

Medication Adherence: Truth and Consequences



Marie T. Brown, MD, Jennifer Bussell, MD, Suparna Dutta, MD, MPH,
Katherine Davis, RN, BSN, Shelby Strong, APN, MSN and
Suja Mathew, MD

ABSTRACT

Improving medication adherence may have a greater influence on the health of our population than in the discovery of any new therapy. Patients are nonadherent to their medicine 50% of the time. Although most physicians believe nonadherence is primarily due to lack of access or forgetfulness, nonadherence can often be an intentional choice made by the patient. Patient concealment of their medication-taking behavior is often motivated by emotions on the part of both provider and patient, leading to potentially dire consequences. A review of the literature highlights critical predictors of adherence including trust, communication and empathy, which are not easily measured by current administrative databases. Multifactorial solutions to improve medication adherence include efforts to improve patients' understanding of medication benefits, access and trust in their provider and health system. Improving providers' recognition and understanding of patients' beliefs, fears and values, as well as their own biases is also necessary to achieve increased medication adherence and population health.

Key Indexing Terms: Medication adherence; Compliance; Nonadherence; Trust; Electronic prescribing. [*Am J Med Sci* 2016;351(4):387–399.]

INTRODUCTION

Approximately 117 million Americans live with at least 1 or more chronic diseases, often requiring multiple lifelong medications for control.¹ Improving medication adherence may have a greater influence on the health of the population than in the discovery of any new therapy. Effective medicines are available for many conditions and yet patients are nonadherent to their medicine 50% of the time. In certain disease states, potentially asymptomatic conditions such as hypertension, the incidence may approach 80%. Patients may conceal their medication-taking behavior, often motivated by emotions on the part of both provider and patient. Patient-related factors have a greater influence predicting adherence than provider-related or payment-related variables.² Although most physicians believe nonadherence is due to lack of access or poor memory, it is often an intentional choice by the patient. Critical predictors of adherence are trust, understanding and provider-patient relationships, which are absent from current databases. Improving medication adherence is the “next frontier in quality improvement.”^{3,4}

METHODS

We conducted a MEDLINE database literature search limited to English language articles published between January 1, 2010 and May 31, 2015, using the following search terms: medication adherence, diabetes mellitus and cardiovascular disease. Of the 684 articles retrieved, those that did not address medication adherence in the abstract were excluded, leaving 149 for inclusion in the review. Additional references were obtained from citations within the retrieved articles.

GENERAL ASPECTS OF MEDICATION ADHERENCE

Medication-taking behavior is complex, requiring multifaceted strategies to effect improvement. Since the 2003 World Health Organization report on medication adherence, little has improved and adherence remains dismal at an estimated 50%.⁵ The “best practices” for disease control are often difficult to attain as the “key”—medication adherence—is needed to reach better health outcomes.

Medication adherence is defined as the extent to which a patient adheres to the prescribed dose and interval of their medication regimen. Patients are considered adherent to their medication when the number of pills absent in a given period divided by the number of pills prescribed by the physician in that same period is greater than 80%. One can miss almost a week of medication during a month and still be considered adherent.

Various other methods have been described to measure medication adherence. Approaches include self-reported surveys, pill counts, drug levels, physiological measures, pharmaceutical claims, electronic medication monitoring and physician ordering in electronic health records (EHRs). Each method has inherent limitations, and a combination of these measures is used in studies, leading to substantial heterogeneity in the evidence base.

Recent literature has used pharmaceutical claims to study medication adherence using insurance-based data sources to evaluate medication refill patterns. This approach provides information on the rate of medication possession by patients, which may or may not accurately correlate with actual medication taking. The pharmaceutical claims report a medication possession

ratio (MPR), a proportion of days covered (PDC) or a cumulative medication gap to provide objective measure of medication adherence information. MPR is the number of days of medication supplied within the refill interval per number of days in the refill interval. To calculate this ratio, at least 2 medication refill dates are needed (eg, index date and at least 1 refill). The PDC is the total days of all drug(s) available per day in the follow-up period. The PDC provides more conservative estimate when multiple medications are used concomitantly. The PDC also avoids double-counting days of medication coverage because a day is only counted if all medications are available on that day. The PDC values range from 0-1. Medication persistence is defined as "the duration of time from initiation to discontinuation of therapy."⁶ This is resulted as the percentage of individuals remaining on therapy (persistent) during a specified time interval. Nonpersistence occurs when the patient stops taking a medication on their own initiative.

