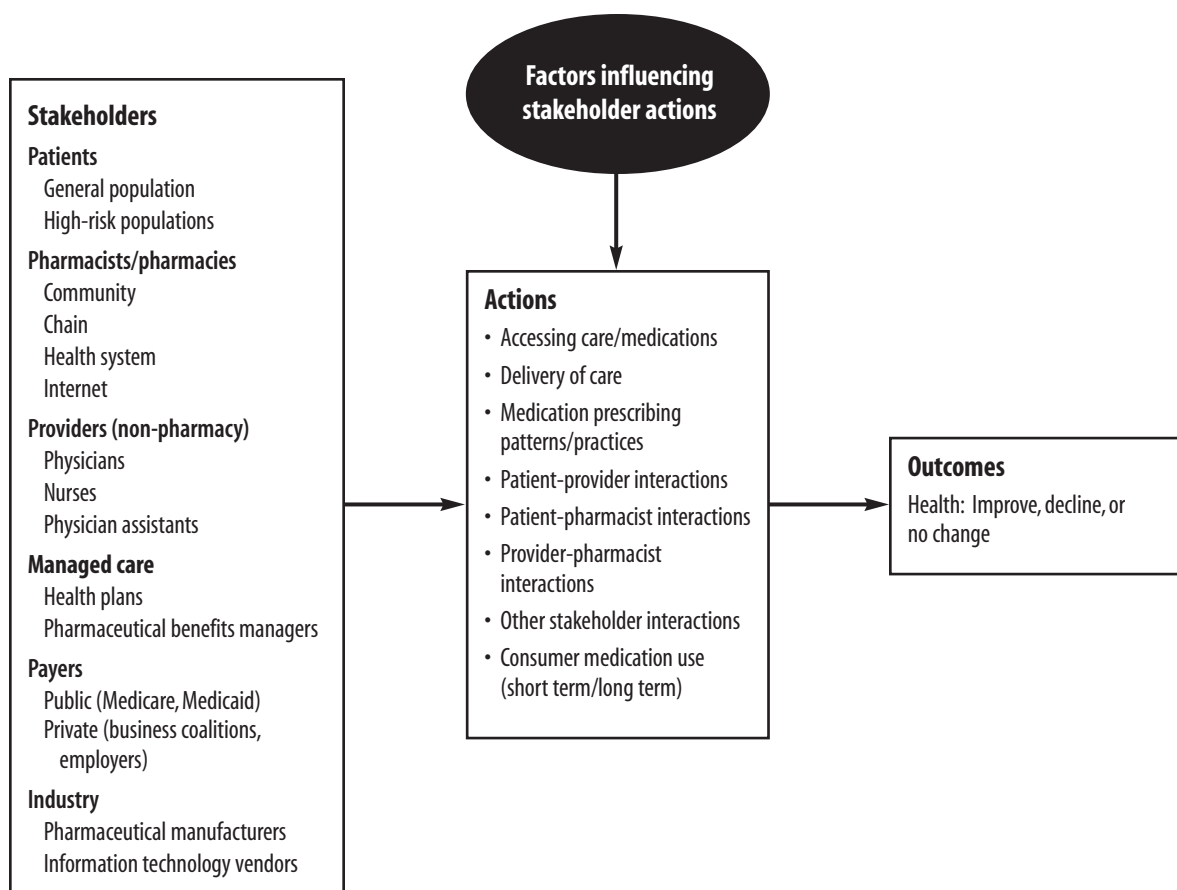
medication adherence, multistakeholder consensus around a comprehensive framework for change, and performance measurement and reporting to drive quality improvement.

Scope of Issues to Be Addressed

A number of sophisticated models have been used to map out the complex system of care and factors affecting patient medication adherence (e.g., figure 1 in appendix D). Figure 1 outlines some of the major stakeholders, actions, process steps related to prescription medication use, and outcomes that should be considered when defining the scope of issues for an action plan. It is not a comprehensive model of all the relevant factors, but is intended to provide a general sense of the breadth of the scope of issues to be considered.

Factors Influencing Stakeholder Actions

A national action plan for improving the use of medications must consider the key leverage points for change at the system, individual provider, and patient levels. Opportunities for improvement could be identified, in large part, by determining what drives stakeholders' actions and interests. Additionally, the various environmental factors (e.g., tools, time, regulations), inter-relational factors (e.g., physician-patient interactions), and individual factors (e.g., patient motivation) should be considered with respect to how they influence stakeholder actions.

Figure 1. Scope of Issues to Consider

Systems. Change at the level of healthcare systems (e.g., hospitals, physician practices, pharmacies) has the potential for wide-spread impact on a large number of consumers. An action plan for improvement recommended through an NQF-convened workshop would be well positioned to address changes at the systems level and should give due consideration to the micro-level variables that affect how those systems operate.

Individual providers. As the intermediaries between systems-level changes and patient-specific factors, the involvement and buy-in of individual pharmacists, physicians, nurses, and other providers is critical to the success of an action plan to improve medication use. Individual providers at the frontline of care bear the responsibility for translating recommendations into practice, and provider buy-in is highly dependent on developing recommendations that are sensitive to the other issues and burdens facing providers.

Patients. A large body of literature documents reasons for patient non-adherence to provider recommendations for treatment—both in medication and other areas (e.g., lifestyle changes, receipt of follow-up care).²³ Overall, non-adherence is generally attributed to either patient understanding and recall of recommended treatment regimens (which may be influenced by language/literacy barriers and provider communication skills) or patient motivation and desire to follow those regimens (which may be due to cultural issues, psychosocial/socioeconomic factors, symptoms of disease). At the same time, most of the literature focuses on patient-related factors instead of examining provider- and system-level communication problems and needed improvements. Patients should be supported, not blamed, when non-adherence occurs, and greater attention to provider and health system-related determinants of poor adherence is needed.²⁴ Broad strategies implemented at the system- or provider-levels must be able to take into account the influence of specific patient-level factors in order to determine the most effective interventions for individual patients.

Identifying Priority Areas

The NQF-endorsed™ framework for hospital performance measurement outlined a number of recommendations to guide the content of a comprehensive hospital performance measurement set.²⁵ The framework serves as a useful model to describe what major priority areas should be addressed in a national action plan and/or a future set of NQF-endorsed

standards in other areas, and it could be adapted for use in framing medication adherence issues. The hospital framework recommended that an overall measure set should:²⁵

- encompass all six healthcare aims as adopted by NQF (i.e., safe, beneficial, timely, patient centered, equitable, and efficient);
- have at least some cross-cutting measures that address the needs of all patients;
- address hospital population condition-specific priorities:
 - all NQF-endorsed national goal areas for quality measurement and reporting (and the domains for measurement in the Agency for Healthcare Research and Quality's *National Healthcare Quality Report*), to the extent that care provided to patients by a hospital is a key leverage point for improving care in that area;
 - conditions or treatments that are in high-risk, high-volume, and/or high-cost or problem-prone areas of care and service for hospital patients and for which key leverage points exist for improving hospital care;
- demographic populations of particular interest (e.g., racial/ethnic populations, children, the elderly, people with disabilities or multiple chronic conditions, rural populations);
- patients with needs across the continuum of care (e.g., prevention, diagnosis, acute treatment, rehabilitation, care for chronic conditions, end-of-life care); and

- major hospital service settings (e.g., emergency, surgery, critical care, obstetric, pediatric, mental health).

Criteria for Evaluating Potential Consensus Standards

Other NQF-endorsed consensus standards, such as the hospital, nursing home, home health, and nursing-sensitive care performance measures, also were selected based on the degree to which they met specific, agreed-upon criteria. Because these criteria also essentially served as a screen that determined what measures or practices met a minimum threshold for consideration as NQF-endorsed standards, the scope of specific standards for improving medication use should be sensitive to the extent to which existing practices or measures meet these criteria, which include:

- **Important.** Consensus standards are most needed in areas reflecting key leverage points for improving quality, with large variation in quality, low levels of overall performance, and population-based disparities.
- **Scientifically acceptable.** Consensus standards should be evidence based and produce consistent and credible results when implemented. They should be well defined and precisely specified, reliable, valid, account for patient preferences and a variety of contexts of settings, risk-adjustable (if applicable), and based on evidence linking them to patient outcomes.
- **Useable.** Consensus standards should consider the extent to which a variety of stakeholders (e.g., providers, consumers, purchasers) can understand the results of the information to be measured or evaluated and the extent to which those stakeholders can use the information to support meaningful decisionmaking.
- **Feasible.** Consensus standards must be feasible to implement, based on the way in which data are obtained within the normal flow of clinical care and the extent to which an action plan can be implemented (e.g., data availability, patient confidentiality, reporting and auditing mechanisms for measures).

Potential Organizing Frameworks

An organizing framework for medication adherence is needed to ensure that recommendations for action are comprehensive, promote improvement across the continuum of care, and reflect the highest priorities for improvement for a variety of stakeholders. This framework could serve as the basis for identifying priority areas for future NQF consensus standards endorsement. Potential frameworks are described below:

- **Barriers.** Framing a set of solutions based on identified barriers to patient adherence could help identify key leverage points for action. Barrier-based models could categorize solutions based on issues at the system, individual provider, or patient level, including physician prescribing; pharmaceutical packaging; pharmacist dispensing; patient use; refills and persistence; patients' beliefs, understanding, and motivations about the drug/disease; insurance/co-pays; and medication side effects.

- **Major risk factors.** A framework could be organized around major risk factors for poor adherence that have been demonstrated in the literature, but such a model must be actionable and clearly linked to specific solutions for change. Agreement around the key risk factors to include would also be needed. One potential model is the World Health Organization's framework, which describes non-adherence as being caused by four interacting elements:⁴
 - healthcare team- and system-related factors – the knowledge, attitudes, and skills of providers within the healthcare system and characteristics of the system itself;
 - condition-related factors – particular demands of illness faced by patients and the cultural meaning of the illness;
 - characteristics of therapies – such as cost/access, regimen complexity, immediacy of beneficial effects, and side effects; and
 - patient-related factors – the resources, knowledge, attitudes, beliefs, perceptions, and expectations of patients.
- **High-risk populations.** By identifying specific populations at risk for poor adherence, healthcare providers could effectively target and tailor interventions based on those populations' needs. Such a framework could define these populations by race, ethnicity, primary language, literacy level, insurance status, educational level, age, gender, or a number of other sociodemographic factors. The feasibility of developing a framework around this model relies on the extent to which a comprehensive and meaningful set of "high-risk" populations could be identified and defined, however, and how well the evidence supports action steps targeted to each of those populations. A single approach that is applicable across all populations, but that is sensitive to the additional needs of high-risk groups, may promote more continuous improvement at the system level.
- **High-priority conditions/diseases.** A broad literature describes how medication adherence varies for certain conditions or diseases – for example, HIV/AIDS, hypertension, and diabetes – where proper medication use is particularly important because of issues such as the cost of treatment and the consequences of poor adherence. Focusing on a few "low-hanging fruit" such as these conditions could efficiently address adherence for the majority of the population that is in the greatest need of intervention. Defining a framework around specific conditions or diseases, however, could result in many important areas being neglected and fail to recognize the many adherence-related issues that are shared across conditions/diseases. Other NQF-endorsed consensus standards have framed measure sets around condition areas (e.g., pneumonia, stroke, and heart failure in hospital care), however, since existing measures were largely developed to address specific high-priority conditions and diseases rather than to address the continuum of care.
- **Specific medications.** A framework could be organized around specific medications or classes of medications. For example, the types of medications could be selected based on their impact on cost, frequency of use/misuse (e.g., antibiotics), seriousness of risks/side effects if taken improperly (e.g., abuse of pain medications), and similarities in usage/dosing regimen-related

issues (e.g., those with complicated regimens) that often result in improper use. However, issues arise in framing a national action plan around specific medications that are similar to those described for a framework based on specific conditions/diseases.

- **Care path.** Following a patient through the various steps and contact points within the healthcare system, from medication prescribing to pharmacy orders to consumer use and persistence, could identify the key leverage points for improving adherence. By identifying the relevant stakeholders and actions within the care path, interventions could focus on points in the process with the greatest potential for change.

Mechanisms for Change

Multiple pathways are available to achieve desired goals with an action plan for medication use improvement. The most effective mechanisms for change should be identified based on consideration of the best pathways for improving quality, such as through change/quality improvement or selection/accountability, as well as what types of policy levers, performance measures, and other strategies can be used to achieve change.

Pathways to Better Quality

NQF's Strategic Framework Board described two major pathways for improving healthcare quality: improvement through selection (e.g., consumers choosing higher-quality providers) and improvement through changes in care (e.g., system reform, provider behavior change).²⁶

Change/Quality Improvement.

Standardized quality measures, practices, and/or related strategies can provide valuable information about how to improve existing processes of care. Change could occur at the system level, individual provider level, or patient level, but a number of different stakeholders could be targeted at each level, including:

- **Pharmacies**—a national initiative to improve adherence that focuses on the pharmacy setting is greatly needed,²⁷ and pharmacies as a stakeholder group are well positioned to implement specific actions that could be extremely effective in reaching consumers.
- **Provider organizations**—the nature of providers' interactions with patients when discussing diagnoses and recommending treatment and medication regimens is an important factor in consumer adherence, and the role of physicians, nurses, physician assistants, and other providers in changing their communication practices and patient interactions is central to improvement.
- **Patients**—given the myriad patient-level factors influencing adherence, finding ways to change consumer behavior regarding their medication-taking practices is a major challenge—and a number of other healthcare stakeholders (in addition to providers) could utilize strategies that would impact adherence on this level.

Selection/Public Reporting and

Accountability. Increasing attention has been given to actively involving stakeholders outside of the traditional healthcare system to leverage change. This would include, for example, consumers

and purchasers of healthcare, who have the ability to drive change by using performance information to select higher-quality health plans and providers, which in turn drives the system to improve. However, consumers and purchasers need publicly reported information that is well designed and meaningful in supporting these quality- and value-based decisions. Mechanisms to improve quality that promote selection and public accountability must take into account the following key issues:

- **Locus of reporting**—the pharmacy (community, chain, health system, and Internet/mail order); physician offices/healthcare facilities; health plans/pharmaceutical benefits management groups; and other relevant stakeholders.
- **Level of accountability**—individual provider, health plans/healthcare organizations, and systems. The level of accountability must be sensitive to issues such as data collection/sample size, risk adjustment, and others that could affect how fairly providers are represented.
- **Target/goals of reporting**—to consumers or purchasers to drive value-based decisionmaking, to physicians, pharmacists, and other providers to support quality improvement efforts, or to other entities such as regulatory and accreditation bodies.

Strategies for Improving Adherence

Existing strategies and interventions to improve adherence on the individual patient level are highly variable and include adherence aids, refill or follow-up reminders, regimen simplification, written

and oral education, and comprehensive medication and disease management.^{27,28,29}

There is no single strategy that emerges as the most effective^{30,31} or even a best approach to measuring adherence, given the limitations in various measurement methods (e.g., pill counts, patient self-reports),^{32,33} and the need to tailor appropriate interventions to patient needs is clear.^{24,27} On a broader systems or provider level, however, other strategies could be used to drive actions that will address adherence issues nationally:

- **Policies, guidelines, and recommendations**—that could be implemented by policymakers and systems-level administrators (e.g., specific requirements around oral or written counseling);
- **Specific practices**—that could be used by individual providers in the care delivery process (e.g., motivational interviewing, follow-up reminders); and
- **Measures**—to evaluate the performance of providers that could be used for quality improvement through change and/or selection (e.g., prescription refill rates at specific pharmacies).

Summary

A national action plan must be based upon consideration of a comprehensive set of factors and be meaningful and actionable by a variety of stakeholders. The major concepts described in this background paper in proposing a preliminary framework have been as follows:

Scope of issues to be addressed—considering the stakeholders involved, the actions related to medication adherence, the

factors that influence various stakeholders' actions, and health outcomes. The scope specifically addressed:

- **Level of change**—system, individual provider, and patient.
- **Priority areas**—national goals for improvement, high-risk populations, high-risk/cost/prevalence conditions and diseases, cross-cutting areas and the continuum of care, key leverage points for improvement, and the breadth of applicable healthcare settings.
- **Criteria**—importance, scientific acceptability, usability, and feasibility for multiple stakeholders.

Organizing framework—categorized by barriers, risk factors, high-risk populations, priority conditions/diseases, specific medications, and the care path.

Mechanisms for change—describing the ideal pathways for quality improvement and what specific standards or other action steps could be pursued to achieve wide-spread change:

- **Pathways to better quality**—change/quality improvement and selection/accountability/public reporting.
- **Strategies for improving adherence**—guidelines, practices, and measures.

References

1. Cherry DK, Burt CW, Woodwell DA. *National Ambulatory Medical Care Survey: 2001 Summary*. Hyattsville, MD: National Center for Health Statistics; 2001.
2. Stagnitti MN. *Trends in Outpatient Prescription Drug Utilization and Expenditures: 1997-2000 – Statistical Brief #1*. Rockville, MD: Agency for Healthcare Research and Quality; July 2003.
3. National Wholesale Druggists' Association. *Industry Profile and Healthcare Factbook*; 1998.
4. World Health Organization (WHO). *Adherence to Long-Term Therapies: Policy for Action (Meeting Report)*. Geneva: WHO; 2001.
5. Haynes RB, Montague P, Oliver T, et al. *Interventions for Helping Patients Follow Prescriptions for Medications*. The Cochrane Library (Oxford); 2001.
6. Bedell SE, Jabbour S, Goldberg R, et al. Discrepancies in the use of medications. *Arch Int Med*. 2000; 160(14):2129-2134.
7. Einarson TR. Drug-related hospital admissions (review). *Ann Pharmacother*. 1993;27(7-8):832-840.
8. U.S. Pharmacopeia, Center for the Advancement of Patient Safety (CAPS). *Examining Medication Errors That Occur in the Patient's Home*. USP Patient Safety CAPSLink; March 2004.
9. U.S. Federal Drug Administration, Center for Drug Evaluation and Research. *National Surveys of Prescription Medicine Information Received by Consumers*. Available at www.fda.gov/cder/Offices/ODS/y2ktitle.htm. Last accessed September 8, 2005.
10. Flores G, Laws MB, Mayo SJ, et al. Errors in medical interpretation and their potential clinical consequences in pediatric encounters. *Pediatrics*. 2003;111(1):6-14.
11. Andrulis D, Goodman N, Pryor C. *What a Difference an Interpreter Can Make: Health Care Experiences of Uninsured with Limited English Proficiency (for the Access Project)*; April 2002.
12. Wilson FL, Racine E, Tekieli V, et al. Literacy, readability, and cultural barriers: critical factors to consider when educating older African Americans about anticoagulation therapy. *J Clin Nurs*. 2003;12:275-282.

13. Estrada CA, Hryniewica MM, Higgs VB, et al. Anticoagulant patient information material is written at high readability levels. *Stroke*. 2000;31:2966-2970.
14. Williams MV, Baker DW, Honig EG, et al. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest*. 1998; 114:1008-1015.
15. Baker DW, Parker RM, Williams MV, et al. The healthcare experience of patients with low literacy. *Arch Fam Med*. 1996;5:329-334.
16. Doak CC, Doak LG, Root JH. The literacy problem. In: *Teaching Patients with Low Literacy Skills*, 2nd ed. Philadelphia: J.B. Lippincott Co.; 1996, 1-9.
17. Weiss BD, ed. *20 Common Problems in Primary Care*. New York: McGraw Hill; 1999, 468-481.
18. Baker DW, Parker RM, Williams MV, et al. Health literacy and the risk of hospital admission. *J Gen Intern Med*. 1998;13:791-798.
19. Smith D. Compliance packaging: a patient education tool. *Am Pharm*. 1989;NS29(2):42-45, 49-53.
20. Institute of Medicine. *Health Literacy: A Prescription to End Confusion*. Washington, DC: National Academies Press; 2004.
21. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs, American Medical Association. Health literacy: report of the Council on Scientific Affairs. *JAMA*. 1999;282(6):525-527.
22. International Conference on Improving Use of Medicines (ICIUM). *Policies and Programmes to Improve Use of Medicines: Recommendations from ICIUM 2004*. Available at www.icium.org. Last accessed September 8, 2005.
23. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004;42(3):200-209.
24. WHO. *Adherence to Long-Term Therapies: Evidence for Action*. Geneva: WHO; 2003.
25. NQF. *A Comprehensive Framework for Hospital Care Performance Evaluation: A Consensus Report*. Washington, DC: NQF; 2003.
26. Berwick DM, James B, Coye MJ. Connections between quality measurement and improvement. *Med Care*. 2003;41(1)(suppl.):I-30-I-38.
27. Krueger KP, Felkey BG, Berger BA. Improving adherence and persistence: a review and assessment of interventions and description of steps toward a national adherence initiative. *J Am Pharm Assoc*. 2003;43:668-679.
28. Fogarty L, Roter D, Larson S, et al. Patient adherence to HIV medication regimens: a review of published and abstract reports. *Patient Educ Couns*. 2002;46:93-108.
29. Pearson S, Ross-Degnan D, Payson A, et al. Changing medication use in managed care: a critical review of the available evidence. *Am J Manag Care*. 2003;9:715-731.
30. Roter DL, Hall JA, Merisca R, et al. Effectiveness of interventions to improve patient compliance: a meta-analysis. *Med Care*. 1998;36(8):1138-1161.
31. Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *Am J Health-Syst Pharm*. 2003; 60:657-675.
32. Burke LE, Ockene IS, eds. *Compliance in Healthcare and Research*. Armonk, NY: Futura Publishing Company; 2001.
33. Wood W, Gray J. An integrative review of patient medication compliance from 1990-1998. *Online J Knowl Synth Nurs*. 2000 Jan 14;7:1.

APPENDIX D

MEDICATION ADHERENCE AND PERSISTENCE

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SUMMARY OF KEY FINDINGS

Adherence and non-adherence are behaviors, so the interventions that work best are those that include patient follow-up. Multifaceted interventions that target specific barriers to adherence are most effective because they address the problems and reinforce positive behaviors. Theory-based or disease-based interventions with follow-up seem to perform the best. Additional information is presented in table 1.

Data on barriers to adherence are conflicting. It is clear that providers need to a) assess patients' understanding of the illness and treatment; b) communicate benefits of the treatment; c) assess patients' readiness to carry out the plan; and d) discuss any barriers or obstacles to adherence that patients may have. Studies have shown that a positive, supporting, and trusting relationship between the patient and provider improves adherence. Individual patient factors also impact adherence. For instance, conditions that slow or inhibit cognition have a negative impact on adherence. Other factors, such as the lack of a support network, limited English proficiency, the inability to obtain and pay for medications, and having severe side effects or the fear of side effects, are all barriers to adherence. Additional information is presented in table 2. Specific products, services, and interventions used to improve adherence are presented in tables 1, 4, 5, and 6.

BACKGROUND AND OBJECTIVES

Overall estimates of adherence to chronic medication regimens range from 17 percent to 80 percent.¹ Studies have shown that non-adherence to medication regimens (or non-persistence) can lead to increases in morbidity, mortality, and healthcare costs.² For example, non-adherence results in more relapses among patients with schizophrenia and significant decreases in ejection fraction in patients with heart failure.³ Patients who did not adhere to their heart failure medication are 1.95 times more likely to die from heart failure compared to adherent patients, and patients who stop taking their beta-blockers have an initial increase in risk of coronary heart disease 4.5 times greater than patients who persist with therapy.⁴ Conversely, improving adherence or persistence can improve clinical outcomes. Lasaffre and colleagues (2003)⁵ reported that the relative risk of a major cardiac event such as a heart attack or death dropped by 5 percent to 0.68 when they excluded patients who did not adhere to their cardiac medications.

Improving adherence can decrease medical resource consumption as demonstrated by Balkrishnan and Christensen,⁶ who found that better adherence to asthma medications in elderly patients decreased hospitalizations by 20 percent. Improving adherence in people with schizophrenia produced a 40 percent drop in hospital days, and the results of a study of psychiatric patients revealed that patients who adhered to

¹ Demyttenaere K, Noncompliance with antidepressants: who's to blame? *Int Clin Psychopharmacol*, 1998;13(Suppl 2):S19-S25; Partridge AH, Avorn J, Wang PS, et al., Adherence to therapy with oral antineoplastic agents [see comment], *Journal of the National Cancer Institute*, 2002;94(9):652-661.

² Schoen MD, DiDomenico RJ, Connor SE, et al., Impact of the cost of prescription drugs on clinical outcomes in indigent patients with heart disease, *Pharmacotherapy*, 2001;21(12):1455-1463; Solomon DK, Portner TS, Bass G, et al., Clinical and economic outcomes in the hypertension and COPD arms of a multicenter outcomes study, *J Am Pharm Assoc*, 1998;38(5):574-585.

³ Miura T, Kojima R, Mizutani M, et al., Effect of digoxin noncompliance on hospitalization and mortality in patients with heart failure in long-term therapy: a prospective cohort study, *Eur J Clin Pharmacol*, 2001;57(1):77-83; Sellwood W, Tarrier N, Demographic factors associated with extreme non-compliance in schizophrenia, *Soc Psychiatry Psychiatr Epidemiol*, 1994;29(4):172-177.

⁴ Miura T, Kojima R, Mizutani M, et al., Effect of digoxin noncompliance on hospitalization and mortality in patients with heart failure in long-term therapy: a prospective cohort study, *Eur J Clin Pharmacol*, 2001;57(1):77-83.

⁵ Lasaffre E, Kocmanova D, Lemos PA, et al., A retrospective analysis of the effect of noncompliance on time to first major adverse cardiac event in the Lescol Intervention Prevention Study, *Clin Ther*, 2003;25(9):2431-47.

⁶ Balkrishnan R, Christensen DB, Inhaled corticosteroid use and associated outcomes in elderly patients with moderate to severe chronic pulmonary disease, *Clin Ther*, 2000;22(4):452-69.

their antipsychotic therapy had more time in remission than non-adherent patients.⁷ Miura and colleagues⁸ also demonstrated that patients who did not adhere to their heart failure therapy had 2.5 times as many hospitalizations as adherent patients.

Based on these studies, the solution seems obvious: simply increase adherence to medication regimens to improve clinical and economic outcomes for patients on chronic therapy. Unfortunately the solution is complicated by the fact that there are multiple reasons for non-adherence/non-persistence, and the solution needs to be tailored to the individual patient's needs. In order to have an impact on adherence, healthcare providers need to understand the barriers to adherence and methods or tools that can be used to overcome these barriers.

Therefore the objectives of this paper are to:

1. describe the barriers to medication adherence and persistence;
2. describe the interventions that have been used to address medication adherence and/or persistence problems; and
3. identify other interventions and compliance aids that can be used by practitioners and organizations to address barriers to medication adherence and/or persistence problems in practice.

METHODS

A literature search was conducted using the CINAHL, IPAB, Ovid MEDLINE, and PsycINFO databases using the keywords (Medication(s) OR Drug(s)? OR Pharmacotherapy) AND (Compliance OR Adherence OR Persistence). Due to changes in healthcare delivery, the availability of good reviews of older literature, and the sheer volume of material, the search focused on articles published in English between 1994 and 2004. A total of 11,981 potential articles were identified and placed in an EndNote database (version 7.0). The abstracts of these potential articles were divided among four reviewers, who categorized the abstracts as related or unrelated to medication adherence/persistence based on the topic of the publication and study design. The unrelated abstracts were removed, and the 2,956 useable abstracts were classified as controlled studies, reports, or reviews and opinions. If the utility of an article could not be determined by reviewing the abstract, then the article was ordered for a full text review. The 2,956 identified articles were combined with key articles already on file, and the references were reviewed to locate other important works. The articles describing controlled studies were reviewed. Keyword searches of the EndNote database were conducted to identify articles dealing with specific issues.

ADHERENCE INTERVENTIONS

The results of studies that have demonstrated the effectiveness of adherence interventions are presented in table 1. The studies examined a number of interventions based on different theories or models, using different samples and a multitude of adherence measures. The study results vary because barriers to adherence can occur at many points in the patient care process, and each of these barriers needs to be targeted on a patient-by-patient basis. Some of the interventions evaluated in the studies address multiple barriers, while others address a single barrier.

⁷Lecompte D, Pelc I, A cognitive-behavioral program to improve compliance with medication in patients with schizophrenia, *Int J Ment Health*, 1996;25(1):51-56; Rzewuska M, Drug maintenance treatment compliance and its correlation with the clinical picture and course of schizophrenia, *Prog Neuropsychopharmacol Biol Psychiatry*, 2002;26(4):811-814.

⁸Miura T, Kojima R, Mizutani M, et al., Effect of digoxin noncompliance on hospitalization and mortality in patients with heart failure in long-term therapy: a prospective cohort study, *Eur J Clin Pharmacol*, 2001;57(1):77-83.

Another issue with the adherence literature is the fact that there is no standard measurement or common criteria for non-adherence. Some studies defined non-adherence as the consumption of less than 80 percent of the prescribed doses; others used 90 percent as the cut-off; while others considered any missed dose to be non-adherent. Similarly, adherence can be measured by devices that record the date and time a bottle is opened, manual pill counts, refill rates, biological concentrations, clinical response to therapy, or by patient self-report. Although these measures may correlate with each other, the results they produce are not directly comparable. All of these factors combined make it difficult to compare the results of studies that are published in the literature.

Table 2 summarizes the controlled studies that have evaluated different interventions and found positive results. The control group is comprised of usual care unless otherwise noted in the table. The studies are sorted into eight categories based on the nature of the intervention. The categories include theory-based interventions, disease-based interventions conducted by providers from a single discipline, disease-based interventions conducted by providers from multiple disciplines, dosage simplifications, reminders, discharge interventions, one-time interventions, and self-care initiatives.

Theory-based interventions are developed to improve the knowledge, skill, and information that patients need to improve adherence based on one of the theories or models presented in table 2. Two of the 11 studies evaluated interventions that were no better than the control group.⁹ Both studies evaluated cognitive behavioral-based counseling sessions in patients with schizophrenia. The controls were general counseling sessions that lasted as long as the intervention sessions. Adherence was improved in both groups in both studies, and non-adherence predicted relapse in one of the studies.

Disease-based interventions are developed based on the skills and knowledge patients need to treat a particular disease. Seven of the 10 studies evaluated multifaceted interventions conducted by providers from multiple disciplines and produced statistically significant results. The three studies that did not produce significant results did have an impact on the clinical outcomes, but not on adherence.¹⁰ Thirteen studies evaluated the impact of disease-based interventions conducted by providers from a single discipline. Six of these failed to produce a statistically significant impact on adherence.¹¹ Although all six studies produced significant clinical improvements, the measures of adherence, insufficient power, or the focus of the interventions resulted in non-significant impacts on adherence.

⁹ O'Donnell C, Donohoe G, Sharkey L, et al., Compliance therapy: a randomised controlled trial in schizophrenia, *BMJ*, 2003;327(7419):834; Sellwood W, Barrowclough C, Tarrier N, et al., Needs-based cognitive-behavioural family intervention for carers of patients suffering from schizophrenia: 12-month follow-up [see comment], *Acta Psychiatr Scand*, 2001;104(5):346-355.

¹⁰ Kutcher S, Leblanc J, Maclaren C, et al., A randomized trial of a specific adherence enhancement program in sertraline-treated adults with major depressive disorder in a primary care setting, *Prog Neuropsychopharmacol Biol Psychiatry*, 2002;26(3):591-596; Rawlings, MK, Thompson MA, Farthing CF, et al., Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients, *J Acquir Immune Defic Syndr*, 2003;34(2):174-183; Weinberger M, Murray MD, Marrero DG, et al., Effectiveness of pharmacist care for patients with reactive airways disease: a randomized controlled trial, *JAMA*, 2002;288(13):1594-1602.

¹¹ Capoccia KL, Boudreau DM, Blough DK, et al., Randomized trial of pharmacist interventions to improve depression care and outcomes in primary care, *Am J Health Syst Pharm*, 2004;61(4):364-372; Hanlon JT, Weinberger M, Samsa GP, et al., A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy, *Am J Med*, 1996;100(4):428-437; Owens D, Carroll A, Fattah S, et al., A randomized, controlled trial of a brief interventional package for schizophrenic out-patients, *Acta Psychiatr Scand*, 2001;103(5):362-369; Patton K, Meyers J, Lewis BE, Enhancement of compliance among patients with hypertension, *Am J Manag Care*, 1997;3(11):1693-1698; Taylor CT, Byrd DC, Krueger K, Improving primary care in rural Alabama with a pharmacy initiative, *Am J Health Syst Pharm*, 2003;60(11):1123-1129; Volume CI, Farris KB, Kassam R, et al., Pharmaceutical care research and education project: patient outcomes, *J Am Pharm Assoc*, 2001;41(3):411-420.

Dosage simplifications are interventions designed to decrease the number of doses a patient has to take in a given day. Reducing the duration of acute therapy or decreasing the number of doses per day improves treatment adherence. Claxton and colleagues¹² reviewed 85 studies and reported that the average rate of adherence for once-a-day dosing was 79 percent (SD 14) across 29 studies compared to 69 percent (SD 15) for BID dosing (32 studies), 65 percent (SD 16) for TID dosing (13 studies), and 51 percent (SD 20) for QID dosing (11 studies). These findings are consistent with the results presented in table 1.

Reminders are interventions used to remind patients to take their medicines. These include alarms, calendars, letters, pamphlets, or telephone calls. Reminders are usually periodic in nature and are generally effective due to this follow-up.

Discharge interventions are those programs initiated before a patient is discharged from the hospital. Four of the eight controlled studies evaluated interventions that were no more effective than the controls.¹³ While most of the interventions used several strategies such as verbal information, written information, and schedules, the four programs that produced significant results all incorporated follow-up contacts with the patient after discharge. Some follow-ups were in person; others were over the telephone. All of the unsuccessful interventions were one-time interventions before the patients were discharged. One of the studies reported on an intervention that produced a large improvement in adherence (27 percent) that was not statistically significant.¹⁴ The study only had 43 patients, so it most likely had insufficient power to detect a difference.

One-time interventions focus on knowledge, skills, or information a patient may need to improve adherence. The key with these interventions is that there is no follow-up. The successful interventions had multiple components, such as counseling, a pill box, a medication calendar, or a devised plan for medication use. The unsuccessful interventions were those that occurred one time with one component, such as written information about the medication.¹⁵

Self-care initiatives are programs used to teach patients to provide their own care. Two of the three studies examining self-care found significant improvements in treatment adherence. The third study, conducted with hypertensive patients, did not find significant differences between the intervention and control groups, but there was a significant intervention by time effect.¹⁶ In other words, adherence was similar at the start of the study, but there was a larger decrease in adherence in the control group over time.

The studies listed in table 1 used a variety of measures of adherence. These measures can be divided into behavioral measures, biochemical measures, and clinical measures. All of these are indirect measures of adherence. Behavioral measures include self-reported adherence to medication regimens, pill counts, refill records, and electronic measures of pill taking. Self-reported adherence rates have been shown to be over-estimated by 200 percent compared to biochemical measures, and provide 1.3 to 2 times higher estimates

¹² Claxton AJ, Cramer J, Pierce C, A systematic review of the associations between dose regimens and medication compliance, *Clin Ther*, 2001;23(8):1296-1310.

¹³ Esposito L, The effects of medication education on adherence to medication regimens in an elderly population, *J Adv Nurs*, 1995;21(5):935-943; Madoff SA, Pristach CA, Smith CM, et al., Computerized medication instruction for psychiatric inpatients admitted for acute care, *MD Comput*, 1996;13(5):427-431, 441; Nazareth I, Burton A, Shulman S, et al., A pharmacy discharge plan for hospitalized elderly patients: a randomized controlled trial, *Age Ageing*, 2001;30(1):33-40; Williford SL, Johnson DF, Impact of pharmacist counseling on medication knowledge and compliance, *Mi Med*, 1995;160(11):561-564.

¹⁴ Esposito L, The effects of medication education on adherence to medication regimens in an elderly population, *J Adv Nurs*, 1995;21(5):935-943.

¹⁵ Bennett JW, Glasziou P, Del Mar C, et al., A computerized prescribing decision support system to improve patient adherence with prescribing: a randomized controlled trial, *Aust Fam Physician*, 2003;32(8):667-671; Lourens H, Woodward MC, Impact of a medication card on compliance in older people, *Aust J Ageing*, 1994;13(2):72-76; Stevens VJ, Shneidman RJ, Johnson RE, et al., *Helicobacter pylori* eradication in dyspeptic primary care patients: a randomized controlled trial of a pharmacy intervention [see comment], *West J Med*, 2002;176(2):92-96.

¹⁶ Vrijens B, Goetghebeur E, Comparing compliance patterns between randomized treatments, *Control Clin Trials*, 1997;18(3):187-203.

of adherence than pill counts in the same patients.¹⁷ This overestimation may stem from the patient's desire to appear compliant or because patients do not remember exactly when they took their medication, so they record the times that they were supposed to take it. Asking the patient about his/her medication-taking within the last 24 to 48 hours (versus the past month) may increase the validity of the information obtained, as will combining the information with other data.¹⁸ Pill counts also appear to overestimate adherence because patients may discard remaining pills if they know that a pill count is going to be conducted. Furthermore, while pill counts provide information about doses removed from the container, we have no way of knowing if the doses were actually consumed or consumed at the correct time. Refill records are a reliable method for determining if someone has picked up the prescription, but they provide no information on a patient's actual medication use. That is, we may know that a patient is coming in on time, but we do not know if that patient took the medication as prescribed.

Biochemical measures that detect the concentration of medications in the patient's blood or urine have also been used to assess compliance. These are objective measures, but they are still indirect measures of compliance. Unfortunately, these measures require assays for each medication and only assess compliance over the past 24 or 48 hours, depending on the half-life of the product. Using biochemical measures to assess long-term compliance with a medication regimen would require multiple blood or urine samples, which are costly and inconvenient for patients.

Clinical measures, such as blood glucose control for diabetics or blood pressure control for hypertensive patients, have also been used as measures of compliance. Since a direct relationship between adherence and clinical control may not exist, it is problematic to use clinical measures as the sole estimate of compliance. Factors such as diet, exercise, and patients' pharmacologic response to the medication may affect their clinical control more than just adherence.

In order to make sense out of these results, an overview of the barriers is presented in table 2, a diagram of the adherence process is presented in figure 1, and an overview of the theories and models that have been used in adherence research is presented in table 3. Additional compliance aids and organizational activities that can improve adherence are listed in tables 4 and 5, respectively.

BARRIERS

Signs of an adherence problem present when a patient does not get a new prescription filled; does not refill a chronic medication as frequently as expected; stops refilling chronic medications; or fails to finish an entire course of an acute medication, such as an antibiotic. The factors that impact adherence in each of these instances are broadly grouped into six categories: patient demographics, patient psychosocial and behavioral characteristics, disease-related issues, family and cultural issues, healthcare system issues, and issues with the treatment plan itself.

Table 2 lists the factors that impact adherence. The evidence supporting the impact of each factor is sometimes mixed. In these cases the effect reported in the most studies is listed first and in bold text. The conflicting results stem, in part, from the fact that the factors were identified from studies that used different study designs ranging from qualitative studies, to exploratory studies, to randomized controlled studies. The studies also used different populations and different measures of adherence or persistence, and, in some cases, the operational definition of a given factor differed from one study to another. A systematic review of each factor was not conducted.

¹⁷ Levine AM, Antiretroviral therapy: adherence, *Clinical Care Options for HIV Online Journal*, 1998;4:1-10; Isaac LM, Tamblyn RM, Compliance and cognitive function: a methodological approach to measuring unintentional errors in medication compliance in the elderly, *Gerontologist*, 1993;33:772-781.

¹⁸ Holzemer WL, Corless IB, Nokes KM, et al., Predictors of self-reported adherence in persons living with HIV disease, *AIDS Patient Care STDS*, 1999;13(3):185-197.

Patient Demographics

Age, low literacy, having insurance coverage, and being homeless had the most consistently reported impact on adherence among the patient demographic factors reported in these studies. Although nine studies found that age did not affect compliance, most of these studies had restricted age ranges, which limited the impact of this factor. Nearly all of the studies that included a wide range of ages reported age as a factor contributing to adherence. Generally speaking, as age increases, adherence also increases, until the seventh decade, and then treatment adherence levels off or begins to decrease.¹⁹ This decrease may be due to other processes associated with aging, such as an increased incidence of dementia or decreased mobility.

The evidence supporting the impact of gender, ethnicity, and marital status is mixed, and these factors are generally thought to play a minor role in adherence. This finding is consistent with other reviews.²⁰ There is some evidence to suggest that the amount of education a patient has plays a role in adherence, but understanding the treatment instructions and the importance of the treatment are probably the more important factors regardless of the patient's level of education. Education and ethnicity are often related to limited English proficiency and low health literacy. For instance, one study found that years of education were correlated with understanding the disease-related terms and prescription directions.²¹ These factors may lead to increased adherence. Limited English proficiency and health literacy will be discussed below.