The EHR that tracks physician ordering and patient refilling of chronic medications now offer an opportunity to capture otherwise undocumented cases of primary nonadherence or nonpersistence. Before EHR medication data, medication adherence may have been greatly overestimated as first-fill rates were not easily available. This is of paramount importance as 25–40% of patients do not fill a primary prescription.⁷ Patients filling index prescriptions (first prescription) is crucial as filling this first prescription has shown to improve clinical outcomes. For example, increasing primary adherence to diabetic or antihypertensive medications yielded a 3-fold reduction in hemoglobin A1c levels and significantly lowered blood pressure readings.^{8,9}

CONSEQUENCES

Medication nonadherence leads to poor outcomes, increasing healthcare service utilization and overall healthcare costs. Nonadherence to cardiovascular medications

has been associated with increased risks of morbidity and mortality.^{10,11} As the U.S. population ages, the need to medically manage multiple chronic illness increases.¹² Medication nonadherence is estimated to lead to between \$100 and \$300 billion of avoidable healthcare costs in the United States annually, representing 3–10% of total U.S. healthcare costs.¹³ It has been estimated that health-related productivity loss costs are 2.3 times higher than the direct healthcare costs.¹⁴

In 2007, Roebuck et al studied the relationship between medication adherence in patients with chronic vascular conditions (congestive heart failure, hypertension, diabetes and dyslipidemia) and the use and cost of healthcare services. In patients with chronic vascular diseases, adherence reduced total annual healthcare spending, despite an increase in pharmaceutical costs. Annually, medication adherence in patients with 1 or more chronic vascular conditions resulted in a reduction of average medical spending by \$8,881 in congestive heart failure, \$4,337 in hypertension and \$4,413 in diabetes (Figure 1).¹⁵ Improved adherence to diabetes medication could avert 699,000 emergency department visits and 341,000 hospitalizations annually, for a saving of \$4.7 billion.¹⁶

TRUTH

Nonadherence to medication is often hidden. The critical first step in improving adherence is uncovering its presence. In a study by Lapane et al,¹⁷ 83% of patients would never tell a provider that they were not going to fill a new prescription, although providers estimated only 9% would withhold such information. Patients are often reluctant to disclose their true medication-taking behavior for a variety of reasons, unsure of their provider's reaction to their nonadherence. Just as illiteracy is often hidden from employers and even family, so nonadherence often remains concealed. Clues to poor literacy include missed appointments, excuses such as leaving

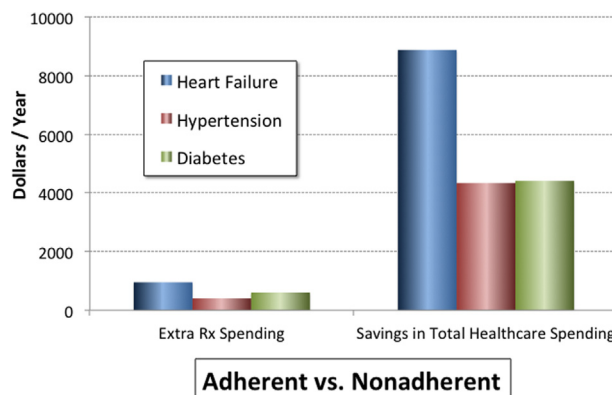


FIGURE 1. Adherence leads to total healthcare savings. This analysis of over 135,000 individuals examined the relationship between medication adherence and the total annual cost of health services with congestive heart failure, hypertension or diabetes or all of these. Increases in medication spending combined with the decreases in medical spending (primarily from lower hospital and emergency room costs) resulted in an average benefit-cost ratio of 10.1:1 for hypertension, 8.4:1 for congestive heart failure and 6.7:1 for diabetes. (Adapted from Roebuck et al.¹⁵)

their eyeglasses at home or promising to read information later. So too, clues to identify nonadherence include nonaligned pill counts, missed refills, escalating therapies without improvement in clinical measures, presence of depression or use of alternative medicines.¹⁸