Family/Cultural Issues

Patients live in a social environment. Social support involves the help that family members, friends, or caregivers provide in assisting the patient with medication regimens. People who believe they have social support have higher treatment adherence. Family cohesion and the stability of the home life are important predictors of adherence. However, when there are too many people in the household, or when too many other people are depending on the patient, treatment adherence suffers. It appears that as people's lives become more chaotic, adherence suffers.²²

Psychosocial and Behavioral Characteristics

The patient's psychosocial and behavioral characteristics also play an important role in treatment adherence. A patient's belief that a medication will work or is working is directly related to treatment adherence, as is the ability to manage side effects and a positive attitude. Healthcare providers can work with patients to impact each of these.

Depression, impaired cognition, anger, stress, anxiety, substance abuse, psychiatric disorders, and low self-efficacy are associated with lower treatment adherence. Self-efficacy is a person's belief or confidence in his/her own ability to carry out a target behavior and the extent to which the behavior is actually carried out correctly.

The evidence to support the impact of locus of control is mixed. Locus of control involves whether the patient believes that what is happening to him/her or the outcomes of treatment are under his/her control (internal locus of control) or out of his/her control (external locus of control).

¹⁹ Mehta S, Moore RD, Graham NM, Potential factors affecting adherence with HIV therapy, *AIDS*, 1997;11(14):1665-1670; Venturini F, Nichol MB, Sung JC, et al., Compliance with sulfonylureas in a health maintenance organization: a pharmacy record-based study, *Ann Pharmacother*, 1999;33(3):281-288.

²⁰ Fogarty L, Roter D, Larson S, et al., Patient adherence to HIV medication regimens: a review of published and abstract reports [see comment], *Patient Educ Couns*, 2002;46(2):93-108.

²¹ Van Servellen G, Brown JS, Lombardi E. et al., Health literacy in low-income Latino men and women receiving antiretroviral therapy in community-based treatment centers, *AIDS Patient Care STDS*, 2003;17(6):283-298.

²² Krueger KP, Felkey BG, Berger BA, Improving adherence and persistence: a review and assessment of interventions and description of steps toward a national adherence initiative [see comment], *J Am Pharm Assoc*, 2003;43(6):668-678; quiz 678-669.

Treatment and Healthcare System Characteristics

One of the most important healthcare system factors impacting adherence is the relationship that providers establish with patients. Ten out of the 12 studies that included this factor found that a trusting, supportive relationship increased adherence.

Other characteristics of the treatment plan and healthcare system also impact treatment adherence. If the patient is unable to read or understand the medication label or if the cap cannot be removed easily, then adherence rates decrease. Conversely, treatment adherence increases when patients understand why a medication is important and how it impacts their disease. This is one of the reasons why positive reinforcement from healthcare providers improves adherence.

Side effects can decrease adherence rates if patients believe they cannot control or manage them. Treatment adherence also decreases as the number of medications increases, particularly when a patient takes more than four medications. The inconvenience and/or embarrassment of the therapy regimen also negatively impact adherence. This may be one of the reasons why Wagner²³ found lower adherence rates among employed subjects.

Limited English Proficiency/Low Health Literacy

Limited English proficiency/low health literacy is a barrier to adherence that deserves special attention. Nearly 90 million people in the United States have literacy skills at or below the high school level. Half of these have trouble finding information in unfamiliar texts such as newspaper articles or prescription labels. Literacy levels are lowest among the elderly, those with fewer years of education, lower socioeconomic levels, minority populations, and those with limited English proficiency.²⁴ Educational and informational materials created by healthcare providers often require that patients have a high school reading level (or higher) in order to understand them.²⁵ The shame or embarrassment of low literacy can be a barrier to healthcare in and of itself. Studies have demonstrated that patients with limited English proficiency have decreased access to healthcare services and perceive lower quality of care when they do receive it.²⁶ Lack of access and low-quality care can also lead to lower adherence, poor health outcomes, and ultimately to utilization of more expensive healthcare resources. This has been demonstrated in three of the studies listed in table 2,²⁷ and in a study which found that patients with limited English proficiency had 6 percent longer hospital stays compared to English-proficient patients ($p < 0.05$).²⁸ Another study in people with diabetes found that patients with lower health literacy were more likely to have worse glycemic control than patients with higher health literacy.²⁹

²³ Wagner G, Placebo practice trials: the best predictor of adherence readiness for HAART among drug users? *HIV Clin Trials*, 2003;4(4):269-281.

²⁴ IOM Committee on Health and Literacy, The extent and associations of limited health literacy. In: Nielsen-Bohlman L, Panzer AM, Kindig DA, eds., *Health Literacy: A Prescription to End Confusion*. Washington, DC: National Academies Press; 2004, 59-107.

²⁵ Ebrahimzadeh H, Davalos R, Lee PP, Literacy levels of ophthalmic patient education materials, *Surv Ophthalmol*, 1997;42(2):152-156.

²⁶ Ortiz F, Fitten LJ, Barriers to healthcare access for cognitively impaired older Hispanics, *Alzheimer Dis Assoc Disord*, 2000;14(3):141-150; Weech-Maldonado R, Morales LS, Elliott M, et al., Race/ethnicity, language, and patients' assessments of care in Medicaid managed care, *Health Serv Res*, 2003;38(3):789-808; Xu KT, Rojas-Fernandez CH, Ancillary community pharmacy services provided to older people in a largely rural and ethnically diverse region: a survey of consumers in West Texas, *J Rural Health*, 2003;19(1):79-86.

²⁷ Kalichman SC, Catz S, Ramachandran B, Barriers to HIV/AIDS treatment and treatment adherence among African-American adults with disadvantaged education, *J Natl Med Assoc*, 1999;91(8):439-446; Kalichman SC, Ramachandran B, Catz S, Adherence to combination antiretroviral therapies in HIV patients of low health literacy [see comment], *J Gen Intern Med*, 1999;14(5):267-273; Miller LG, Liu H, Hays RD, et al., Knowledge of antiretroviral regimen dosing and adherence: a longitudinal study [see comment], *Clin Infect Dis*, 2003;36(4):514-518.

²⁸ John-Baptiste A, Naglie G, Tomlinson G, et al., The effect of English language proficiency on length of stay and in-hospital mortality [see comment], *J Gen Intern Med*, 2004;19(3):221-228.

²⁹ Schillinger D, Piette J, Grumbach K, et al., Closing the loop: physician communication with diabetic patients who have low health literacy [see comment], *Arch Intern Med*, 2003;163(1):83-90.

Interventions have been developed and studied which improve knowledge and understanding about disease and treatments in low health literacy patients. An instructional module targeting limited English proficiency patients was studied in a group of HIV patients. They were predominately male and 75 percent of the sample spoke Spanish in their homes. The intervention increased the subjects' knowledge of the disease and therapy, but it had no effect on self-reported adherence rates.³⁰ Other studies that have evaluated verbal messages and visual aids have reported increases in knowledge about the disease and its treatment and improvements in health outcomes.³¹

Patient-Provider Relationships

In order to effectively combat problems with adherence and persistence, healthcare providers have to work with patients to accurately identify and address each patient's unique barriers to adherence and persistence. Before this can happen, the providers have to establish a supportive therapeutic relationship with their patients. Unfortunately a productive interaction between the patient and provider is not always achieved. Svarstad and colleagues³² have studied patient counseling and the use of written information in community pharmacies. Their research concludes the following:

- Pharmacist monitoring positively influences patient satisfaction and adherence with antidepressant therapy.
- The quality of pharmacist monitoring after the first fill affects the quality of patient feedback regarding medication-related problems and concerns. The initial encounter helps form patients' beliefs about the therapy. Therefore, benefits and expectations need to be addressed.
- The provision of written information with prescriptions is becoming a routine practice in community pharmacies (87 percent of study patients received written information).
- Wide variability in the length and quality of the information exists. Most leaflets did not contain information that met usefulness guidelines for patients. Notably absent was sufficient information about contraindications, precautions, and how to avoid harm while using the medicine.
- Patients are more likely to receive written information in pharmacies with more staff present. Chain pharmacies are more likely to provide information and more likely to provide quality information.
- Too often, written information is used as a substitute for verbal counseling.
- Twenty-five percent of pharmacists never talked with the study shoppers, and 47 percent of all shoppers never received any oral drug information from pharmacy staff.
- The content and style of counseling that does take place in community pharmacies is suspect. Very little information is provided about the drug in verbal counseling other than the information provided on the prescription label. A majority of shoppers received no information about how long to take the drug, how to manage adverse effects, precautions, or when the medicine should begin to work. Only 5 percent of the shoppers received information leaflets containing this information, and only 8 percent of those shoppers were encouraged to read the leaflets.

³⁰ Van Servellen G, Chang B, Garcia L, et al., Individual and system level factors associated with treatment nonadherence in human immunodeficiency virus-infected men and women, *AIDS Patient Care STDS*, 2002;16(6):269-281.

³¹ Hussey LC, Minimizing effects of low literacy on medication knowledge and compliance among the elderly, *Clin Nurs Res*, 1994;3(2):132-145; Mulrow C, Bailey S, Sonksen PH, et al., Evaluation of an audiovisual diabetes education program: negative results of a randomized trial of patients with non-insulin-dependent diabetes mellitus, *J Gen Intern Med*, 1987;2(4):215-219; Okonkwo PO, Akpala CO, Okafor HU, et al., Compliance to correct dose of chloroquine in uncomplicated malaria correlates with improvement in the condition of rural Nigerian children, *Trans R Soc Trop Med Hyg*, 2001;95(3):320-324.

³² Bultman D, Svarstad BL, Effects of pharmacist monitoring on patient satisfaction with antidepressant therapy, *J Am Pharm Assoc*, 2002;42(1):36-43; Svarstad BL, Bultman DC, Mount JC, et al., Evaluation of written prescription information provided in community pharmacies: a study in eight states, *J Am Pharm Assoc*, 2003;43(3):383-393; Svarstad BL, Bultman DC, Mount JK, Patient counseling provided in community pharmacies: effects of state regulations, pharmacist age, and busyness, *J Am Pharm Assoc*, 2004;44(1):22-29.

- Less than half of the shoppers (48 percent) were asked any questions to assess prior use, medical history, understanding of the illness and treatment, etc.
- Age of the pharmacist and how busy the pharmacist is affect counseling practices more than type of practice.
- The quality and amount of counseling about medications in community pharmacies is woefully inadequate and does not meet the intent of OBRA 90 provisions. However, states where more stringent regulations exist tend to have better pharmacist counseling. This certainly has public policy implications regarding the setting of standards to elevate practice and protect patients.

The interaction between physicians and patients has been studied by Sleath, Roter, and colleagues.³³ They found that many patients express complaints and adherence problems to their physicians (20 percent now versus 14 percent for data collected in the 1970s). While no patient demographic characteristics differentiated the number of complaints or adherence problems, patients' physical health, as rated by their physicians, was a significant factor. The more ill the patient was, the more they complained. While the majority of physicians responded to patients' complaints by changing the patients' medications, educating the patient, and listening to the complaint, physicians ignored 33 percent of patients who expressed an adherence problem. This study did not examine the effect of the physicians' responses on adherence. In 1995, Roter³⁴ proposed relationship-centered medicine as an approach for facilitating patient compliance. The focus was on the communication skills used by the healthcare provider. The approach, based upon evidence-based research, advocated the following principles:

1. Respect the patient's perspective regarding the illness and treatment.
2. Do not use drug therapy as an expediency or simply as a way to satisfy the patient.
3. Provide a diagnostic and treatment rationale to the patient.
4. Negotiate a plan with the patient and expect problems.
5. Share expertise with the patient in a way that is useful to the patient—find out what the patient knows about the illness.
6. Ensure that communication with the patient has cognitive and emotional significance.
7. Ask about a patient's adherence in a non-judgmental and non-threatening manner. Monitor compliance each visit.
8. If compliance problems are discovered, use a collaborative approach that involves the patient in decisionmaking and solutions.

A PATIENT-FOCUSED PROCESS

A process that a healthcare provider can use to efficiently assess a patient and determine the appropriate next step is presented in figure 1. This represents a visual summary of the literature on improving treatment adherence with medication regimens. The boxes with dark borders represent decision points (things the provider needs to do), the boxes with dotted borders represent favorable responses by the patient, and the boxes with the double border represent barriers that the patient and provider must address. The solid black arrows show the flow, and the broken or dotted arrows indicate relationships between the boxes, illustrating the circular nature of this process. The entire flowchart incorporates the theories, models, and patient characteristics that are predictive of or associated with treatment adherence. Table 3 supports this flowchart by summarizing the theories/models depicted in this flowchart. Appendix A of this paper contains a more detailed synopsis of these theories and models.

³³ Sleath B, Chewning B, Svarstad B, et al., Patient expression of complaints and adherence problems with medications during chronic disease medical visits, *J Soc Adm Pharm*, 2000;17(21):71-80.

³⁴ Roter D, Advancing the physician's contribution to enhancing compliance, *Journal of Pharmacoepidemiology*, 1995;3(2):37-48.

Table 4 presents medication adherence aids and evaluates their effectiveness in overcoming four specific barriers to adherence: remembering to take the medicine; remembering if the medicine was taken; reducing the regimen complexity; and remembering to refill the prescription. These ratings are based on one author's experience and are the types of aids that were used in some of the interventions listed in table 1 and mentioned in figure 1.

Table 5 describes aids that can be implemented at the organizational level to help providers improve treatment adherence. The expected impact, providers involved, and the technological requirements of each initiative are described. This table was developed from one author's experience and a survey of the literature.

Table 6 lists other initiatives that have been reported to the National Quality Forum. These initiatives cover an array of services ranging from specific adherence interventions to disease management programs.

This paper surveys literature from the past 10 to 15 years. The findings are similar with reviews conducted by Haynes and colleagues between 1980 and 2002 indicating that the fundamental adherence issues have not changed.³⁵

TAKE HOME POINTS

The following points summarize this vast body of literature:

- No single approach is enough to ensure patient compliance.
- Any attempts to improve compliance must involve the patient in the decisionmaking process. Patients must be partners in the process.
- Compliance with short-term therapy falls off rapidly unless the patient is properly educated about how long the medicine needs to be used, the intended effects, and what the patient can expect.
- For long-term therapies, the benefit of the therapy must be clear, the barriers must be discussed and strategies for overcoming them determined, regimens need to be tailored to patient's daily routines, patients must be supervised more closely, including follow-up care, and compliance and good or improving performance needs to be rewarded. Contracts should be considered in which rewards of compliance are negotiated with the healthcare provider. In addition, involving the patient in setting goals of treatment that are relevant to the patient improves adherence.
- Social support, involving family members, is helpful in improving patient compliance, particularly with chronic asymptomatic illnesses.
- The complexity of the treatment regimen is related to compliance. The more complex the regimen, the higher the rates of non-adherence.
- The quality of the clinical setting affects compliance. Patients who experience long wait times and a lack of continuity of care are more likely to be non-compliant.
- Individual counseling and assisting the patient in identifying lifestyle cues to help patients take medications improves treatment adherence, while group sessions may be helpful for some patients with chronic illnesses.
- Measures of adherence are often correlated with one another, but they rarely produce the same estimate of adherence. The advantages and disadvantages of any adherence measure should be kept in mind when it is being used.
- Current methods for improving adherence are often complex and do not produce consistent improvements. New ways of thinking and more comprehensive approaches are needed.

³⁵ Haynes RB, Strategies for enhancing patient compliance, *Drug Ther*, 1980;January:147-154; Haynes RB, Wang E, Da Mota Gomes M, A critical review of interventions to improve compliance with prescribed medications, *Patient Educ Couns*, 1987;(10):155-166; Haynes RB, McDonald PM, Garg AX, Helping patients follow prescribed treatment, *JAMA*, 2002;288(12):2880-2883; McDonald PM, Garg AX, Haynes RB, Interventions to enhance patient adherence to medication regimens, *JAMA* 2002;288(12):2868-2879.

Figure 1. The Adherence Process Flowchart

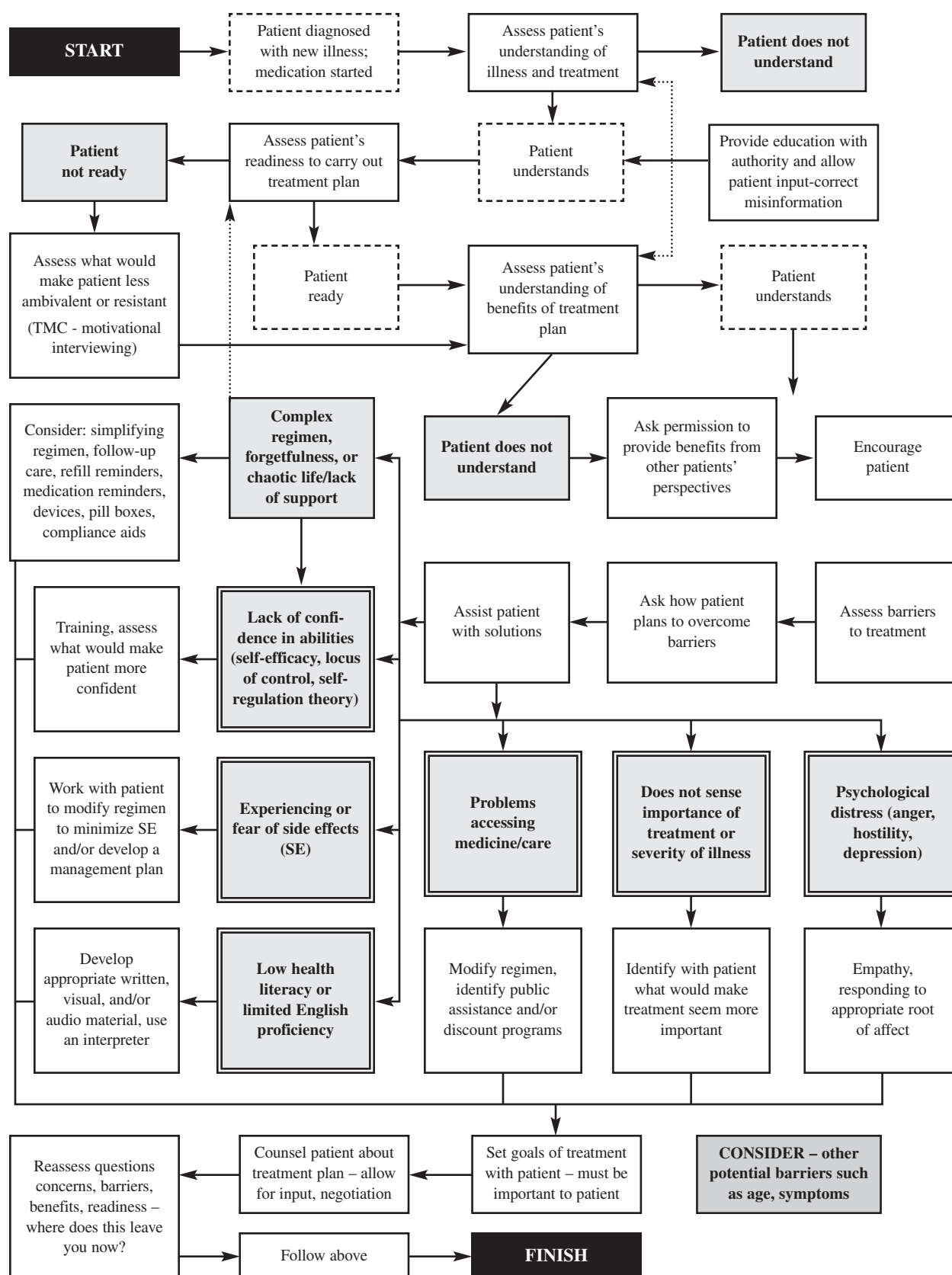


Table 1. Adherence Interventions Reported in the Literature

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Theory-Based Interventions							
(Kemp, Hayward, Applewhaite, et al.)	1996	RCT	Psychiatric illness	47	4 to 6 sessions that lasted 10 to 60 minutes and focused on the patient's history and knowledge of his/her condition, the benefits and drawbacks of therapy, the patient's ambivalence, and discrepancies between the patient's actions and beliefs	Observer using a 7-point scale ranging from 1 (partial refusal of therapy) to 7 (taking responsibility for their treatment)	5.2 times more likely to be compliant than control (p<0.05)
(Lin et al.)	2003	RCT	Depression – HMO setting	386	Motivational interviewing x 5 (in person and telephone) sessions	Self-reported persistence	13% INC (p<0.05)
(Miklowitz, George, Richards, et al.)	2003	RCT	Bipolar disorder	101	Family-focused therapy (21 1-hour sessions broken into 3 content areas: psychoeducation, communication enhancement, and problem-solving skills training) vs. intensive crisis management (control)	An independent observer of medication consumption and patient self-report (rated on a 3-point scale from 1 (no adherence) to 3 (perfect adherence))	4.67% INC (p=0.04)
(Rapoff et al.)	2002	RCT	Juvenile rheumatoid arthritis	34	Registered nurse administered education and behavioral intervention	Percentage of doses taken within 2 hrs of prescribed time measured by MEMS cap	20.8% INC (p=0.02)
(Razali, Hasanah, Khan, et al.)	2000	RCT	Psychiatric illness	143	Culturally modified family therapy (the intervention); behavior family therapy (the control)	Being 90% compliant with therapy from a self-reported 6 point scale assessing the proportion of doses taken	30% INC (p<0.001)
(Saunders, Wilkinson, Phillips)	1995	RCT	Methadone program participants	116	Motivational interview intervention program	Persistence with therapy	18.9% INC (p=0.03)

INC = increase in adherence from the control group to the intervention group • NR = not reported

Table 1. Adherence Interventions Reported in the Literature (continued)

Theory-Based Interventions (continued)						
AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE
(Margolin, Avants, Warburton, et al.)	2003	RCT	HIV and substance abuse problems	69	Enhanced methadone maintenance program (6 months of daily methadone and weekly individual substance abuse counseling and case management along with a 6-session HIV risk-reduction program that included individualized feedback, video-based needle cleaning demonstrations, harm reduction role playing and activities, and harm reduction kits); HIV+ Harm reduction Program (6 months of daily methadone and weekly individual substance abuse counseling and case management along with a 6-session HIV risk-reduction program that included individualized feedback, video-based needle cleaning demonstrations, harm reduction role playing and activities, and harm reduction kits plus twice weekly group sessions that address the medical, emotional, and spiritual needs of the subjects based on cognitive remediation strategies); historic control	13% INC (p=0.02)
	2004	Pretest-posttest design	Asthma	46	NHLBI information booklet; Protection Motivation Theory (PMT) tapes; PMT based audiotapes and booklet; standard provider education (control)	Pharmacy Records 33% INC (p=0.02); 8% INC (NS); 43% INC (p=0.04) (each compared to control)
(Schmaling, Blume, Afari)	2001	RCT	Asthma (adults)	25	Educational session accompanied with motivational interviewing (individual feedback, information about asthma, coaching on inhaler technique, and a booklet given to all patients to reinforce these lessons)	Motivation to comply with their asthma regimen 40.9% INC (p<0.05)

INC = increase in adherence from the control group to the intervention group • NR = not reported

Table 1. Adherence Interventions Reported in the Literature (continued)

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Theory-Based Interventions (continued)							
(Ngho, Shepherd)	1997	RCT - pretest posttest design	Non-literate women receiving antibiotics	78	Visual aids alone; visual aids with advance organizers (culturally specific medication information)	Percentage of doses taken	17.1% INC (p<0.05); 12.02% INC (p<0.05) (compared to control)
Disease-Based Interventions							
(Bouvy et al.)	2003	RCT	Congestive heart failure	152	Structured pharmaceutical care with monthly follow-up and communication with physician	Days without therapy measured by MEMS cap	33% INC (p<0.05)
(Cramer, Rosenheck)	1999	RCT	Psychiatric illness	45	Life skill training, dosing cues, digital display of number of doses that day, and monthly follow-up	Proportion of days with correct number of doses measured by MEMS cap	19% INC (p=0.008)
(Katon et al.)	2001	RCT	Major depression – adults	386	Relapse prevention (written plan, prodromal symptom recognition, 2 primary care visits, 3 follow-up telephone calls)	Proportion of patient refilling medications necessary to receive adequate doses of medication	13.5% INC (p<0.001)
(Katon et al.)	1995	RCT	Major depression – adults	217	Several educational sessions, video education, and written material aimed at educating the patient about the disease state and facilitating the interaction between the provider and the patient	Pharmacy refills (picking up within 3 days of due date)	25.5% INC (p<0.01)
(Peveler, George, Kinnmonth, et al.)	1999	RCT	Using tricyclic antidepressants	213	Written information plus drug counseling at 2 and 8 weeks; written information (leaflet); drug counseling at 2 and 8 weeks	Self-reported persistence	24% INC; 6% INC; 16% INC (p<0.05)
(Tan, Yong, Wan, et al.)	1997	Pretest-posttest with control group (quasi-experimental)	Elderly with diabetes	302	6 individual education sessions and 4 group sessions	Self-report—take medication daily as prescribed	3.5% INC (p<0.05)

INC = increase in adherence from the control group to the intervention group • NR = not reported

Table 1. Adherence Interventions Reported in the Literature (continued)

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Disease-Based Interventions (continued)							
(Rand, Nides, Cowles, et al.)	1995	RCT	Smokers with lung disease 35 to 65 years old	0	MD medical education, classes, regimen tailoring with active drug; MD medical education, classes, regimen tailoring with placebo	Self-report	11.8% INC (NR)
(Dixon, Weiden, Torres, et al.)	1997	Pretest-posttest design	Homeless and psychiatric illness	70	Assertiveness training	Persistence with therapy	28% INC (p<0.005)
(Gani et al.)	2001	RCT	Allergic rhinitis	101	Drug therapy + nasal spray training; or drug therapy + nasal spray training + a disease orientation class (vs. drug therapy alone)	Diaries and returned canisters	8.6% INC (p=0.001); 16.67% INC (p=0.001)
(Lowe, Raynor, Purvis, et al.)	2000	RCT	Elderly using ≥3 meds	161	Visits by 3 pharmacists to assess knowledge, provide education, address packaging problems	Proportion of correct doses taken	11.8% INC (p<0.0001)
(Piette et al.)	2000	RCT	Diabetes	248	Biweekly automated assessment calls and self-care education provided by a registered nurse	Self-reported missing doses or discontinuation	21% INC (p=0.003)
(Stewart, Eales, Davis)	2003	RCT	Adults with hypertension	83	Usual care (home-based exercise program, medications, and monthly education session focusing on normal blood pressure, medication information, smoking cessation, etc.) vs. monthly telephone follow-up with usual care	Persistence with treatment program	23.5% INC (p=0.007)
(Sturges, McElnay, Hughes, et al.)	2003	RCT	Elderly using ≥4 meds	191	Coordinated, structured pharmaceutical care	Proportion of patients who were compliant by self report	32.6% INC (p<0.05)
(Varma, McElnay, Hughes, et al.)	1999	RCT	Elderly with congestive heart failure	83	Systematic pharmaceutical care (medication information and education, dosage simplification or changes if necessary, education about lifestyle changes, and written information); usual care	Proportion of pts with MPR between 80 and 120%	46% INC (p=0.039)

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Table 1. Adherence Interventions Reported in the Literature (continued)

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Dose Simplification							
(Bukstein et al.)	2003	RCT- crossover design I	Children with asthma	666	Once daily therapy vs. 4-times-a-day therapy (control)	Proportion of days with correct number of doses	16.6% INC (p<0.001)
(Doren, Reuther, Minne, et al.)	1995	RCT	Postmenopausal women	140	Single combination tablet 12 days a month vs. 2 individual tablets daily (control)	Self-report by interview	24% INC (NR)
(Laine, Estrada, Trujillo, et al.)	1996	RCT	<i>H. pylori</i> eradication adults (PUD or dyspepsia)	150	7 day course of twice-daily triple therapy; or 10 day course of twice-daily triple therapy; compared to a 14-day course (control)	Percent taking 80% or more of the regimen by pill count	10% INC (p=0.03); 4% INC (p=0.03)
(Mounier-Vehier et al.)	1998	RCT	Hypertension	103	Once a day therapy vs. twice a day therapy (control)	Proportion of doses taken by pill count and MEMS	11.3% INC (p<0.0001)
(Stoloff, Stempel, Meyer, et al.)	2004	Retro- spective claims database study	Asthma	1660	2 medications in single inhaler vs. 2 medications in 2 inhalers (control)	Medication possession ratio (MPR) measured by claims data	11.2% INC (p<0.05)
(Taylor, Shoheiber)	2003	Retro- spective claims database study	Hypertension	573 2	2 medications in single capsule vs. 2 medications in 2 capsules (control)	MPR measured by claims data	7% INC (p<0.001)
Reminders with and without Feedback							
(Azrin, Teichner)	1998	RCT	Psychiatric illness	27	Education, pill box, and skill development; or family support plus, education, pill box and skill development compared to education only (the control) (skills developed include using the pill box, taking medications, getting refills, communicating with the pharmacist, setting appointments, using alcohol, and managing side effects)	Proportion of pills taken based on pill count	22% (p<0.05) INC; 19% (p<0.05) INC

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Table 1. Adherence Interventions Reported in the Literature (continued)

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Reminders with and without Feedback (continued)							
(Frick, Lavreys, Mandaliya, et al.)	2001	RCT	Women using multivitamins	120	Alarm device	Proportion of doses taken within two hours of the expected time as measured by an electronic cap	10% INC (p<0.001)
(Hoffman et al.)	2003	RCT	Patients receiving new prescriptions	956 4	Monthly informational letters sent to patients and their prescribers	MPR measured by pharmacy data	1.4% INC (p<0.01)
(Jacobson et al.)	1999	RCT	Pts ≥65 yrs or with chronic disease	433	1-page low-literacy reminder about vaccinations	Proportion vaccinated	16.1% INC (p<0.001)
(Laster, Martin, Fleming)	1996	One group pretest posttest study	Glaucoma	13	Medication alarm device	Self-report	12.6% INC (p<0.01)
(Perri, Martin, Pritchard)	1995	Randomized pretest posttest controlled study	Community pharmacy patients	186	Prescription vial counter cap	The difference between the expected and actual days between refills	40.6% INC (p=0.036)
Discharge Counseling							
(Lipton, Bird)	1994	RCT	Medicare recipients using ≥3 meds	232	Pharmacists provide pharmaceutical care in hospital and during 4 follow-up visits over 3 months. (Pharmaceutical care is medication information and education, dosage simplification or changes if necessary, education about lifestyle changes, and written information)	Percentage of correct responses from an interview covering knowledge, regularity of medication taking, frequency of doses, amount, missed doses	14.6% INC (p<0.001)
(Naunton, Peterson)	2003	RCT	Elderly using ≥4 meds	121	Pharmacist discharge counseling and 5th-day home visit to provide pharmaceutical care	Self-report of never "missing a dose"	43% INC (p<0.0001)
(Rich, Gray, Beckham, et al.)	1996	RCT	Elderly with congestive heart failure	156	Multidisciplinary discharge counseling program with intensive follow-up	Proportion of doses taken assessed by pill count	6.8% INC (p=0.003)

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Table 1. Adherence Interventions Reported in the Literature (continued)

AUTHOR	YEAR OF PUBLICATION	DESIGN	CONDITIONS OR CHARACTERISTICS OF SAMPLE	n	INTERVENTION(S)	MEASURE OF ADHERENCE	EFFECT
Discharge Counseling (continued)							
(Smith et al.)	1997	RCT	Elderly	53	Discharge counseling, pharmaceutical care plan, follow-up home visit	Not stated (likely self-report or pill count)	42.1% INC (p<0.001)
One-Time Intervention							
(Lee et al.)	1999	RCT	<i>H. pylori</i> eradication adults (peptic ulcer disease or dyspepsia)	125	Written and oral medication counseling, a medication calendar, and a pill box	Percentage taking 90% or more of medications based on pill count	31% INC (p<0.01)
(Okonkwo, Akpala, Okafor, et al.)	2001	RCT	Children with malaria	632	Pictorial medication instruction; pictorial and verbal medication instruction usual care	Proportion of patients consuming all their medication	15% INC; 36% INC (p<0.001) for each compared to usual care
(Putnam, Finney, Barkley, et al.)	1994	RCT	College students using antibiotics	60	Commitment counseling (subjects committed to adhere, information was provided to them, and they developed strategies to remember to take the medications)	Percent of doses taken based on pill count from home visit	11% INC (p<0.05)
Self-Care							
(Berg, Dunbar-Jacob, Sereika)	1997	RCT	Asthma (rural dwelling)	55	Self-management program consisting of 6 sessions covering self-management skills, asthma triggers, prevention of attacks, relaxation techniques, psychological responses to asthma, and problem-solving skills	Proportion of doses taken measured by MDI Chronolog (electron device similar to MEMS)	17% INC (p<0.05)
(Lowe, Raynor, Courtney, et al.)	1995	RCT	Inpatients discharged from hospital	88	Inpatient self-medication program with education	Pill count	12% INC (p<0.02)

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Table 2. Factors That Impact Adherence

FACTOR	EFFECT ON ADHERENCE	NUMBER OF STUDIES	AUTHORS
Patient Demographics			
Age (younger less/older more adherent)	Increase	11	(Agarwal, Sharma, Kishore Kumar, et al., 1998; Branin, 2003; Coldham, Addington, 2002; Daniels, Rene, Daniels, 1994; Degli Esposti et al., 2002; Mehta et al., 1997; Peters, Horne, Kong, et al., 2001; Rand et al., 1995; Van Servellen et al., 2003; van Servellen, Chang, Garcia, et al., 2002; Venturini et al., 1999; Wagner, 2002)
	None	9	(Ayres, Hoon, Franzoni, et al., 1994; Brus, van de Laar, Taal, et al., 1999; Colom et al., 2000; Coons et al., 1994; Dew, Roth, Thompson, et al., 1996; Erlen, Sereika, Cook, et al., 2002; Evangelista et al., 2003; Kane, Cohen, Aikens, et al., 2001; Kyngas, 2000)
Education (having more)	Increase	3	(Gago et al., 2000; Kalichman, Ramachandran, Catz, 1999; Rand et al., 1995)
	None	2	(Ayres et al., 1994; Brus et al., 1999)
	Decrease	1	(Daniels et al., 1994)
Insurance (having insurance)	Increase	2	(Asawavichienjinda, Sittthi-Amorn, Tanyanont, 2003; Wagner, 2002)
Low literacy	Decrease	3	(Kalichman, Catz, Ramachandran, 1999; Kalichman, Ramachandran, Catz, 1999; Miller et al., 2003)
Homelessness	Decrease	1	(Wagner, 2003)
Employment status (being employed)	Decrease	1	(Wagner, 2003)
	None	1	(Wagner, 2002)
Ethnicity (being Caucasian) (from a minority group/born outside the United States)	None	2	(Ayres et al., 1994; Wagner, 2002)
	Increase	1	(Pettinger et al., 1999)
	Decrease	2	(Kalichman, Ramachandran, Catz, 1999; van Servellen et al., 2002)
Gender (being male)	None	7	(Brus et al., 1999; Coldham et al., 2002; Colom et al., 2000; Coons et al., 1994; Dew et al., 1996; Gago et al., 2000; Kyngas, 2000)
	Increase	3	(Asawavichienjinda et al., 2003; Daniels et al., 1994; Degli Esposti et al., 2002)
	Decrease	2	(Kane et al., 2001; van Servellen et al., 2002)
Marital status (being married) (being single)	None	3	(Ayres et al., 1994; Daniels et al., 1994; Gago et al., 2000)
	Increase	2	(Kane et al., 2001; Rand et al., 1995)
	Increase	1	(Wagner, 2002)
Living arrangement	None	1	(Coons et al., 1994)

Table 2. Factors That Impact Adherence (continued)

FACTOR	EFFECT ON ADHERENCE	NUMBER OF STUDIES	AUTHORS
Family/Cultural Issues			
Support (family, social, or caregiver)	Increase None	5 1	(Cohen, Rogers, Burke, et al., 1998; Coldham et al., 2002; Dew et al., 1996; Kalichman, Ramachandran, Catz, 1999; Wagner, 2003) (Brus et al., 1999)
Household size (large)	None Decrease	2 1	(Ayres et al., 1994; Kyngas, 2000) (Wagner, 2002)
Responsibility for others' care	Decrease	1	(Wagner, 2003)
Family cohesion	Increase	1	(Embry, 2003)
Family adaptability	Increase	1	(Eddy et al., 1998)
Stable home environment	Increase	1	(Wagner, 2003)
Patient Psychosocial and Behavioral Characteristics			
Belief medications are working/hope they will work (efficacy)	Increase None	7 1	(Alice, Mostashari, Friedland, 2001; Anastasio et al., 1994; Bruckert, Simonetta, Giral, 1999; Fraser, Hadjimichael, Vollmer, 2001; Holzemer et al., 1999; Lin et al., 2003; Malcolm, Ng, Rosen, et al., 2003) (Wagner, 2002)
Belief medications are not important or they're harmful	Decrease	4	(Agarwal et al., 1998; Cohen et al., 1998; Cooper et al., 2002; Peters et al., 2001)
Depression	Decrease Increase None	8 2 1	(Carney, Freedland, Eisen, et al., 1995; Carrieri et al., 2003; Ciechanowski, Katon, Russo, 2000; Coldham et al., 2002; Gordillo, del Amo, Soriano, et al., 1999; Mohr et al., 1997; Wagner, 2003; Wang et al., 2002) (Ayres et al., 1994; Branim, 2003) (Dew et al., 1996)
Other neuropsychological disorders	Decrease	2	(Colom et al., 2000; Wagner, 2002)
Lower cognitive function or impairment	Decrease	6	(Barat, Andreasen, Damsgaard, 2001; Coldham et al., 2002; Cuffel, Alford, Fischer, et al., 1996; Jeste et al., 2003; Wagner, 2003; Wagner, 2002)
Forgetfulness	Decrease	5	(Asawavichienjinda et al., 2003; Cohen et al., 1998; Conway, Pond, Hamnett, et al., 1996; Erlen et al., 2002; Walsh, Horne, Dalton, et al., 2001)
Self-efficacy (increased)	Increase None	5 2	(Auamnoy, 2000; Brus et al., 1999; Dew et al., 1996; Fraser et al., 2001; Wagner, 2003) (Branim, 2003; Wagner, 2002)
Anger	Decrease	5	(Christensen, Moran, Lawton, et al., 1997; Dew et al., 1996; Dodds, 1997; Duncan, Rogers, 1998; Penkower et al., 2003)

Table 2. Factors That Impact Adherence (continued)

FACTOR	EFFECT ON ADHERENCE	NUMBER OF STUDIES	AUTHORS
Patient Psychosocial and Behavioral Characteristics (continued)			
Psychological stress	Decrease	4	(Coons et al., 1994; Eddy et al., 1998; Laidlaw, Beeken, Whitney, et al., 1999; Patton et al., 1997)
Anxiety	Decrease	3	(Dew et al., 1996; Embry, 2003; Wagner, 2002)
	Increase	1	(Ayres et al., 1994)
Health status	Decrease	2	(Coldham et al., 2002; Segal, Tamir, Ish-Shalom, 2003)
	None	1	(Coons et al., 1994)
Having comorbid conditions	None	1	(Coons et al., 1994)
Alcohol/tobacco/substance abuse	Decrease	4	(Coldham et al., 2002; Daniels et al., 1994; Kyngas, 2000; Wagner, 2003)
	None	1	(Colom et al., 2000)
Tired of taking medications	Decrease	1	(Cohen et al., 1998)
Exercise (regular)	Increase	1	(Ayres et al., 1994)
Ability to manage side effects	Increase	1	(Lin et al., 2003)
Motivation	Increase	2	(Kyngas, 2000; Malcolm, Ng, Rosen, et al., 2003)
	None	1	(Wagner, 2002)
Life satisfaction	None	1	(Coons et al., 1994)
Hopelessness	Decrease	1	(van Servellen et al., 2002)
Locus of control (increased)	Increase	2	(Laidlaw et al., 1999; McDonald-Miszczak, Maki, Gould, 2000)
	Decrease	1	(Cooper et al., 2002)
No locus of control	Increase	1	(Wang et al., 2002)
	None	3	(Budd, Hughes, Smith, 1996; Hargrave, Remler, 1996; Lin, Liang, 1997)
Positive attitude	Increase	1	(Kyngas, 2000)
Vigor/fighting spirit	Increase	3	(Ayres et al., 1994; Cohen et al., 1998; Kyngas, 2000)
Sense of mastery	None	1	(Dew et al., 1996)
Use of avoidance coping skills	Decrease	1	(Dew et al., 1996)
Use of active behavioral or cognitive behavioral coping skills	None	1	(Dew et al., 1996)
Use of playful coping skills	None	1	(Lin et al., 2003)

Table 2. Factors That Impact Adherence (continued)