In clinical practice, assessing adherence is usually accomplished by self-report. Studies have shown that this may overestimate adherence by 200%.¹⁹ Asking the patient if they are taking their medicines is necessary but not sufficient. The veracity of the patient's response may depend on how the question is asked and who is making the inquiry. During medication reconciliation, a member of the healthcare team reviews the list of medications and asks if refills are needed, inquires about side effects and affordability and adds any new medicines or supplements to the medication profile. An opportunity to discuss whether or not a patient is regularly taking the medicines or has stopped a medicine or has questions about the medicines is rarely provided. An assumption is made that if the list on screen matches the pill bottles at home then adherence has been addressed. The important question of whether the medicines are actually being taken often has not been asked. Therapeutic decisions are then based on inaccurate assumptions of adherence, which can lead to escalation of therapies if clinical metrics such as HbA1c or blood pressure are not at goal. This may lead to catastrophic consequences, especially upon hospital admission, as the patient can be abruptly started on their listed medicines with resultant hypotension or hypoglycemia. These symptoms may occur days after admission and not be readily attributed to medicines started in the hospital.

A Nonaccusatory Approach Is Critical

The manner in which the patient is queried regarding their medication-taking behavior has a great influence on whether the patient shares their actual adherence history. A consistently blame-free environment must be present for the patients to feel comfortable sharing their nonadherence, whether by direct inquiry or completion of a questionnaire. If patients reveal that they have not been adherent and the response by any healthcare team member is less than empathetic, the patient may avoid future revelations of their nonadherent behavior.

Who Assesses Adherence Influences the Response

It is often unclear who has ultimate responsibility for assessing adherence in any given practice setting. Encouraging patients to disclose their behaviors may be challenging as well as time-consuming, often assigned to the medical assistant or patient tech. That person may or may not have the trust of the patient or the skills or both to evaluate adherence. The most effective person to assess adherence is the healthcare team member who the patient most trusts and the most

experienced person at suspecting and identifying nonadherence, which may vary by practice.

Increased adherence has been demonstrated in studies which reflect social or cultural interactions between patient and physician such as sex concordance or country of physician's education. Familiarity with the provider or the institution increases adherence as demonstrated by studies measuring the influence of continuity of care (ongoing relationship over time), especially in patients with diabetes.^{3,20}

Emotional Barriers to Revealing True Medication-Taking Behavior

What motivates patients to conceal actual medication-taking behavior? Patients' emotions may suppress the truth. Several emotions or biases are common.

Social Desirability Bias: Patients Tell the Provider What They Think the Provider Wants to Hear²¹

Patients' actions are based on their knowledge and experience as are providers. Knowing that the provider believes that the medicine should be taken, failing to follow the recommendations might be viewed as an affront to the skill and competence of the provider. When nonadherent patients do not have the opportunity to discuss their concerns about a medicine, they may feel that they have no alternative to offending the clinician but to hide their actions. Once nonadherence is identified, the provider may respond emotionally, feeling angry and frustrated that their advice was not followed (why is my advice not followed or trusted?), hopeless that as providers they have done their job (I am providing evidence-based recommendations), betrayed that the patient was not more forthcoming (why would my patient hide it from me?) or irritated that they incorrectly escalated therapy based on wrong patient-provided information. All these reactions contribute to the patient's unwillingness to be honest. People prefer to answer in the affirmative leading to "white coat adherence" (initiating medications 1 or 2 days before office visit). Adherence for several days to insulin results in glucose at control, however, only when hemoglobin A1c testing became routine could adherence over 3 months be assessed accurately.

Fear of Being Admonished or Punished

The provider-patient relationship may be viewed as unequal. The provider is often viewed as having more education, knowledge and power. Finding that advice is not being followed may result in reprimands for patients' "foolishness," accusations of distrust in the provider or lack of appreciation for the provider's time. These all result in an unpleasant experience that the patient is likely to avoid in the future, promoting the cycle of nondisclosure.

As more pay for performance models are instituted, poorly controlled blood pressure and diabetes measures may adversely affect the physician's personal income and publicly reported quality-of-care measures may reflect poorly on the provider. Patient and physician can appear in this case to be adversaries rather than partners. Unintended consequences may occur, subtly encouraging the patient to seek care elsewhere.

Fear of Embarrassment

Patients may be embarrassed to reveal that their financial situation prevented their ability to obtain their medicines. Altruism, placing the needs of others before one's own may lead patients to sacrifice financial resources to provide support for other family members' needs. Altruism is valued by physicians and patients alike and is a key attribute of our profession, but the same motivation may contribute to patients' nonadherence. Patients may fear appearing foolish or less educated by asking questions regarding the need for or duration of a medicine regimen.

ASSESSING ADHERENCE, TRUST AND LITERACY

Measurement of adherence is a complex process with no gold standard. Numerous methods have been used. Direct measurements of adherence (body fluid assays of drug or direct observation of taking medicines) are resource driven and not well adapted to clinical use. Indirect measurements, both subjective and objective, rely on self-reporting such as the Morisky Scale, TABS: Tool for Adherence Behaviour Screening, MAR-scale: Medication Adherence Reasons-scale, pill counts either manually or electronically and increasingly, review of pharmacy refill records such as MedsIndex, MPR.²² Relying on the latter, especially mail order refills, assumes that because the patient is in possession of the medicine, the medicine is being taken. This results in overestimation of adherence. Refills obtained from alternative pharmacies may lead to underestimation.²³ The 8-item or 4-item Morisky Scale is frequently used. It is simple, measures intentional and unintentional causes of nonadherence, has been validated across disease states and internationally and is available in a short form for screening. Simple self-reported measures of nonadherence have been shown to be valid even in depressed patients.²⁴ Multiple methods may be required to identify patients most in need of intervention.

Important factors influencing adherence including trust, patient understanding and satisfaction, provider-patient communication and social support cannot be easily obtained from administrative databases. Efforts to measure the quality of the physician-patient relationship have been elusive. Current interventions have had a small influence on improving adherence, therefore measurement of additional factors influencing adherence are vital. The 10-item Health Care System Distrust Scale

developed by Rose et al²⁵ is 1 such tool. Once non-adherence is identified, the critical second step lies in understanding the reason for nonadherence.

Institutions adopting "universal precautions" against nonadherence and health illiteracy, encourage clinicians to assume patients may not take their medicine or understand directions until proven otherwise. Instead of asking "do you have any questions?" and asking "what are your questions?," allowing the patient to feel that asking questions is normal and welcomed.

OBSTACLES TO ADHERENCE: PATIENT PERSPECTIVE

Mistrust

Studies have demonstrated a direct effect of trust in the physician or health system on medication nonadherence, delay in seeking care and failure to keep appointments. This effect is unrelated to racial and ethnic concordance of patient and provider.²⁶ Although trust is increasingly identified as an important predictor of adherence, widespread healthcare-related distrust has grown significantly and is pervasive among all socio-demographic groups. Determinants of this mistrust include less continuity of care with personal physicians, increased access to and conflicting medical information, cost containment strategies that include restricted access, disclosures of unethical research, medical errors and malpractice. Increasing distrust may annul advancements in medical knowledge, negatively impacting patient satisfaction, adherence and patient-provider relationships (Figure 2).²⁵

Mistrust, though prevalent in all sociodemographic groups, is consistently higher in certain minorities. In view of the health disparities and historical treatment of the African-American community, trust plays an even greater determinant of healthcare outcomes in this population. Racial discrimination, centuries of mistreatment and the infamous Federally funded clinical Tuskegee Syphilis Study performed in the latter half of the 20th century contribute to mistrust especially among African Americans. The U.S. Public Health Service enrolled 399 impoverished farmers with syphilis and observed the natural history of syphilis from 1932-1972 withholding penicillin after it became available.^{27,28} Research studies that contradict prior guidelines such as the effect of estrogen on heart disease, may lead to confusion and continued mistrust from the patients' perspective as do frequent drug recalls.