FACTOR	EFFECT ON ADHERENCE	NUMBER OF STUDIES	AUTHORS
Treatment Plan Issues			
Side effects or fear of side effects	Decrease	9	(Alice et al., 2001; Anastasio et al., 1994; Bruckert et al., 1999; Cohen et al., 1998; Conway et al., 1996; Cooper et al., 2002; Demyttenaere et al., 2001; Laidlaw et al., 1999; Segal et al., 2003)
	None	1	(Coldham et al., 2002)
High price/economic issues	Decrease	4	(Asawavichienjinda et al., 2003; Cohen et al., 1998; Laidlaw et al., 1999; Segal et al., 2003)
Embarrassment/cause of social isolation/inconvenience	Decrease	4	(Altice et al., 2001; Conway et al., 1996; Segal et al., 2003; Walsh et al., 2001)
Number of medications (taking 3 or more)	Decrease	3	(Barat et al., 2001; Coons et al., 1994; Kane et al., 2001)
	None	1	(Pettinger et al., 1999)
Doses per day (higher number)	Decrease	1	(Barat et al., 2001)
	None	1	(Wagner, 2002)
Regimen complexity	Decrease	2	(Altice et al., 2001; Cooper et al., 2002)
	None	1	(Wagner, 2002)
Previous adherence	Increase	2	(Pettinger et al., 1999; Wagner, 2003)
Satisfaction with treatment information	Increase	1	(Horne, Hankins, Jenkins, 2001)
Disease-Related Issues			
Severity of disease	Decrease	3	(Ayres et al., 1994; Kyngas, 2000; Wagner, 2002)
	Increase	2	(Gao, Nau, Rosenbluth, et al., 2000; Pettinger et al., 1999)
	None	1	(Ayres et al., 1994)
More symptoms	Decrease	2	(Peters et al., 2001; Wagner, 2002)
Monitoring symptoms	None	1	(Lin et al., 2003)
Age of onset	None	1	(Colom et al., 2000)
Episodic course of illness	Decrease	1	(Agarwal et al., 1998)
Length of illness (longer duration)	None	1	(Gago et al., 2000)
	Decrease	1	(Ayres et al., 1994)
	Decrease	1	(Agarwal et al., 1998)

Table 2. Factors That Impact Adherence (continued)

FACTOR	EFFECT ON ADHERENCE	NUMBER OF STUDIES	AUTHORS
Disease-Related Issues (continued)			
Knowledge of disease	Increase None	1 1	(Wagner, 2002) (Conway et al., 1996)
Perceived risk/susceptibility	Increase None	1 1	(Gao et al., 2000) (Bruckert et al., 1999)
Perceived threat of disease to well-being	Decrease	1	(Kyngas, 2000)
Lack of a perceived threat of disease to wellbeing	Decrease	1	(Cooper et al., 2002)
Viral load in HIV patients	None	1	(Wagner, 2002)
Healthcare System Issues			
Positive/supportive/trusting relationship with provider	Increase	10	(Alice et al., 2001; Ayres et al., 1994; Breen, Thornhill, 1998; Ciechanowski, Katon, Russo, et al., 2001; Fraser et al., 2001; Hausman, 2001; Malcolm, Ng, Rosen, et al., 2003; Olfson et al., 2000; Taylor, Galbraith, Mills, 2002; van Servellen et al., 2002)
More outpatient visits	None	2	(Chadwick, 2001; Fenichel, 1999)
Lack of medications	Increase	2	(Conway et al., 1996; Daniels et al., 1994)
Access to care	Decrease	2	(Cohen et al., 1998; Erlen et al., 2002)
Male providers	Increase	1	(van Servellen, et al., 2002)
Younger providers	Increase	1	(Degli Esposti et al., 2002)
	Increase	1	(Degli Esposti et al., 2002)

Table 3. Models and Theories Useful for Improving Adherence*

AUTHORS	MODELS	KEY CONCEPTS	APPLICATION
(Kasl, Cobb, 1996)	Stages of Health Behavior	<ul style="list-style-type: none"> Health behavior—to prevent illness or to detect it at an asymptomatic stage Illness behavior—in the presence of symptoms, to obtain diagnosis and to discover suitable treatment Sick-role behavior—to receive treatment aimed at restoration of health or at healing disease progression in the presence of a defined illness 	<ul style="list-style-type: none"> A basic understanding of the stages a person may be in is not specific enough to help healthcare providers in decisionmaking
(Carroll et al., 2001)	Contingency Management	<ul style="list-style-type: none"> Highly desired behaviors contingent upon low desired behaviors Rewards given for low desired behavior (gift for taking medicine) 	<ul style="list-style-type: none"> Very useful for shaping desired behaviors
(Cox, 1998)	Social Support	<ul style="list-style-type: none"> Assistance that family or friends can provide to help patient “stay on track” 	<ul style="list-style-type: none"> Mixed research results Problem may be that healthcare provider does not involve family enough upfront
(Moore, 1995)	Theory of Planned Action	<ul style="list-style-type: none"> Intention to perform a behavior is the immediate determinant of an attempt to perform the behavior The individual’s beliefs that specific persons or groups think s/he should or should not perform the behavior and his/her motivation to comply with the specific referents 	<ul style="list-style-type: none"> Extremely useful to consider using these concepts as part of the assessment strategy
(Bastardo, Kimberlin, 2002)	Theory of Planned Behavior	<ul style="list-style-type: none"> Behavior intention—likelihood of performing behavior Behavioral belief—performance is associated with certain outcomes Evaluation—value attached to a behavior outcome Normative belief—whether each referent approves or disapproves of the behavior Motivation to do what each referent thinks Control belief—perceived likelihood of occurrence of helping or constraining condition 	<ul style="list-style-type: none"> Extremely useful to consider using these concepts as part of the assessment strategy Some problems with social desirability when asking patients about intentions to use medicines
(Adams, Scott, 2000; Cohen, Parikh, Kennedy, 2000; Scott, 2002; Steele et al., 2001)	Health Belief Model (Value – Expectancy Theory)	<ul style="list-style-type: none"> The value placed by an individual on a particular goal The individual’s estimate of the likelihood that a given action will achieve the goal <p>Dimensions of the Health Belief Model:</p> <ul style="list-style-type: none"> Perceived susceptibility (re-susceptibility) to condition Perceived severity of condition Perceived benefits of accepting recommended action Perceived barriers of accepting recommended action Strategies to activate one’s readiness Cues to action Self-efficacy—one’s confidence in ability to take action 	<ul style="list-style-type: none"> Useful to consider using these concepts as part of the assessment strategy Perceived severity of illness and perceived benefits of treatment are most predictive of adherence Patient education about illness and benefits of treatment are critical Most studies show the model to be only modestly useful in predicting compliance

*Material adapted from *Patient Adherence Outcome Indicators and Measurement in Case Management Healthcare*, Hamilton GA, RN, DNSc, HOD (hon.), 1999, Paper 1 of 3, Council for Case Management Accountability. With permission of the Case Management Society of America (www.cmsa.org).

Table 3. Models and Theories Useful for Improving Adherence* (continued)

AUTHORS	MODELS	KEY CONCEPTS	APPLICATION
(Dracup, Meleis, 1982)	Interactionist Approach (Symbolic Interaction) Role theory	<ul style="list-style-type: none"> The act of adherence/ non-adherence involves behaviors that are demanded by the performance of a new role The individual's self-concept is a reflection of his/her total repertoire of roles, well, at-risk, or self-role The counter roles played by healthcare provider and family influence adherence if complementary or congruent The periodic evaluations of role enacted by self and those in counter roles in which adherence is evaluated in light of the treatment plan 	<ul style="list-style-type: none"> An understanding of the roles in which people are engaged is helpful to the healthcare provider as a part of the overall assessment
(Budd et al., 1996; Christensen, Wiebe, Lawton, 1997; Hargrave, Remler, 1996; Lin, Liang, 1997; McDonald-Miszczak et al., 2000; Wang et al., 2002)	Locus of Control	<ul style="list-style-type: none"> Internal locus of control (outcomes of treatment under patient's control) External locus of control (outcome of treatment is out of patient's control) 	<ul style="list-style-type: none"> Mixed results in studies mostly showing no correlation between locus of control and compliance Methods of measurement vary widely in the literature Paper and pencil measures may be too difficult for population under study to complete accurately
(Aunannoy, 2000; Berg, 1995; Berg et al., 1997; Brus et al., 1999; Fraser et al., 2001)	Self-Efficacy	<ul style="list-style-type: none"> Person's belief or confidence in his/her own ability to carry out a target behavior Part of Trans-theoretical Model of Change 	<ul style="list-style-type: none"> Extremely powerful concept Good research evidence shows strong correlation between self-efficacy and adherence Should be assessed by healthcare providers
(Willey et al., 2000)	Trans-theoretical Model and Stages of Change	<p>Stages of Change</p> <ul style="list-style-type: none"> Pre-contemplation—has no intention to take action within the next 6 months Contemplation—intends to take action within the next 6 months Preparation—intends to take action within the next 30 days and has taken some behavioral steps in this direction Action—has changed overt behavior for less than 6 months Maintenance—has changed overt behavior for more than 6 months <p>Self-efficacy</p> <ul style="list-style-type: none"> Confidence that one can engage in the behavior across different challenging situations Temptation to engage in the unhealthy behavior across different challenging situations Decisional balance Pros and cons evaluated Processes of change—overt and covert activities that people use to progress through the 6 stages 	<ul style="list-style-type: none"> Really useful way to approach assessment. Some of the strongest evidence for success with adherence is coming from this model Documented evidence of predictive ability of model and ability to improve treatment outcomes

*Material adapted from *Patient Adherence Outcome Indicators and Measurement in Case Management Healthcare*, Hamilton GA, RN, DNSc, HOD (hon.), 1999, Paper 1 of 3, Council for Case Management Accountability. With permission of the Case Management Society of America (www.cmsa.org).

Table 3. Models and Theories Useful for Improving Adherence* (continued)

AUTHORS	MODELS	KEY CONCEPTS	APPLICATION
(Miller, Rollnick, 2002; Berger, Hudmon, et al. 2004)	Motivational Interviewing	<ul style="list-style-type: none">• Ambivalence• Resistance• Dissonance• Readiness to change	<ul style="list-style-type: none">• By assessing ambivalence and resistance, interventions strategies may be individualized• Shows much promise for improving persistence and adherence• Evidence exists that shows significant impact on adherence and persistence

*Material adapted from *Patient Adherence Outcome Indicators and Measurement in Case Management Healthcare*, Hamilton GA, RN, DNSc, HOD (hon.), 1999, Paper 1 of 3, Council for Case Management Accountability. With permission of the Case Management Society of America (www.cmsa.org).

Table 4. Medication Memory Aids

TOOLS	EFFECTIVENESS IN ADDRESSING BARRIER			
	REMEMBERING TO TAKE THE MEDICINE	REMEMBERING IF MEDICINE WAS TAKEN	REDUCING THE REGIMEN COMPLEXITY	REMEMBERING TO REFILL THE PRESCRIPTION
Alarm devices	+++ (Check patient's hearing before using)	+	+	+
Automatic delivery to home				+++
Bingo cards, pill boxes	–	+++	+++	–
Calendars	++ (If properly placed)	++ (If marked off)	++	++ (If included with refill)
Conspicuous sticker placed where it would be noticed	++	–	–	+
Electronic-mail messages				++
Medicine placed where it would be noticed	++	–	–	–
Multidose envelopes	– (Can be portable)	+++	+++	+
Patient diaries	+	++ (If entry made immediately)	–	–
Printed information and materials	+	–	++	+
Provider follow-up	(Reinforcement only)	(Problem solving)	–	++
Refill reminder letters				++
Refill reminder postcards				++
Refill telephone calls				++
Stickers on medicine vials that may be scratched or punched out	+	+++ (If scratch or punch-out variety)	+	+
Tailoring to patient routine	++	–	–	–
Tokens, rewards	+			+

+++ = Very effective solution for the given barrier

++ = Good solution for the given barrier

+ = Limited effectiveness for given solution

– = Poor solution for the given barrier

Table 5. Organizational-Level Technological Initiatives

INITIATIVE	EXPECTED IMPACT	EXPECTED DISCIPLINE(S) INVOLVED	EXPECTED TECHNOLOGICAL REQUIREMENTS
Adherence DUR flags at point of dispensing	Increased persistence and identification of adherence problems	Pharmacist	Pharmacy management system/database
Adherence-focused point of information kiosks	Education for all illiteracies and languages	Pharmacist	Kiosk and interface/barcode scanner
Compliance agents	Identification of adherence problem	Pharmacist	Workstation and application
e-health web sites	Telecommunication, health behavior prompting, and information retrieval	All	Server system
POC multimedia assets	Education for low or no literacy	Pharmacist	Clinical workstation
Computerized prescriber order entry (CPOE)	Decrease drug defaulting, enhanced refill authorization, telecommunication	Prescribers, pharmacists	System with integration and PDA selection
Electronic health record (EHR) community/enterprise delivered	Telecommunication, coordination of care, patient prompting, collaboration, and information	All (with patients)	System with web expression
Central fulfillment	Decreased distribution channel with optional courier/mail delivery	Pharmacist	Facility and integration to pharmacies
Adherence incentives to professionals	Increased attention to problem	Pharmacist, physician	Employers, payers, regulators
Will call tracking/telephony	Increased acute and chronic regimen initiation/persistence	Pharmacist	System with integration to pharmacy management system

Adapted from: Felkey, Fox, 2003.

Table 6. Local, State, and National Initiatives

SPONSORING ORGANIZATION	NAME AND DESCRIPTION OF THE INITIATIVE	TARGET POPULATION
American Heart Association (AHA)	<i>Get With the Guidelines</i> : an educational program to improve adherence to treatment guidelines after a cardiovascular event or stroke. Includes modules on CAD and stroke designed to leverage the “teachable moment” following an acute event.	Physicians and hospitals
AHA and National Committee for Quality Assurance	<i>Heart/Stroke Recognition Program</i> : a program that recognizes physicians in outpatient settings who prevent heart disease and strokes by improving preventive care. The program uses performance measures based on evidence-based guidelines.	Physicians and other healthcare providers
AHA	<i>AHA Compliance Action Program</i> : A web-based educational sheet containing tips for providers and patients to improve treatment adherence	Patients and healthcare providers
AHA and Joint Commission on Accreditation of Healthcare Organizations	<i>Primary Stroke Center Certification</i> : Certification program for Primary Stroke Centers based on evidence-based guidelines including treatment adherence.	Healthcare organizations
AHA and Council for Affordable Quality Healthcare (CAQH)	<i>Heartbeat for Life</i> : a program to improve adherence to beta-blocker therapy following an acute MI. Educational materials are distributed through member health plans and hospitals.	Patients and healthcare providers
Texas Pharmacy Association and AstraZeneca	<i>Texas Hispanic Healthcare Initiatives</i> : a coalition has orchestrated or designed interventions to improve cardiovascular care in the TX Hispanic population through diabetes education and disease management. The targeted interventions are based on existing resources, technologies, best practices, evidence based medicine, and outcomes studies.	Pharmacists and Hispanic patients with diabetes
IPRO (The Quality Improvement Organization for New York State) and Centers for Medicare and Medicaid Services	<i>Diabetes Self-management Education Program</i> : Community based diabetes education and self-management program providing culturally appropriate information. The program uses the Centers for Disease Control and Prevention’s “Take Charge of your Diabetes” curriculum and is attempting to minimize healthcare disparity in New York City. Nursing students and Department for the Aging interns conduct the sessions, and patients are recruited through flyers, web sites, and public service announcements.	African Americans with diabetes
United States Pharmacopeia’s Center for the Advancement of Patient Safety	<i>Think it Through</i> : A brochure created in conjunction with other national healthcare organizations to maximize benefits and minimize errors associated with medication use.	Patients and healthcare providers
University of Mississippi	<i>Pharmaceutical Care Clinics</i> : Pharmacists run disease specific clinics that help patients manage their medications, improve treatment adherence and therapy outcomes. Interventions are evidenced based and outcomes of the programs are monitored.	Patients with specific conditions such as diabetes, asthma, dyslipidemia, etc.
National Council on Parent Information and Education (NCPIE)	<i>Public Awareness Campaigns</i> : “Medicine: Before you take it, talk about it.” Provides a list of questions that patients should ask their healthcare providers. They also distribute a medication card and sponsor the national “Talk About Prescriptions” month each October.	Patients
Food and Drug Administration (FDA) and NCPIE	<i>Take Time to Care</i> : An outreach program developed by the FDA Office of Women’s Health to encourage low-income and minority women to use medications appropriately. The program is modeled after NCPIE’s educational programs.	Patients
Emory University	<i>Low health literacy research projects</i> focusing on pictorial medication cards and reminders.	Low health literacy/ limited English proficiency patients
Plaza Pharmacy and Wellness Center and the City of Asheville and the North Carolina Pharmacy Association	<i>The Asheville Project</i> : Pharmaceutical care program for at risk patients designed to help patients manage their medications, improve treatment adherence and therapy outcomes.	Patients with diabetes and asthma
Plaza Pharmacy and Wellness Center and the American Pharmacy Association	<i>Project Impact</i> : A national pharmacy based program to improve treatment adherence and outcomes for lipid lowering therapy. The program includes training for pharmacists and outcomes monitoring. The interventions are evidence based.	Patients with hyperlipidemia

Table 6. Local, State, and National Initiatives (continued)

SPONSORING ORGANIZATION	NAME AND DESCRIPTION OF THE INITIATIVE	TARGET POPULATION
AnMed Health	<i>Universal Medication Form:</i> A patient-driven tool to help the patient and their providers manage their medication regimens. It is a large type medication lists with areas for directions, notes, start and stop dates, along with other information such as contact information, allergies, and immunizations. Written at the 5th-grade reading level or below. Available in English or Spanish.	Patients
Massachusetts Coalition for the Prevention of Medical Errors	<i>Ambulatory Medication Workgroup:</i> Identifies best practices to decrease med errors, develops tools and educational programs to promote their adoption and supports consumer education.	Healthcare providers and patients
Massachusetts Coalition for the Prevention of Medical Errors	<i>“Your Role in Safe Medication Use”:</i> Patient educational brochure to encourage patients to become a member of the healthcare team. Available in English and Spanish	Patients
Massachusetts Coalition for the Prevention of Medical Errors	<i>Medication Safe Practices for Physician Offices and Ambulatory Settings:</i> A guide with tips to minimize medication errors	Physician offices and clinics
Massachusetts Coalition for the Prevention of Medical Errors	<i>Draft Opportunities to Improve Care:</i> Ambulatory Medication: A white paper recommending a set of safe practices to minimize medication errors in the ambulatory setting	Healthcare providers
Massachusetts Coalition for the Prevention of Medical Errors	<i>Patient Medication List:</i> Prototype for High Risk Patients: a consumer-based list of medication with larger font than the typical wallet card.	Patients
Various Chain Pharmacies	Use of call center staff to contact patients to remind them to refill medication or pick up meds that have been filled	Patients
Various Chain Pharmacies	Product or disease focused programs: Disease or product education information is provided to patient with or without refill reminders. Generally funded in part or in whole by a pharmaceutical manufacturer.	Patients