Financial relationships between physicians and pharmaceutical companies have been highlighted and legislation has been enacted to prevent undue influence on physicians. In a study by Grande et al, 55% of patients believed their physician received gifts from pharmaceutical companies. Younger patients and those of higher socioeconomic status were more likely to believe that gifts were received by their physicians, and this belief

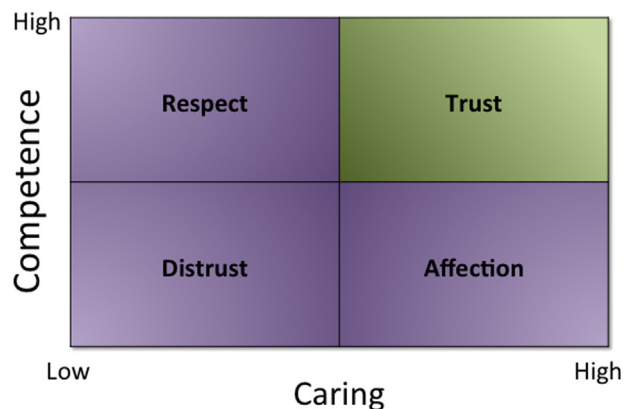


FIGURE 2. Building Trust. Trust is a critical factor in an effective relationship. A provider perceived as competent but uncaring would be respected but not trusted. A provider perceived as caring but incompetent would be viewed with affection but not trusted. Trust develops when both caring and competence are present. (Adapted with permission from Paling J.⁴¹)

was associated with lower physician trust and twice the distrust in the healthcare system.²⁹

Patients' Beliefs and Preferences

Goethe's statement that "belief is not the beginning but the end of all knowledge" highlights the importance of understanding the power of beliefs and how difficult they are to counter by relying purely on additional educational materials. The latter has been shown to be ineffective in the face of strong belief, yet often the only tool relied upon to change behaviors. Individual patients' adherence is influenced by their time perspective.³⁰ Some patients are oriented to the present and others to the future, resulting in a preference for immediate rewards versus delayed gratification. Stressing the need to ingest a medicine now, to reap abstract rewards in the distant future may not be considered an imperative, as patients may not feel they have a future to look forward to.³¹ Taking a medicine to prevent death from a heart attack in some distant future may not motivate a patient, as they may feel succumbing in this way may be preferable to a death from cancer or stroke.

Latino cultural concepts such as "machismo" versus "caballerismo" were found by Galvan et al³² to have effects on adherence. The stereotypical machismo characteristics of being strong, invulnerable and in control were associated with nonadherence and denial of illness. Patients believing that God or a higher power determined their health were more likely to be non-adherent, and this is of greater significance in the African-American community.³³ Patients may be adherent to one medicine and nonadherent to another depending on varying attitudes about each of the medicines, referred to as selective adherence.

Low Health Literacy or Numeracy

An enormous barrier to the health of the population is poor literacy. This is often hidden during the healthcare encounter. More than 85% of patients ashamed of

their reading limitations hid their limited literacy from coworkers and approximately 50% hid it from their children.³⁴ The U.S. Department of Education landmark study in 2003 noted that only 12% of American adults had "proficient" health literacy, whereas 35% have basic or below basic health literacy, resulting in their inability to read a medicine bottle or poison warning.³⁵

Numeracy, referring to the ability to understand numbers, is a key element of health literacy, and low numeracy scores are associated with lower understanding, less use of health information and more health crises. Calculating the difference between a sale price and a regular price was difficult for almost half the population according to the National Adult Literacy Survey. Even literate patients are often challenged by poorly written or contradictory instructions as demonstrated by a study of highly educated patients in which 16% incorrectly answered questions about which number represents the larger risk—1%, 5% or 10%. Almost one-quarter of medical students also have been found to have difficulty with basic numerical tasks.³⁶ Less numerate patients do not trust information provided in numerical form and are more likely to view it as inaccurate while they are more likely to base decisions on non-numeric sources including emotions and trust or distrust in their health system.³⁷

Patients often lack an understanding of the need for chronic daily medicine, as missing a dose in most asymptomatic conditions rarely leads to an immediate undesirable symptom. Recommending an action such as taking a pill every day so that something would not happen is counterintuitive. Understanding the difference between "controlled" and "cured" leads to misunderstanding and leads to a sense of "dependence" on a drug. Campaigns against drug dependence are pervasive, highlighting the national epidemic of substance abuse and drug dependence. It is challenging for patients to understand if they are on lifelong therapy and why they would not become dependent on it. Patients may be concerned that if hypertension is only

controlled when taking the medicine, they may have become “dependent.”