REFERENCES

- Adams J, Scott J. Predicting medication adherence in severe mental disorders. *Acta Psychiatr Scand*. 2000;101(2):119-124.
- Agarwal MR, Sharma VK, Kishore Kumar KV, et al. Non-compliance with treatment in patients suffering from schizophrenia: a study to evaluate possible contributing factors. *Int J Soc Psychiatry*. 1998;44(2):92-106.
- Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis Process*. 1991;50:179-211.
- Ajzen I. From intentions to action: a theory of planned behavior. In: Kuhl J, Beckman J, eds. *Action Control: From Cognition to Behavior*. New York: Springer-Verlag; 1985, 11-39.
- Ajzen I, Madden, TJ. Prediction of goal-directed behavior: attitudes, intentions, and perceived behavioral control. *J Exp Soc Psychol*. 1986;22:453-474.
- Altice FL, Mostashari F, Friedland GH. Trust and the acceptance of and adherence to antiretroviral therapy. *J Acquire Immune Defic Syndr*. 2001;28(1):47-58.
- Anastasio GD, Little JM, Jr, Robinson MD, et al. Impact of compliance and side effects on the clinical outcome of patients treated with oral erythromycin. *Pharmacotherapy*. 1994;14(2):229-234.
- Asawavichienjinda T, Sitthi-Amorn C, Tanyanont W. Compliance with treatment of adult epileptics in a rural district of Thailand. *J Med Assoc Thai*. 2003;86(1):46-51.
- Auamnoy T. Self-efficacy and non-adherence in post-renal transplant patients. *University of Iowa*. US; 2000, 1.
- Ayres A, Hoon PW, Franzoni JB, et al. Influence of mood and adjustment to cancer on compliance with chemotherapy among breast cancer patients. *J Psychosom Res*. 1994;38(5):393-402.
- Azrin NH, Teichner G. Evaluation of an instructional program for improving medication compliance for chronically mentally ill outpatients. *Behavior Research and Therapy*. 1998;36(9):849-861.
- Balkrishnan R, Christensen DB. Inhaled corticosteroid use and associated outcomes in elderly patients with moderate to severe chronic pulmonary disease. *Clin Ther*. 2000;22(4):452-69.
- Barat I, Andreassen F, Damsgaard EM. Drug therapy in the elderly: what doctors believe and patients actually do. *Brit J Clin Pharmacol*. 2001;51(6):615-622.
- Bastardo YM, Kimberlin CL. Predicting adherence to antiretroviral therapy: an application of an extended theory of reasoned action (APS-P-203). *International Pharmaceutical Federation World Congress*. 2002;62:73.
- Becker MH. The health belief model and sick role behavior. *Health Educ Monogr*. 1990;2:409-419.
- Becker MH, Drachman RH, Kirscht JP. Predicting mother's compliance with pediatric medical regimens. *J Pediatr*. 1972;81:843-856.
- Becker MH, Haefner DP, Kasl SA, et al. Selected psychosocial models and correlates of individual health-related behaviors. *Med Care*. 1977;15(Suppl):27-46.
- Becker MH, Maiman LA. Strategies for enhancing patient compliance. *J Community Health*. 1980;6(2):113-135.
- Becker MH, Maiman LA. Sociobehavioral determinants of compliance with health and medical care recommendations. *Med Care*. 1975;12:10-24.
- Bennett JW, Glasziou P, Del Mar C, et al. A computerized prescribing decision support system to improve patient adherence with prescribing: a randomized controlled trial. *Aust Fam Physician*. 2003;32(8):667-671.
- Berg J. An Evaluation of a Self-Management Program for Adults with Asthma. University of Pittsburgh Doctoral Dissertation (237 p);1995.
- Berg J, Dunbar-Jacob J, Sereika SM. An evaluation of a self-management program for adults with asthma. *Clin Nurs Res*. 1997;6(3):225-238.
- Berger BA, Hudmon KS, Liang H. Predicting treatment discontinuation among patients with multiple sclerosis: application of the transtheoretical model of change. *J Am Pharm Assoc*. 2004;44(4):445-454.
- Bouvy ML, Heerdink ER, Urquhart J, et al. Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: a randomized controlled study. *J Card Fail*. 2003;9(5):404-411.
- Branin JJ. Correlates of strategy use in medication adherence among older adults. *The Claremont Graduate University*. US; 2003, 1.
- Breen R, Thornhill JT. Noncompliance with medication for psychiatric disorders: reasons and remedies. *CNS Drugs*. 1998;9(6):457-471.
- Bruckert E, Simonetta C, Giral P. Compliance with fluvastatin treatment characterization of the noncompliant population within a population of 3845 patients with hyperlipidemia. CREOLE Study Team. *J Clin Epidemiol*. 1999;52(6):589-594.
- Brus H, van de Laar M, Taal E, et al. Determinants of compliance with medication in patients with rheumatoid arthritis: the importance of self-efficacy expectations. *Patient Educ Couns*. 1999;36(1):57-64.
- Budd RJ, Hughes IC, Smith JA. Health beliefs and compliance with antipsychotic medication. *Br J Clin Psychol*. 1996;35(Pt 3):393-397.
- Bukstein DA, Bratton DL, Firriolo KM, et al. Evaluation of parental preference for the treatment of asthmatic children aged 6 to 11 years with oral montelukast or inhaled cromolyn: a randomized, open-label, crossover study. *J Asthma*. 2003;40(5):475-485.
- Bultman DC, Svarstad BL. Effects of pharmacist monitoring on patient satisfaction with antidepressant therapy. *J Am Pharm Assoc*. 2002;42(1):36-43.
- Capoccia KL, Boudreau DM, Blough DK, et al. Randomized trial of pharmacist interventions to improve depression care and outcomes in primary care. *Am J Health Syst Pharm*. 2004;61(4):364-372.
- Carney RM, Freedland KE, Eisen SA, et al. Major depression and medication adherence in elderly patients with coronary artery disease. *Health Psychol*. 1995;14(1):88-90.

- Carrieri MP, Chesney MA, Spire B, et al. Failure to maintain adherence to HAART in a cohort of French HIV-positive injecting drug users. *Int J Behav Med.* 2003;10(1):1-14.
- Carroll KM, Ball SA, Nich C, et al. Targeting behavioral therapies to enhance naltrexone treatment of opioid dependence: efficacy of contingency management and significant other involvement. *Arch Gen Psychiatry.* 2001;58(8):755-761.
- Cattaneo MJ, Sengupta N, Nichol MB. Factors associated with compliance: analysis of the patient's health belief model. *ASHP Midyear Clinical Meeting.* 1999;34(Dec):P-444E.
- Cegala DJ, Marinelli T, Post D. The effects of patient communication skills training on compliance [see comment]. *Arch Fam Med.* 2000;9(1):57-64.
- Chadwick NB. The therapeutic alliance, awareness, and medication compliance in the treatment of schizophrenia. *Medical Coll Georgia.* US; 2001, 1.
- Christensen AJ, Moran PJ, Lawton WJ, et al. Monitoring attentional style and medical regimen adherence in hemodialysis patients. *Health Psychol.* 1997;16(3):256-262.
- Christensen AJ, Wiebe JS, Lawton WJ. Cynical hostility, powerful others control expectancies, and patient adherence in hemodialysis. *Psychosom Med.* 1997;59(3):307-312.
- Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med.* 2000;160(21):3278-3285.
- Ciechanowski PS, Katon WJ, Russo JE, et al. The patient-provider relationship: attachment theory and adherence to treatment in diabetes. *Am J Psychiatry.* 2001;158(1):29-35.
- Claxton AJ, Cramer J, Pierce C. A systematic review of the associations between dose regimens and medication compliance. *Clin Ther.* 2001;23(8):1296-1310.
- Cohen I, Rogers P, Burke V, et al. Predictors of medication use, compliance and symptoms of hypotension in a community-based sample of elderly men and women. *J Clin Pharm Ther.* 1998;23(6):423-432.
- Cohen NL, Parikh SV, Kennedy SH. Medication compliance in mood disorders: relevance of the Health Belief Model and other determinants. *Primary Care Psychiatry.* 2000;6(3):101-110.
- Coldham, EL, Addington J, Addington D. Medication adherence of individuals with a first episode of psychosis. *Acta Psychiatr Scand.* 2002;106(4):286-290.
- Colom F, Vieta E, Martinez-Aran A, et al. Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry.* 2000;61(8):549-555.
- Conway, SP, Pond MN, Hamnett T, et al. Compliance with treatment in adult patients with cystic fibrosis. *Thorax.* 1996;51(1):29-33.
- Coons SJ, Sheahan SL, Martin SS, et al. Predictors of medication noncompliance in a sample of older adults. *Clin Ther.* 1994;16(1):110-117.
- Cox LE. The relative influence of social support on the medication compliance of people with HIV infection. *Virginia Commonwealth University.* US; 1998, 1.
- Cramer JA, Rosenheck R. Enhancing medication compliance for people with serious mental illness. *J Nerv Ment Dis.* 1999;187(1):53-55.
- Cuffel BJ, Alford J, Fischer EP, et al. Awareness of illness in schizophrenia and outpatient treatment adherence. *J Nerv Ment Dis.* 1996;184(11):653-659.
- Daftary MN, Goolsby T, Dutta A, et al. Possible factors influencing non-adherence to antiretrovirals in an ambulatory HIV population. *ASHP Midyear Clinical Meeting.* 2002;37(Dec):P-618E.
- Daniels DE, Rene AA, Daniels VR. Race—an explanation of patient compliance: fact or fiction? *J Natl Med Assoc.* 1994;86(1):20-25.
- Degli Esposti E, Sturani A, Di Martino M, et al. Long-term persistence with antihypertensive drugs in new patients. *J Hum Hypertens.* 2002;16(6):439-444.
- Demyttenaere K, Mesters P, Boulanger B, et al. Adherence to treatment regimen in depressed patients treated with amitriptyline or fluoxetine. *J Affect Disord.* 2001;65(3):243-252.
- Demyttenaere K. Noncompliance with antidepressants: who's to blame? *Int Clin Psychopharmacol.* 1998;13(Suppl 2):S19-S25.
- Dew MA, Roth LH, Thompson ME, et al. Medical compliance and its predictors in the first year after heart transplantation. *J Heart Lung Transplant.* 1996;15(6):631-645.
- DiClemente CC, Prochaska JO. Self-change and therapy change of smoking behavior: a comparison of processes of change in cessation and maintenance. *Addict Behav.* 1982;7:133-142.
- Dixon L, Weiden P, Torres M, et al. Assertive community treatment and medication compliance in the homeless mentally ill. *Am J Psychiatry.* 1997;154(9):1302-1304.
- Dodds JA. Anger, hostility and psychological reactance: Implications for intervention and medical adherence in the coronary patient. *Kent State University.* US; 1997, 1.
- Doren M, Reuther G, Minne HW, et al. Superior compliance and efficacy of continuous combined oral estrogen-progestogen replacement therapy in postmenopausal women. *Am J Obstet Gynecol.* 1995;173(5):1446-1451.
- Dracup KA, Meleis AI. Compliance: an interactionist approach. *Nurs Res.* 1982;31(1):31-36.
- Duncan JC, Rogers R. Medication compliance in patients with chronic schizophrenia: implications for the community management of mentally disordered offenders. *J Forensic Sci.* 1998;43(6):1133-1137.
- Ebrahimzadeh H, Davalos R, Lee PP. Literacy levels of ophthalmic patient education materials. *Surv Ophthalmol.* 1997;42(2):152-156.

- Eddy ME, Carter BD, Kronenberger WG, et al. Parent relationships and compliance in cystic fibrosis. *J Pediatr Health Care*. 1998;12(4):196-202.
- Ehmke DA, Stehbins JA, Young L. Two studies of compliance with daily prophylaxis in rheumatic fever patients in Iowa. *Am J Public Health*. 1980;70:1189-1193.
- Embry LM. Predictors of treatment adherence in pediatric cancer patients. *University of Southern Mississippi*. US; 2003, 1.
- Erlen JA, Sereika SM, Cook RL, et al. Adherence to antiretroviral therapy among women with HIV infection. *JOGN Nurs*. 2002;31(4):470-477.
- Esposito L. The effects of medication education on adherence to medication regimens in an elderly population. *J Adv Nurs*. 1995;21(5):935-943.
- Evangelista L, Doering LV, Dracup K, et al. Compliance behaviors of elderly patients with advanced heart failure. *J Cardiovasc Nurs*. 2003;18(3):197-206; quiz 207-208.
- Felkey BG, Fox BI. Technology to support patient compliance with medication regimens. *Computertalk*. January 2003.
- Fenichel A. The relationship between healthcare clinicians' relational abilities and psychosocial orientation to patient care, and patient adherence with medical treatment. *Columbia University*. US; 1999, 1.
- Fogarty L, Roter D, Larson S, et al. Patient adherence to HIV medication regimens: a review of published and abstract reports [see comment]. *Patient Educ Couns*. 2002;46(2):93-108.
- Fraser C, Hadjimichael O, Vollmer T. Predictors of adherence to Copaxone therapy in individuals with relapsing-remitting multiple sclerosis. *J Neurosci Nurs*. 2001;33(5):231-239.
- Frick PA, Lavreys L, Mandaliya K, et al. Impact of an alarm device on medication compliance in women in Mombasa, Kenya. *Int J STD AIDS*. 2001;12(5):329-333.
- Gago C, Gruss E, Gonzalez S, et al. Compliance of haemodialysis patients with prescribed medication. *EDTNA ERCA J*. 2000;26(4):4-6.
- Gani F, Pozzi E, Crivellaro MA, et al. The role of patient training in the management of seasonal rhinitis and asthma: clinical implications. *Allergy*. 2001;56(1):65-68.
- Gao X, Nau DP, Rosenbluth SA, et al. The relationship of disease severity, health beliefs and medication adherence among HIV patients. *AIDS Care*. 2000;12(4):387-398.
- Gordillo V, del Amo J, Soriano V, et al. Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. *AIDS*. 1999;13(13):1763-1769.
- Green LW, Levine DM, Wolle J, et al. Development of randomized patient education experiments with urban poor hypertensives. *Patient Counseling and Health Education*. 1979;1:106-111.
- Hanlon JT, Weinberger M, Samsa GP, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *Am J Med*. 1996;100(4):428-437.
- Hargrave R, Remler MP. Noncompliance. *J Natl Med Assoc*. 1996;88(1):7, 11.
- Hausman A. Taking your medicine: relational steps to improving patient compliance. *Health Market Q*. 2001;19(2):49-71.
- Haynes RB. Strategies for enhancing patient compliance. *Drug Ther*. 1980; January:147-154.
- Haynes RB, McDonald PM, Garg AX. Helping patients follow prescribed treatment. *JAMA*. 2002;288(12):2880-2883.
- Haynes RB, Wang E, da Mota Gomes M. A critical review of interventions to improve compliance with prescribed medications. *Patient Educ Couns*. 1987;10:155-166.
- Hochbaum GM. Why people seek diagnostic x-rays? *Public Health Rep*. 1956;71:337-380.
- Hoffman L, Enders J, Luo J, et al. Impact of an antidepressant management program on medication adherence. *Am J Manag Care*. 2003;9(1):70-80.
- Holzemer WL, Corless IB, Nokes KM, et al. Predictors of self-reported adherence in persons living with HIV disease. *AIDS Patient Care STDs*. 1999;13(3):185-197.
- Horne R, Hankins M, Jenkins R. The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research [see comment]. *Qual Health Care*. 2001;10(3):135-140.
- Hussey LC. Minimizing effects of low literacy on medication knowledge and compliance among the elderly. *Clin Nurs Res*. 1994;3(2):132-145.
- IOM Committee on Health and Literacy. The extent and associations of limited health literacy. In: Nielsen-Bohlman L, Panzer AM, Kindig DA, eds. *Health Literacy: A Prescription to End Confusion*. Washington, DC: The National Academies Press; 2004, 59-107.
- Isaac LM, Tamblin RM. Compliance and cognitive function: a methodological approach to measuring unintentional errors in medication compliance in the elderly. *Gerontologist*. 1993;33:772-781.
- Jacobson TA, Thomas DM, Morton FJ, et al. Use of a low-literacy patient education tool to enhance pneumococcal vaccination rates: a randomized controlled trial. *JAMA*. 1999;282(7):646-650.
- Janz NK, Becker MH. The health belief model: a decade later. *Health Educ Q*. 1984;11:1-47.
- Jeste SD, Patterson TL, Palmer BW, et al. Cognitive predictors of medication adherence among middle-aged and older outpatients with schizophrenia. *Schizophr Res*. 2003;63(1-2):49-58.
- John-Baptiste A, Naglie G, Tomlinson G, et al. The effect of English language proficiency on length of stay and in-hospital mortality [see comment]. *J Gen Intern Med*. 2004;19(3):221-228.
- Kalichman SC, Catz S, Ramachandran B. Barriers to HIV/AIDS treatment and treatment adherence among African-American adults with disadvantaged education. *J National Med Assoc*. 1999;91(8):439-446.

- Kalichman SC, Ramachandran B, Catz S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy [see comment]. *J Gen Intern Med*. 1999;14(5):267-273.
- Kane SV, Cohen RD, Aikens JE, et al. Prevalence of nonadherence with maintenance mesalamine in quiescent ulcerative colitis. *Am J Gastroenterol*. 2001;96(10):2929-2933.
- Kasl SA, Cobb S. Health behavior, illness behavior, and sick role behavior: I. Health and illness behavior. *Arch Environ Health*. 1966;12:246-266.
- Katon W, Rutter C, Ludman EJ, et al. A randomized trial of relapse prevention of depression in primary care. *Arch Gen Psychiatry*. 2001;58(3):241-247.
- Katon W, Von Korff M, Lin E, et al. Collaborative management to achieve treatment guidelines: impact on depression in primary care. *JAMA*. 1995;273(13):1026-1031.
- Katz EC, Brown BS, Schwartz RP, et al. Role induction: a method for enhancing early retention in outpatient drug-free treatment. *J Consult Clin Psychol*. 2004;72(2):227-234.
- Kegeles SS. Why people seek dental care: a test of conceptual formulation. *J Health Human Behav*. 1963;4:166-173.
- Kemp R, Hayward P, Applewhite G, Compliance therapy in psychotic patients: randomised controlled trial [see comment]. *BMJ*. 1996;312(7027):345-349.
- Kettler LJ, Sawyer SM, Winefield HR, et al. Determinants of adherence in adults with cystic fibrosis. *Thorax*. 2002;57:459-464.
- Krueger KP, Felkey BG, Berger BA. Improving adherence and persistence: a review and assessment of interventions and description of steps toward a national adherence initiative [see comment]. *J Am Pharm Assoc*. 2003;43(6):668-678; quiz 678-679.
- Kutcher S, Leblanc J, MacLaren C, et al. A randomized trial of a specific adherence enhancement program in sertraline-treated adults with major depressive disorder in a primary care setting. *Prog Neuropsychopharmacol Biol Psychiatry*. 2002;26(3):591-596.
- Kyngas H. Compliance with health regimens of adolescents with epilepsy. *Seizure*. 2000;9(8):598-604.
- Laidlaw JK, Beeken JE, Whitney FW, et al. Contracting with outpatient hemodialysis patients to improve adherence to treatment. *ANNA J*. 1999;26(1):37-40.
- Laine L, Estrada R, Trujillo M, et al. Randomized comparison of differing periods of twice-a-day triple therapy for the eradication of *Helicobacter pylori*. *Aliment Pharmacol Ther*. 1996;10(6):1029-1033.
- Laster SF, Martin JL, Fleming JB. The effect of a medication alarm device on patient compliance with topical pilocarpine. *J Am Optom Assoc*. 1996;67(11): 654-658.
- Lecompte D, Pelc I. A cognitive-behavioral program to improve compliance with medication in patients with schizophrenia. *Int J Ment Health*. 1996;25(1):51-56.
- Lee M, Kemp JA, Canning A, et al. A randomized controlled trial of an enhanced patient compliance program for *Helicobacter pylori* therapy. *Arch Intern Med*. 1999;159(19):2312-2316.
- Lesaffre E, Kocmanova D, Lemos PA, et al., A retrospective analysis of the effect of noncompliance on time to first major adverse cardiac event in the Lescol Intervention Prevention Study. *Clin Ther*. 2003;25(9):2431-47.
- Levine AM. Antiretroviral therapy: adherence. *Clinical Care Options for HIV Online Journal*. 1998;4:1-10.
- Liang H. *Decreasing Medication Dropout: A Study to Develop and Evaluate Intervention Software Using the Transtheoretical Model of Change and Motivational Interviewing*. Auburn University; 2003.
- Lin CC, Liang CC. The relationship between health locus of control and compliance of hemodialysis patients. *Kaohsiung J Med Sci*. 1997;13(4):243-254.
- Lin EH, Von Korff M, Ludman EJ, et al. Enhancing adherence to prevent depression relapse in primary care. *Gen Hosp Psychiatry*. 2003;25(5):303-310.
- Lipton HL, Bird JA. The impact of clinical pharmacists' consultations on geriatric patients' compliance and medical care use: a randomized controlled trial. *Gerontologist*. 1994;34(3):307-315.
- Lourens H, Woodward MC. Impact of a medication card on compliance in older people. *Aust J Ageing*. 1994;13(2):72-76.
- Lowe, CJ, Raynor DK, Courtney EA, et al. Effects of self medication programme on knowledge of drugs and compliance with treatment in elderly patients [see comment]. *BMJ*. 1995;310(6989):1229-1231.
- Lowe, CJ, Raynor DK, Purvis J, et al. Effects of a medicine review and education programme for older people in general practice. *Br J Clin Pharmacol*. 2000;50(2):172-175.
- Madoff SA, Pristach CA, Smith CM, et al. Computerized medication instruction for psychiatric inpatients admitted for acute care. *MD Comput*. 1996;13(5):427-431, 441.
- Magura S, Laudet AB, Mahmood D, et al. Adherence to medication regimens and participation in dual-focus self-help groups. *Psychiatr Serv*. 2002;53(3):310-316.
- Malcolm SE, Ng JJ, Rosen RK, et al. An examination of HIV/AIDS patients who have excellent adherence to HAART. *AIDS Care*. 2003;15(2):251-261.
- Margolin A, Avants S, Warburton LA, et al. A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. *Health Psychol*. 2003;22(2):223-228.
- McDonald PM, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication regimens. *JAMA*. 2002;288(12):2868-2879.

- McDonald-Miszczak L, Maki SA, Gould ON. Self-reported medication adherence and health status in late adulthood: the role of beliefs. *Exp Aging Res*. 2000;26(3):189-207.
- Mehta S, Moore RD, Graham NM. Potential factors affecting adherence with HIV therapy. *AIDS*. 1997;11(14):1665-1670.
- Miklowitz DJ, George EL, Richards JA, et al. A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. *Arch Gen Psychiatry*. 2003;60(9):904-912.
- Miller LG, Liu H, Hays RD, et al. Knowledge of antiretroviral regimen dosing and adherence: a longitudinal study [see comment]. *Clin Infect Dis*. 2003;36(4):514-518.
- Miller NH, Hill M, Kottke T, et al. The multilevel compliance challenge: recommendations for a call to action—a statement for healthcare professionals. *Circulation*. 1997;95:1085-1090.
- Miller WR, Rollnick S. *Motivational Interviewing: Preparing People for Change*, 2nd ed. New York: Guilford Press; 2002.
- Miura T, Kojima R, Mizutani M, et al. Effect of digoxin noncompliance on hospitalization and mortality in patients with heart failure in long-term therapy: a prospective cohort study. *Eur J Clin Pharmacol*. 2001;57(1):77-83.
- Mohr DC, Goodkin DE, Likosky W, et al. Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis. *Arch Neurol*. 1997;54(5):531-533.
- Moore SJ. Individuals' beliefs concerning adherence to prescribed antihypertensive medication regimens. Indiana University School of Nursing Dissertation, 1995.
- Mounier-Vehier C, Bernaud C, Carre A, et al. Compliance and antihypertensive efficacy of amlodipine compared with nifedipine slow-release. *Am J Hypertens*. 1998;11(4 Pt 1):478-486.
- Mulrow C, Bailey S, Sonksen PH, et al. Evaluation of an Audiovisual Diabetes Education Program: negative results of a randomized trial of patients with non-insulin-dependent diabetes mellitus. *J Gen Intern Med*. 1987;2(4):215-219.
- Naunton M, Peterson GM. Evaluation of home-based follow-up of high-risk elderly patients discharged from hospital. *Journal of Pharmacy Practice and Research*. 2003;33(3):176-182.
- Nazareth I, Burton A, Shulman S, et al. A pharmacy discharge plan for hospitalized elderly patients: a randomized controlled trial. *Age Ageing*. 2001;30(1):33-40.
- Ngoh LN, Shepherd MD. Design, development, and evaluation of visual aids for communicating prescription drug instructions to nonliterate patients in rural Cameroon. *Patient Educ Couns*. 1997;31(3):245-261. Corrected and republished from *Patient Educ Couns*. 1997;30(3):257-270.
- Norcross JC, Prochaska JO, DiClemente CC. Self-change of psychological distress: laypersons' vs. psychologists' coping strategies. *J Clin Psychol*. 1986;42:834-840.
- O'Donnell C, Donohoe G, Sharkey L, et al. Compliance therapy: a randomised controlled trial in schizophrenia. *BMJ*. 2003;327(7419):834.
- Okonkwo, PO, Akpala CO, Okafor HU, et al. Compliance to correct dose of chloroquine in uncomplicated malaria correlates with improvement in the condition of rural Nigerian children. *Trans R Soc Trop Med Hyg*. 2001;95(3):320-324.
- Olfson M, Mechanic D, Hansell S, et al. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. *Psychiatr Serv*. 2000;51(2):216-222.
- Ortiz F, Fitten LJ. Barriers to healthcare access for cognitively impaired older Hispanics. *Alzheimer Dis Assoc Disord*. 2000;14(3):141-150.
- Owens D, Carroll A, Fattah S, et al. A randomized, controlled trial of a brief interventional package for schizophrenic out-patients. *Acta Psychiatr Scand*. 2001;103(5):362-369.
- Partridge AH, Avorn J, Wang PS, et al. Adherence to therapy with oral antineoplastic agents [see comment]. *J Natl Cancer Inst*. 2002;94(9):652-661.
- Patton K, Meyers J, Lewis BE. Enhancement of compliance among patients with hypertension. *Am J Manag Care*. 1997;3(11):1693-1698.
- Penkower L, Dew MA, Ellis D, et al. Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients. *Am J Transplant*. 2003;3(11):1418-1425.
- Perri M, Martin BC, Pritchard FL. Improving medication compliance: a practical intervention. *J Pharm Technol*. 1995;11(4):167-172.
- Peters KF, Horne R, Kong F, et al. Living with Marfan syndrome II: medication adherence and physical activity modification. *Clin Genet*. 2001;60(4):283-292.
- Peterson GM, McLean S, Senator GB. Determinants of patient compliance, control, presence of complications, and handicap in non-insulin-dependent diabetes. *Aust N Z J Med*. 1984;14:135-141.
- Pettinger MB, Waclawiw MA, Davis KB, et al. Compliance to multiple interventions in a high risk population. *Ann Epidemiol*. 1999;9(7):408-418.
- Peveler R, George C, Kinmonth AL, et al. Effect of antidepressant drug counselling and information leaflets on adherence to drug treatment in primary care: randomised controlled trial [see comment]. *BMJ*. 1999;319(7210):612-615.
- Piette JD, Weinberger M, McPhee SJ, et al. Do automated calls with nurse follow-up improve self-care and glycemic control among vulnerable patients with diabetes? *American J Med*. 2000;108(1):20-27.
- Prochaska JO, DiClemente CC. Common processes of self-change in smoking, weight control and psychological distress. In: Shiffman S, Wills TA, eds., *Coping and Substance Abuse*. New York, NY: Academic Press; 1985, 345-363.
- Prochaska JO, DiClemente CC. *The Transtheoretical Approach: Crossing Traditional Boundaries of Therapy*. Homewood, IL: Dow Jones-Irwin; 1984.
- Prochaska JO, Velicer WF, Guadagnoli E, et al. Patterns of change: dynamic typology applied to smoking cessation. *Multivar Behav Res*. 1991;26:83-107.

- Putnam DE, Finney JW, Barkley PL, et al. Enhancing commitment improves adherence to a medical regimen. *J Consult Clin Psychol*. 1994;62(1):191-194.
- Rand CS, Nides M, Cowles MK, et al. Long-term metered-dose inhaler adherence in a clinical trial: The Lung Health Study Research Group. *Am J Respir Crit Care Med*. 1995;152(2):580-588.
- Rapoff MA, Belmont J, Lindsley C, et al. Prevention of nonadherence to nonsteroidal anti-inflammatory medications for newly diagnosed patients with juvenile rheumatoid arthritis. *Health Psychol*. 2002;21(6):620-623.
- Rawlings MK, Thompson MA, Farthing CF, et al. Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients. *J Acquir Immune Defic Syndr*. 2003;34(2):174-183.
- Razali SM, Hasanah CI, Khan UA, et al. Psychosocial interventions for schizophrenia. *Journal of Mental Health*. 2000;9(3):283-289.
- Rich MW, Gray DB, Beckham V, et al. Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure. *Am J Med*. 1996;101(3):270-276.
- Rosenstock IM. What research in motivation suggests for public health. *Am J Health Promot*. 1960;50:295-302.
- Roter D. Advancing the physician's contribution to enhancing compliance. *Journal of Pharmacoepidemiology*. 1995;3(2):37-48.
- Rzewuska M. Drug maintenance treatment compliance and its correlation with the clinical picture and course of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*. 2002;26(4):811-814.
- Samet JH, Libman H, Steger KA, et al. Compliance with zidovudine therapy in patients infected with human immunodeficiency virus, type 1: a cross-sectional study in a municipal hospital clinic. *Am J Med*. 1992;92:495-502.
- Saunders B, Wilkinson C, Phillips M. The impact of a brief motivational intervention with opiate users attending a methadone programme. *Addiction*. 1995;90(3):415-424.
- Schaffer SD, Tian L. Promoting adherence: effects of theory-based asthma education. *Clin Nurs Res*. 2004;13(1):69-89.
- Schillinger D, Piette J, Grumbach K, et al. Closing the loop: physician communication with diabetic patients who have low health literacy [see comment]. *Arch Intern Med*. 2003;163(1):83-90.
- Schmaling KB, Blume AW, Afari N. A randomized controlled pilot study of motivational interviewing to change attitudes about adherence to medications for asthma. *J Clin Psychol Med Settings*. 2001;8(3):167-172.
- Schoen MD, DiDomenico RJ, Connor SE, et al. Impact of the cost of prescription drugs on clinical outcomes in indigent patients with heart disease. *Pharmacotherapy*. 2001;21(12):1455-1463.
- Scott J. Using Health Belief Models to understand the efficacy-effectiveness gap for mood stabilizer treatments. *Neuropsychobiology*. 2002;46(Suppl 1):13-15.
- Segal E, Tamir A, Ish-Shalom S. Compliance of osteoporotic patients with different treatment regimens. *Isr Med Assoc J*. 2003;5(12):859-862.
- Sellwood W, Barrowclough C, Tarrier N, et al. Needs-based cognitive-behavioural family intervention for carers of patients suffering from schizophrenia: 12-month follow-up [see comment]. *Acta Psychiatr Scand*. 2001;104(5):346-355.
- Sellwood W, Tarrier N. Demographic factors associated with extreme non-compliance in schizophrenia. *Soc Psychiatry Psychiatr Epidemiol*. 1994;29(4):172-177.
- Sleath B, Chewning B, Svarstad B, et al. Patient expression of complaints and adherence problems with medications during chronic disease medical visits. *J Soc Adm Pharm*. 2000;17(21):71-80.
- Smith L, McGowan L, Moss-Barclay C, et al. An investigation of hospital generated pharmaceutical care when patients are discharged home from hospital. *Br J Clin Pharmacol*. 1997;44(2):163-165.
- Solomon DK, Portner TS, Bass GE, et al. Clinical and economic outcomes in the hypertension and COPD arms of a multicenter outcomes study. *J Am Pharm Assoc*. 1998;38(5):574-585.
- Steele RG, Anderson B, Rindel B, et al. Adherence to antiretroviral therapy among HIV-positive children: examination of the role of caregiver health beliefs. *AIDS Care*. 2001;13(5):617-629.
- Stevens VJ, Shneidman RJ, Johnson RE, et al. Helicobacter pylori eradication in dyspeptic primary care patients: a randomized controlled trial of a pharmacy intervention [see comment]. *West J Med*. 2002;176(2):92-96.
- Stewart AV, Eales CJ, Davis KA. Effect of a telephonic intervention on the adherence of patients with hypertension. *South African Journal of Physiotherapy*. 2003;59(1):29-36.
- Stoloff SW, Stempel DA, Meyer J, et al. Improved refill persistence with fluticasone propionate and salmeterol in a single inhaler compared with other controller therapies [see comment]. *J Allergy Clin Immunol*. 2004;113(2):245-251.
- Sturgess IK, McElnay JC, Hughes CM, et al. Community pharmacy based provision of pharmaceutical care to older patients. *Pharm World Sci*. 2003;25(5):218-226.
- Svarstad, B.L., Bultman, D.C., Mount, J.K. Patient counseling provided in community pharmacies: effects of state regulations, pharmacist age, and busyness. *J Am Pharm Assoc*. 2004;44(1):22-29.
- Svarstad BL, Bultman DC, Mount JK, et al. Evaluation of written prescription information provided in community pharmacies: a study in eight states. *J Am Pharm Assoc*. 2003;43(3):383-393.
- Swanson AJ, Pantalon MV, Cohen KR. Motivational interviewing and treatment adherence among psychiatric and dually diagnosed patients. *J Nerv Ment Dis*. 1999;187(10):630-635.
- Tan AS, Yong LS, Wan S, et al. Patient education in the management of diabetes mellitus. *Singapore Med J*. 1997;38(4):156-160.

- Taylor AA, Shoheiber O. Adherence to antihypertensive therapy with fixed-dose amlodipine besylate/benazepril HCl versus comparable component-based therapy. *Congest Heart Fail*. 2003;9(6):324-332.
- Taylor CT, Byrd DC, Krueger K. Improving primary care in rural Alabama with a pharmacy initiative. *Am J Health Syst Pharm*. 2003;60(11):1123-1129.
- Taylor SA, Galbraith SM, Mills RP. Causes of non-compliance with drug regimens in glaucoma patients: a qualitative study. *J Ocul Pharmacol Ther*. 2002;18(5):401-409.
- Van Servellen G, Brown JS, Lombardi E, et al. Health literacy in low-income Latino men and women receiving antiretroviral therapy in community-based treatment centers. *AIDS Patient Care STDS*. 2003;17(6):283-298.
- Van Servellen G, Carpio F, Lopez M, et al. Program to enhance health literacy and treatment adherence in low-income HIV-infected Latino men and women. *AIDS Patient Care STDS*. 2003;17(11):581-594.
- Van Servellen G, Chang B, Garcia L, et al. Individual and system level factors associated with treatment nonadherence in human immunodeficiency virus-infected men and women. *AIDS Patient Care STDS*. 2002;16(6):269-281.
- Varma S, McElnay JC, Hughes CM, et al. Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. *Pharmacotherapy*. 1999;19(7):860-869.
- Venturini F, Nichol MB, Sung JC, et al. Compliance with sulfonylureas in a health maintenance organization: a pharmacy record-based study. *Ann Pharmacother*. 1999;33(3):281-288.
- Volume CI, Farris KB, Kassam R, et al. Pharmaceutical care research and education project: patient outcomes. *J Am Pharm Assoc*. 2001;41(3):411-420.
- Vrijens B, Goetghebeur E. Comparing compliance patterns between randomized treatments. *Controlled Clin Trials*. 1997;18(3):187-203.
- Wagner G. Placebo practice trials: the best predictor of adherence readiness for HAART among drug users? *HIV Clin Trials*. 2003;4(4):269-281.
- Wagner GJ. Predictors of antiretroviral adherence as measured by self-report, electronic monitoring, and medication diaries. *AIDS Patient Care STDS*. 2002;16(12):599-608.
- Wang PS, Bohn RL, Knight E, et al. Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors. *J Gen Intern Med*. 2002;17(7):504-511.
- Weech-Maldonado R, Morales LS, Elliott M, et al. Race/ethnicity, language, and patients' assessments of care in Medicaid managed care. *Health Serv Res*. 2003;38(3):789-808.
- Weinberger M, Murray MD, Marrero DG, et al. Effectiveness of pharmacist care for patients with reactive airways disease: a randomized controlled trial [see comment]. *JAMA*. 2002;288(13):1594-1602.
- Willey C, Redding C, Stafford J, et al. Stages of change for adherence with medication regimens for chronic disease: development and validation of a measure. *Clin Ther*. 2000;22(7):858-871.
- Williford SL, Johnson DF. Impact of pharmacist counseling on medication knowledge and compliance. *Mil Med*. 1995;160(11):561-564.
- Xu KT, Rojas-Fernandez CH. Ancillary community pharmacy services provided to older people in a largely rural and ethnically diverse region: a survey of consumers in West Texas. *J Rural Health*. 2003;19(1):79-86.

APPENDIX A

THEORIES USED IN ADHERENCE RESEARCH AND PRACTICE

Behavioral strategies recognize that adherence to medication regimens requires behavior change. Medications have to be incorporated into patients' daily routines. New habits and behaviors have to be incorporated for effective disease management. For example, patients with diabetes have to take medication, exercise, change eating habits, and monitor their blood glucose—all requiring behavior change. This section attempts to explain behavioral correlates of adherence. Topics such as self-management, self-regulation, self-efficacy, motivational interviewing, readiness for change, and the theory of reasoned action will be covered to identify what factors seem to best predict treatment adherence.

MOTIVATION TO CHANGE

In a study by Carroll and colleagues, contingency management (CM) was employed to increase compliance with naltrexone regimens for patients with opioid drug dependence.¹ Contingency management is a behavioral intervention in which highly desired behaviors are contingent upon performing low-desired behaviors. For example, receiving a gift or reward is contingent upon taking medicine as directed. Recently detoxified opioid-dependent subjects were randomly assigned to: (1) standard naltrexone treatment, given 3 times a week for 12 weeks; (2) naltrexone treatment plus contingency management (CM) for 12 weeks, with delivery of vouchers contingent on naltrexone compliance and drug-free urine specimens; or (3) naltrexone treatment, CM for 12 weeks, plus significant other (SO) involvement, where a family member was invited to participate in up to 6 family counseling sessions. Subjects who received CM had significant improvements in treatment retention (7.4 vs. 5.6 weeks; $P=.05$) and reduction in opioid use (19 vs. 14 opioid-free urine specimens; $P=.04$).

Motivational interviewing is an approach to improving adherence first reported in the addiction literature.² It is a process used to determine readiness to engage in a target behavior (taking a medicine as prescribed) in order to apply specific skills and strategies based upon the patient's level of readiness. Motivational interviewing is used to stimulate or enhance the patient's intrinsic motivation in order to address and resolve ambivalence and resistance.

It is based upon the Transtheoretical Model of Change (TMC). The transtheoretical model for behavior change targets common theoretical elements identified through the analysis of numerous therapy approaches.³ The model provides a framework for understanding behavior change. The model can help healthcare providers to understand various types of behavior change, as well as help them to develop stage-specific interventions. The majority of the empirical groundwork for the model derives from smoking cessation studies,⁴ but the model has also proven its value in addressing other health-related

¹ Carroll KM, Ball SA, Nich C, et al., Targeting behavioral therapies to enhance naltrexone treatment of opioid dependence: efficacy of contingency management and significant other involvement, *Arch Gen Psychiatry*, 2001;58(8):755-761.

² Miller WR, Rollnick S, *Motivational Interviewing: Preparing People for Change*, 2nd ed.; 2002, 428.

³ Prochaska JO, DiClemente CC, *The Transtheoretical Approach: Crossing Traditional Boundaries of Therapy*, Homewood, IL: Dow Jones-Irwin; 1984.

⁴ DiClemente CC, Prochaska JO, Self-change and therapy change of smoking behavior: a comparison of processes of change in cessation and maintenance, *Addict Behavior*, 1982;7:133-142.

behaviors. The model has been applied to smoking, weight control,⁵ psychological distress,⁶ alcohol abuse,⁷ exercise,⁸ and psychiatric disorders.⁹

The TMC has been used successfully to predict patient dropout from drug therapy.¹⁰ In a study of 531 patients, key transtheoretical model concepts (pros and cons of change) allowed for the successful prediction of dropout from the use of Avonex, a medication used for multiple sclerosis, in over 82 percent of the patients. In a study of asthma patients, subjects who received an educational intervention plus motivational interviewing showed a stable or increased readiness to use their asthma medications over time, compared with subjects who received the educational intervention only. Those receiving the educational intervention only showed a decreased readiness to use their medications over time.¹¹

Motivational interviewing was used to improve outpatient treatment adherence among psychiatric and dually diagnosed inpatients. Swanson et al. studied 121 psychiatric inpatients, 93 (77 percent) of whom had concomitant substance abuse/dependence disorders. Subjects were randomly assigned to: a) standard treatment (ST), including pharmacotherapy, individual and group psychotherapy, activities therapy, milieu treatment, and discharge planning; or b) ST plus 15 minutes of motivational interviewing early in the hospitalization and a 1-hour motivational interview before discharge (ST+MI). Motivational interview techniques included reflective listening, discussion of treatment obstacles, and elicitation of motivational statements. Results indicated that the patients in the ST+MI group were significantly more likely to attend their first outpatient appointment (47 percent) than the ST only group (21 percent) overall, and for dually diagnosed patients (42 percent for ST+MI vs. 16 percent for ST only).¹²

Liang used motivational interviewing to create software to be used by a pharmaceutical company's call center to prevent dropout from drug therapy.¹³ Prior to the initiation of the software intervention, the company reported a dropout rate of nearly 13 percent. The intervention was used for three months on a group of patients matched to a control group who received the usual level of care. The dropout rate in the treatment group was 1.2 percent (n=169). This was statistically significantly lower than the control group (p=0.001).