Complex written instructions may be challenging to understand even for the most motivated patient. The number of variables regarding timing for each medicine (empty stomach, full stomach, at bedtime, avoiding lying down, avoiding certain foods, etc.), frequency of doses, varied prescribers, varied pharmacies, varied date of refills, co-pays, tiers, formulary, nonformulary, daily and weekly may simply be too confusing or too time-consuming to manage. Increased frequency of doses is inversely related to adherence as with each additional daily dose, adherence decreases by 10%.

Conflicting Medical Information

The study of patients with chronic illness by Carpenter et al³⁸ found that greater than 80% of patients received conflicting information from physicians, media and the internet, and they were associated with lower adherence. This has been clearly demonstrated by noting that when web-searching the term *vaccination*, greater than 70% of findings are antivaccine, contributing to alarming low adherence to vaccine recommendations.³⁹ Direct to consumer medicine advertisements include a long list of side effects, often including “death” followed by a solicitation for legal services if harmed, consequently leaving the patient at best perplexed and at worst fearful of taking the medicine.

Fear of Side Effects

Patients fear that medicines may do more harm than good. Side effects experienced personally or by others and concern regarding potential side effects influences behavior.⁴⁰ When patients feel forced to choose between side effects or control of an asymptomatic surrogate marker, it is not surprising that the patient may intentionally nonadhere. When uncertainty exists about risk and benefits, people tend to either fully accept or reject the evidence. Patients are more likely to assess risk emotionally than by weighing the facts.⁴¹

Three-quarter of patients in 1 study reported that potential adverse medication effects were not discussed by their physician.¹⁷ Side effects such as hair loss, ace inhibitor-related chronic cough, weight gain, sexual dysfunction from selective serotonin reuptake inhibitor drugs, impotence, fatigue, depression from beta blockers and gynecomastia from spironolactone frequently occur with commonly used drugs. Diarrhea upon initiation of metformin is to be expected and yet patients may not be aware that resolution would occur within the week if metformin is continued. Restarting the drug after a brief 3-day drug holiday may result in recurrence of the initial diarrhea necessitating re-titration.

Depression

Patients with depression are 3 times more likely to have poor medication adherence and poor health

behavior.⁴² Depression is common especially in patients with diabetes and contributes to poor adherence to medication, physical inactivity, poor glycemic control, reduced quality of life, disability and increased health-care cost.⁴³⁻⁴⁷ The American Diabetes Association has modified its guidelines to recommend routine screening for depression in diabetic patients, especially in patients with poor adherence.⁴⁸ Even subclinical depression symptoms represent a major prognostic risk factor for poor medication adherence and poor health behavior. During a year-long evaluation, less than half of the patients with depression were recognized, less than one-third of depressed patients received antidepressant prescriptions and only approximately 7% of patients received adequate psychotherapeutic treatment.⁴⁹ Serna et al⁵⁰ noted that in patients treated for depression, adherence was only 22% among patients during the first 4 months of treatment and 56% of patients discontinued medicine within 1 year.

Forgetfulness

Forgetting to take medicines is a common reason for nonadherence but accounts for only 30% of all nonadherence, although providers incorrectly attribute a greater proportion of nonadherence to this barrier.⁵¹ Identifying the type of forgetting is critical to properly tailoring a solution. A busy person who missed a few pills due to work or life pressures requires a different intervention than the patient with mild cognitive impairment.