Willey and colleagues applied the stages of change model to understanding why and how patients fail to take their medicines.¹⁴ They constructed a staging algorithm to measure stage of change (SOC) for medication taking involving patients with HIV and patients with hypertension. Predictive validity between the SOC scale, and electronically monitored medication taking was strongly supported by significant associations (p<0.03) over a 30-day period (n=85). The authors state, "Behavior-change theory suggests

⁵ Prochaska JO, DiClemente CC, Common processes of self-change in smoking, weight control and psychological distress. In: Shiffman S, Wills TA, eds., *Coping and Substance Abuse*. New York: Academic Press; 1985:345-363.

⁶ Norcross JC, Prochaska JO, DiClemente CC, Self-change of psychological distress: laypersons' vs. psychologists' coping strategies, *J Clin Psychol*, 1986;42:834-840.

⁷ DiClemente CC, Hughes SO, Stages of change profiles in outpatient alcoholism treatment, *J Subst Abuse*, 1990;2(2):217-235.

⁸ Marcus BH, Rakowski W, Rossi JS, Assessing motivational readiness and decision making for exercise, *Health Psychology*, 1992;11(4):257-261.

⁹ McConaughy EA, Prochaska JO, Velicer WF, Stages of change in psychotherapy: measurement and sample profiles, *Psychotherapy: Theory, Research & Practice*, 1983; 20(3):368-375.

¹⁰ Berger BA, Hudmon KS, Liang H, Predicting treatment discontinuation among patients with multiple sclerosis: application of the transtheoretical model of change, *J Am Pharm Assoc*, 2004; 44(4):445-454.

¹¹ Schmalting KB, Blume AW, Afari N, A randomized controlled pilot study of motivational interviewing to change attitudes about adherence to medications for asthma, *J Clin Psychol in Med Settings*, 2001;8(3):167-172.

¹² Swanson AJ, Pantalon MV, Cohen KR, Motivational interviewing and treatment adherence among psychiatric and dually diagnosed patients, *J Nerv Ment Dis*, 1999;187(10):630-635.

¹³ Liang H, Decreasing medication dropout: a study to develop and evaluate intervention software using the transtheoretical model of change and motivational interviewing, *Auburn University*; 2003.

¹⁴ Willey C, Redding C, Stafford J, et al., Stages of change for adherence with medication regimens for chronic disease: development and validation of a measure, *Clin Ther*, 2000;22(7):858-871.

that tailored intervention strategies are more effective than uniform health-promotion messages. Our validated 2-item measure of SOC for medication adherence can be used to match communication strategies to individual motivation and readiness for adherence with chronic disease medication regimens.”¹⁵

FISHBEIN’S THEORY OF REASONED ACTION

The theory of reasoned action (TRA) states that for a person to engage in a volitional behavior is a strong predictor of the actual behavior, provided that the intention and the behavior take place within a relatively short time span, the behavior is under the individual’s control, and that the behavior is repeatable. This would appear to make medication-taking behavior a candidate for study using the TRA. Moore used the TRA to examine patients’ beliefs and adherence to antihypertensive regimens.¹⁶ Using a convenience sample of 100 patients whose average age was 66, it was found that attitude and past behavior predicted treatment adherence more than other parts of the model. In a study of treatment adherence to antihypertensive medications involving 114 patients, Noel found that while attitude was correlated with behavioral intention, the correlation between behavioral intention and behavior was not significant.¹⁷ Moreover, Noel found significant correlations between a validated social desirability measure and behavioral intentions and behavior. Taking medicine as prescribed may simply be a socially desirable behavior (in regard to intentions) and therefore, the TRA may not always be an appropriate model for use in predicting adherence to medication regimens. In another study employing the TRA, Bastardo found that in HIV-infected individuals there was a relationship between intention to take antiviral medications as prescribed and adherence.”¹⁸ It was concluded that the TRA was useful in predicting adherence in patients with HIV.

LOCUS OF CONTROL

Locus of control involves whether the patient believes that what is happening to him/her or the outcomes of treatment are under his/her control (internal locus of control) or out of his/her control (external locus of control). It is hypothesized that patients with a high internal locus of control are more likely to be compliant with medication regimens.

Budd and colleagues found no correlation between locus of control and compliance.¹⁹ Christensen found that more positive health outcomes in hemodialysis patients are mediated by locus of control. That is, patients who did not believe that positive health outcomes were contingent upon following the advice of significant powerful others (healthcare providers) were more likely to be non-compliant and have negative health outcomes.²⁰ In a study of 31 black males with epilepsy, Hargrave found no significant correlation between locus of control and medication regimen compliance.²¹ Lin and Liang found no significant correlation between locus of control (as measured by the Multidimensional Health Locus of Control instrument) and compliance to medication regimens in hemodialysis patients.²² Another study examined locus of control and self-reported medication adherence in 90 elderly adults (average age was 71.7)

¹⁵ Ibid., 868.

¹⁶ Moore SJ, Individuals’ beliefs concerning adherence to prescribed antihypertensive medication regimens, Indiana University School of Nursing Dissertation, 1995.

¹⁷ Noel OR, Adherence to antihypertensive medication regimens: An application of the Fishbein Behavioral Intention Model, Auburn University Doctoral Dissertation, 1993.

¹⁸ Bastardo YM, Kimberlin CL, Predicting adherence to antiretroviral therapy: an application of an extended theory of reasoned action (APS-P-203), *International Pharmaceutical Federation World Congress*, 2002;62(73).

¹⁹ Budd RJ, Hughes IC, Smith JA, Health beliefs and compliance with antipsychotic medication, *Br J Clin Psychol*, 1996;35(Pt 3):393-397.

²⁰ Christensen AJ, Moran PJ, Lawton WJ, et al., Monitoring attentional style and medical regimen adherence in hemodialysis patients, *Health Psychol*, 1997;16(3):256-262.

²¹ Hargrave R, Remler MP, Noncompliance, *J Natl Med Assoc*, 1996;88(1):7, 11.

²² Lin CC, Liang CC, The relationship between health locus of control and compliance of hemodialysis patients, *Kaohsiung J Med Sci*, 1997;13(4):243-254.

and found a significant correlation.²³ Wang reported a significant positive relationship between locus of control and compliance for those patients who perceived that their health is controlled by external factors.²⁴ This is contrary to what one would expect.

Like so much of the other literature examining other factors affecting compliance, the literature on the impact of locus of control is mixed. There are a few possible explanations. One, the methods of measuring compliance vary significantly (self-report versus electronic monitoring versus pill count, etc.). Many of these methods are known to be unreliable. Also, locus of control is generally measured through the use of paper and pencil instruments. It is not clear whether many of the populations studied were able to fill out the instruments accurately. Often, psychometric data are not included in studies using measurement instruments.

THE HEALTH BELIEF MODEL

This model examines patients' health beliefs about their illness and its treatment. Constructs include perceived susceptibility to the illness, perceived benefits of treatment, and perceived severity of the illness. Numerous studies have tested the ability of the health belief model to predict adherence to medication regimens.

A study by Adams and Scott examined the ability of health belief model (HBM) constructs to predict medication regimen treatment adherence in patients with affective disorder and schizophrenia (n=39).²⁵ The results indicated that perceived severity of illness and perceived benefits of treatment explained 43 percent of the variance in adherence behavior. A study by Cattaneo revealed that the HBM constructs weakly explained compliance behavior in 7,000 patients.²⁶ The model had marginal explanatory power (R squared=0.1428). In a study by Scott, the results revealed that demographic and diagnostic variables did not predict adherence to medication regimens. Furthermore, subjects' beliefs about themselves and their control over the disorder were more important for predicting adherence than the side effects of the medication.²⁷

In a study of HIV-positive children, Steele and colleagues examined the role of parental health beliefs on adherence to antiretroviral therapy in their children.²⁸ All participants were low-income African Americans. There was no significant relationship between HBM constructs measured (parental perceived vulnerability, barriers) and adherence. A review of the literature by Cohen from 1985 to 2000 concluded that the HBM is only modestly useful in distinguishing people who adhere to their medication regimens from those who do not.²⁹ That is consistent with this review.

²³ McDonald-Miszczak L, Maki SA, Gould ON, Self-reported medication adherence and health status in late adulthood: the role of beliefs, *Exp Aging Res*, 2000;26(3):189-207.

²⁴ Wang PS, Bohn RL, Knight E, et al., Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors, *J Gen Intern Med*, 2002;17(7):504-511.

²⁵ Adams J, Scott J, Predicting medication adherence in severe mental disorders, *Acta Psychiatr Scand*, 2000;101(2):119-124.

²⁶ Cattaneo MJ, Sengupta N, Nichol MB, Factors associated with compliance: analysis of the patient's health belief model, *ASHP Midyear Clinical Meeting*, 1999;34(Dec):P-444E.

²⁷ Scott J, Using health belief models to understand the efficacy-effectiveness gap for mood stabilizer treatments. *Neuropsychobiology*, 2002;46(Suppl 1):13-15.

²⁸ Steele RG, Anderson B, Rindel B, et al., Adherence to antiretroviral therapy among HIV-positive children: examination of the role of caregiver health beliefs, *AIDS Care*, 2001;13(5):617-629.

²⁹ Cohen NL, Parikh SV, Kennedy SH, Medication compliance in mood disorders: relevance of the Health Belief Model and other determinants, *Primary Care Psychiatry*, 2000,6(3):101-110.

SELF-EFFICACY

Self-efficacy is a person's belief or confidence in his/her own ability to carry out a target behavior and the extent to which the behavior is actually carried out correctly. Numerous studies have examined the relationship between self-efficacy and treatment adherence.

In a study by Auamnoy, self-efficacy was measured to examine if it predicted adherence to medication regimens for self-administration of three classes of drugs; antihypertensive agents, antirejection agents, and antibiotics.³⁰ Self-efficacy not only significantly predicted adherence, it also predicted quality of life measures. Specifically, a patient's effective ability to take their medications on a regular schedule is a direct function of self-confidence in readiness to do so. It is interesting to note that self-confidence and readiness are hallmarks of the TMC and motivational interviewing.

Research by Berg and Berg and colleagues demonstrated that a self-management program given to asthma patients significantly increased compliance with inhaled medications.³¹ Patients with rheumatoid arthritis were studied to examine which factors correlated with compliance with medication regimens.³² Factors included personal factors, demographic variables, disease-related factors, barriers to compliance, and self-efficacy. Only self-efficacy correlated highly with compliance ($r=0.58$, $p<0.001$). In a logistic regression analysis, only self-efficacy was associated with adherence greater than 80 percent.

Fraser examined factors associated with adherence to copaxone therapy, an injection used for multiple sclerosis using logistic regression as well. The four predictors of adherence were self-efficacy (control), hope, perception that the doctor was the most supportive of the individual taking Copaxone, and no previous use of other immunomodulators. There was a direct correlation between the individual's likely adherence to Copaxone therapy and their MS Self-Efficacy Control Subscale score. Similarly the higher an individual scored on the Herth Hope Index (HHI), the more likely the individual will adhere to Copaxone therapy.³³

Numerous other articles in the literature support self-efficacy as a significant predictor of treatment adherence with drug therapy.

DEPRESSION

Many studies have examined the impact of depression on compliance. Generally, it has been found that patients with chronic illnesses who are depressed have significantly lower rates of compliance. In a study by Mohr and colleagues, 35 of the 85 patients reported new or increased depression within 6 months of initiating therapy with IFN beta-1b. Patients who experienced psychotherapy or antidepressant therapy were more than twice as likely to stay on drug (86 percent versus 38 percent) than patients who were not treated for depression ($p=0.03$). Treatment adherence patterns were consistent across various sites.³⁴

³⁰ Auamnoy T, Self-efficacy and non-adherence in post-renal transplant patients, *University of Iowa*, US; 2000, 1.

³¹ Berg J, *An Evaluation of a Self-Management Program for Adults with Asthma*, University of Pittsburgh. Doctoral Dissertation (237 p);1995; Berg J, Dunbar-Jacob J, Sereika SM, An evaluation of a self-management program for adults with asthma, *Clin Nurs Res*, 1997;6(3):225-238.

³² Brus H, van de Laar M, Taal E, et al., Determinants of compliance with medication in patients with rheumatoid arthritis: the importance of self-efficacy expectations, *Patient Educ Couns*, 1999;36(1):57-64.

³³ Fraser C, Hadjimichael O, Vollmer T, Predictors of adherence to Copaxone therapy in individuals with relapsing-remitting multiple sclerosis, *J Neurosci Nurs*, 2001;33(5):231-239.

³⁴ Mohr DC, Goodkin DE, Likosky W, et al., Treatment of depression improves adherence to interferon beta-1b therapy for multiple sclerosis, *Arch Neurol*, 1997;54(5):531-533.

In a year-long study of 496 patients with high blood pressure, clinical depression was significantly associated with non-compliance (95 percent confidence interval, odds ratio of .87 to .99).³⁵ Carney and associates studied the impact of depression on medication taking for elderly patients with coronary heart disease.³⁶ Medication adherence was assessed over a three-week period using an electronic monitoring device. Depressed patients adhered to therapy regimens on 45 percent of the days, while non-depressed patients adhered on 69 percent of the days ($p<0.02$). It appears that major depression may have a significant impact on adherence in coronary heart disease. Depression was also significantly associated with non-adherence in a study of 96 patients taking antiretroviral therapy.³⁷ Similar findings in regards to HIV-positive patients were reported in other studies.³⁸

Numerous other studies focusing on managing chronic illnesses report a strong negative correlation between depression and medication regimen adherence. It is vital that practitioners be aware of the effects of depression on adherence. If depression is suspected, tools such as the Beck Inventory should be used to identify or rule out clinical depression.

SOCIAL SUPPORT

Patients live in a social environment. Social support involves help that family members or significant others may provide in assisting the patient with medication regimen adherence. Therefore, the degree of social support may be a mediating factor in treatment adherence.

Cox examined the impact of social support on compliance in patients with HIV disease.³⁹ In her study of 179 HIV infected patients, Cox attempted to discern the relative influence of specific social support indicators between groups of patients labeled “Good Compliers” and “Poor Compliers,” as measured by clinician and study participant ratings. The investigator concluded that higher levels of social support did not appear to be significantly correlated with higher levels of medication compliance. Emotional support was significant as examined with independent samples, t-tests, and discriminant function techniques. The level of emotional support and employment status were used to distinguish “Good Compliers” from “Poor Compliers.” Other studies showed weak or no correlation between social report and compliance. What is problematic about many of these studies is that most measures of social support are self-reported measures.

STRESS AND ANXIETY

Much research has evaluated the impact of psychological distress on treatment adherence. In a study of over 1,000 adults over the age of 55, measures of psychological distress and medication compliance were collected from structured interviews, and psychological distress was significantly negatively correlated with medication compliance ($p<0.05$).⁴⁰ Eddy and colleagues found that psychological stress between

³⁵ Wang PS, Bohn RL, Knight E, et al., Noncompliance with antihypertensive medications: the impact of depressive symptoms and psychosocial factors, *J Gen Intern Med*, 2002;17(7):504-511.

³⁶ Carney RM, Freedland KE, Eisen SA, et al., Major depression and medication adherence in elderly patients with coronary artery disease, *Health Psychol*, 1995;14(1):88-90.

³⁷ Carrieri MP, Chesney MA, Spire B, et al., Failure to maintain adherence to HAART in a cohort of French HIV-positive injecting drug users, *Int J Behav Med*, 2003;10(1):1-14.

³⁸ Daftary MN, Goolsby T, Dutta A, et al., Possible factors influencing non-adherence to antiretrovirals in an ambulatory HIV population, *ASHP Midyear Clinical Meeting*, 2002;37(Dec):P-618E; Gordillo V, del Amo J, Soriano V, et al., Sociodemographic and psychological variables influencing adherence to antiretroviral therapy, *AIDS*, 1999;13(13):1763-1769.

³⁹ Cox LE, The relative influence of social support on the medication compliance of people with HIV infection, *Virginia Commonwealth University*, US; 1998.

⁴⁰ Coons SJ, Sheahan SL, Martin SS, et al., Predictors of medication noncompliance in a sample of older adults, *Clin Ther*, 1994;16(1):110-117.

parents and their children with cystic fibrosis had a significant impact on treatment adherence.⁴¹ The stress is usually precipitated from disagreements between the parents and children about treatment plans. Stress was also associated with poorer disease outcomes in these subjects. The impact of a self-help group on stress and treatment adherence in patients with psychiatric disorders was examined in a study by Magura and colleagues.⁴² The self-help group meetings focused on reducing or resolving stressful life events. Attendance at the meetings was strongly associated with improved medication compliance.

In a before-and-after study of patients with hypertension, nurses provided patients with interventions on a periodic basis to deal with stress, improve compliance with medication regimens, and educate patients about their illness and its treatment.⁴³ Statistically significant reductions in blood pressure resulted ($p=0.01$) and there was a relationship between improved adherence and decreased blood pressure even though the overall adherence rate did not change significantly over the year. The effect of a telephonic behavior change program was measured in a study by Stewart et al.⁴⁴ The treatment group received this intervention and the control did not. The intervention focused on psychological distress and modification of health behaviors. The treatment group showed statistically significant ($p<0.01$) greater adherence, better knowledge of hypertension, and better control than the control group, and had greater exercise capacity, greater reduction in weight, and were less tired and had less headaches and dizziness.

Embry examined the impact of psychological variables on treatment adherence in pediatric cancer patients.⁴⁵ Family cohesion was positively correlated with adherence, while parental anxiety, child anxiety, and externalizing behavior problems were negatively correlated with adherence. Regression analyses indicated that parental anxiety, child anxiety, and the child's fear of death and danger were significant predictors of adherence, and together accounted for nearly 28 percent of the variance in adherence rates. Overall, it appears that reduction in psychological distress has a positive impact on medication regimen compliance.

ANGER

Another form of psychological distress is anger. Dodds examined anxiety, hostility, and psychological reactance and their impact on treatment adherence in patients with coronary heart disease.⁴⁶ The relationship between anger and adherence was studied controlling for hostility, psychological reactance, and their interactions. The study sample was small (84 patients), predominantly male (76 percent) and Caucasian (85 percent) with 76 percent having the diagnosis more than five years. The study group had more anger and lower adherence relative to norm groups. Anger was correlated with poor adherence controlling for hostility, and psychological reactance, however, none of the other variables and none of the interactions among the variables showed a statistically significant correlation to adherence.

⁴¹ Eddy ME, Carter BD, Kronenberger, WG, et al., Parent relationships and compliance in cystic fibrosis, *J Pediatr Health Care*, 1998;12(4):196-202.

⁴² Magura S, Laudet AB, Mahmood D, et al., Adherence to medication regimens and participation in dual-focus self-help groups, *Psychiatr Serv*, 2002;53(3):310-316.

⁴³ Patton K, Meyers J, Lewis BE, Enhancement of compliance among patients with hypertension, *Am J Manag Care*, 1997;3(11):1693-1698.

⁴⁴ Stewart AV, Eales CJ, Davis KA, Effect of a telephonic intervention on the adherence of patients with hypertension, *South African Journal of Physiotherapy*, 2003;59(1):29-36.

⁴⁵ Embry LM, Predictors of treatment adherence in pediatric cancer patients, *University of Southern Mississippi*, US; 2003, 1.

⁴⁶ Dodds JA, Anger, hostility and psychological reactance: implications for intervention and medical adherence in the coronary patient, *Kent State University*, US; 1997, 1.

Penkower and colleagues examined the impact of various forms of psychological distress on adherence in 22 adolescent renal transplant patients aged 13-18. The results indicated that adolescents with excessive anger were at greater risk for subsequently missing medications than adolescents without excessive anger. However, similar results were not seen for other forms of psychological distress such as anxiety and depression.⁴⁷

In a study conducted by Duncan and Rogers, anger was a key symptom associated with non-compliance with medication regimens for patients with schizophrenia.⁴⁸ Christensen reports that higher hostility in patients is significantly associated with poorer compliance and health in hemodialysis patients.⁴⁹ Numerous other studies reported similar findings. As reported on other studies of psychological distress and non-compliance, it seems clear that anger is associated with non-compliance. It will take a very caring, clear, and skillful practitioner to recognize and confront a patient's anger in dealing with non-compliance.

⁴⁷ Penkower L, Dew MA, Ellis D, et al, Psychological distress and adherence to the medical regimen among adolescent renal transplant recipients, *Am J Transplant*, 2003;3(11):1418-1425.

⁴⁸ Duncan JC, Rogers R, Medication compliance in patients with chronic schizophrenia: implications for the community management of mentally disordered offenders, *J Forensic Sci*, 1998;43(6):1133-1137.

⁴⁹ Christensen AJ, Wiebe JS, Lawton WJ, Cynical hostility, powerful others control expectancies, and patient adherence in hemodialysis, *Psychosom Med*, 1997;59(3):307-312.

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