Demographics

Generally as age increases, so does adherence. The influence of marital status, sex, ethnicity and level of education on adherence is mixed. Understanding, recognizing and agreeing with the treatment plan is more importantly associated with adherence than is formal level of education. Patient-provider race concordance plays a minor role in the relationship as long as there is a shared understanding of the goals of the visit. Black patients' adherence levels were reflective of their perceived quality of communication with their white providers.⁵²

OBSTACLES TO ADHERENCE: PROVIDER PERSPECTIVE

Unaware of Patient's Nonadherence

Physicians may count on the medication reconciliation process to reveal nonadherence and are unaware of barriers to revealing the truth of patient's medication-taking behavior. Few physicians ask patients detailed questions about medication adherence to reveal missed medications or doses of medications. Physicians may not have the skills to unmask medication-taking behavior. Simply asking a question, “Are you taking your medications?” is inadequate. The art of unmasking medication nonadherence requires direct, open-ended

questions spoken in an encouraging manner. Believing that medication nonadherence is the “fault” of the patient is an uninformed and destructive model. The physician may feel time pressured, burdened or lack motivation to ask more detailed questions to assess medication adherence.⁵³ Physician burnout is associated with reduced adherence to treatment plans leading to decreased clinical outcomes.⁵⁴

Uncoordinated Care and Polypharmacy

Patients with chronic medical diseases are susceptible to polypharmacy, often taking 5 or more medications for their medical disorder.⁵⁵ Having multiple physicians including primary physicians, consultants and out of network physicians caring for 1 patient may increase the risk of inappropriate polypharmacy. Approximately 28% of older people in the United States are receiving polypharmacy.⁵⁶ Refill consolidation refers to the number of pharmacy visits required to obtain prescribed medications. Ideal refill consolidation is provided by mail order as no visits are necessary. Greater numbers of prescribers and pharmacies, and less refill consolidation are associated with decreased medication adherence.

Every year, 1 in 3 adults aged 65 years or older have 1 or more adverse reactions to a medication or medications.^{12,57} The total estimated healthcare expenditures related to the use of potentially inappropriate medications is \$7.2 billion.⁵⁸ The American Geriatric Society Beers Criteria is designed to improve care of older adults by reducing their exposure to potentially inappropriate medications. These medications should be avoided as they have a greater risk of harm than benefit, for people aged 65 years and older.⁵⁹

Failure to Communicate Critical Information

When prescribing a new medication, physicians often fail to communicate critical information of medication use to patients. Physicians discuss adverse effects, the frequency of medication and timing of dosing less than 60% of the time. When prescribing lifelong therapy, most physicians do not address the duration of therapy.⁶⁰ Not surprisingly, some patients stop medications if the directions state “Take 1 pill every day for 90 days,” by taking the directions literally. Most physicians fail to inform the patient of the need for lifelong therapy for several reasons. Survey results indicate that physicians fear doing so would lengthen the visit, or cause patient resistance or a sense of futility, as well as being uncomfortable delivering unwelcome messages.

SYSTEM OBSTACLES

Cost and Access

Co-payments have a negative influence on adherence. Each co-pay dollar is associated with a diminished

odds ratio of adherence by 0.55.⁶¹ Barely 21% of physicians reported knowledge of their patients’ out-of-pocket expenses.⁶² Though decreasing co-pays or cost improves adherence, studies have shown that even when medicine is free or co-pays are decreased, lowering cost has only a small influence on improving adherence.⁶³ Social disparities, even in systems with universal access, still affect medication adherence.⁶⁴

Generic Medications

Approximately, 80% of all medications prescribed are now generic, which has increased access and lowered costs. However, U.S. trademark laws result in the physical appearance of generic pills varying greatly. Changing sources of each generic drug may lead to its changing appearance each time it is refilled. Each generic medication may change its appearance at each refill, leading to highly variable appearance of their pills over the course of a year.

Hospital Discharge

Hospital discharge can be a complex, challenging transition, often confusing for patients and caregivers and can contribute to medication nonadherence, errors and adverse events. Estimates suggest that almost half of patients encounter at least 1 medical error after discharge, most commonly involving medications and anywhere between 12–23% of patients experience an adverse drug event.^{65,66} At least half of patients have at least 1 unintended medication discrepancy on admission, many potentially harmful. The most common discrepancy is omission of a home medication. Restricted hospital formularies may necessitate medication changes in the hospital that are not always reversed on discharge. When discharging a patient, physicians typically go over the medication list very quickly (if at all), and may explain the discharge plan utilizing medical jargon. Physicians tend to overestimate their communication skills as well as patients’ comprehension of their explanations, may not leave enough time for questions, and confirm patient understanding only 15% of the time.^{67,68} Discharge summaries, designed to help facilitate transitions in care, are not available 75% of the time by the first postdischarge. On a review of discharge summaries, a list of discharge medications were absent from 2–40% of summaries.⁶⁹

SOLUTIONS

A review of 78 randomized trials found relatively few complex interventions and no one simple intervention to improving long-term medication adherence and health outcomes.⁷⁰ A variety of approaches are necessary.

Patient Solutions

“Brown bag review” refers to a patient bringing in all medicines to each clinic visit in order for the provider to assess medication-taking behavior by pill count, refills

and discussion. Together the provider and patient can discuss each drug while looking at the medicine together. This is an opportunity to remind the patient that the color and shape of a drug may change over time as the source of generic drugs changes. Providing a simple list of an individual's medications before the visit in the waiting room for review, can save time and begin the reconciliation process. Instructions to circle the medications for which refills are needed and put a question mark next to any medication for which the patient questions the need, facilitates assessment of medication-taking behavior without lengthening the visit. "Ask me 3" is a publicly available communication tool provided by the Partnership for Clear Health Communication and encourages patients to become active members of the team.

The program encourages each patient to ask the following questions:

- (1) What is my main problem?
- (2) What do I need to do?
- (3) Why is it important for me to do this?

Education and Health Literacy

As patients may recall as little as 50% of content discussed during a medical encounter, for patient education to be effective it must be multipronged, individualized and delivered in a variety of methods and settings outside the examining room.⁷¹ Numerous resources are available in multiple languages and rely heavily on pictographs or video.

PROVIDER SOLUTIONS

Assume Nonadherence

Inquiring about medication-taking behavior in a non-judgmental and blame-free atmosphere is key. All members of the team must adhere to this approach. If a patient confides their nonadherent behavior to a team member, only to have the physician reprimand the patient for their aberrant behavior, the patient may conceal the nonadherence from all team members.

Develop a Trusting Relationship

In order to develop trust, patients must perceive that the provider has both a high level of competence as well as a sense that the provider cares for the health of the patient to develop trust (Figure 2). Trust develops with time and may require several visits with the same provider over months and years. Providing the "golden moment" upon first meeting a patient, giving them undivided, uninterrupted attention takes less than 1 minute and sets the tone for an effective encounter. Patient-centered communication can enhance patient trust and promote active patient involvement in the medical decision-making process.

Referring patients to peer-reviewed websites domains such as .org, .edu and .gov provides a more consistent evidence-based resource. For patients requesting a "natural" medicine, reassurance that metformin is derived from the French lilac may improve acceptance of the therapy.

Oral hypoglycemic medications adherence decreased in patients with diabetes when patient-physician communication is suboptimal.⁷² In a study of patients with human immunodeficiency virus infection, an 18% increased odds of adherence was associated with a 1-point increase in patient trust.⁷³ Highlighting and celebrating even small achievements leads to continued engagement.

Physician communication training programs may significantly improve the physician's ability to engage in patient-centered communication and elevate patient satisfaction. Available, organization-supported communication courses, coaching programs or educational resources to improve the quality of communication between provider and patient are needed.

Once nonadherence is identified, responding to the patient with appreciation for being forthcoming and sharing their behavior is critical. Recognizing their reason for nonadherence as legitimate leads to a fruitful nonconfrontational discussion is followed by a tailored solution. Responding with motivational interviewing techniques is helpful.

Improve Continuity of Care

Long-term relationships between physicians and patients are important in developing trust, effective communication and continuity of care. These interpersonal relationships may lead to better information sharing, as physicians are more familiar with their patient's medical history and medication usage. Longitudinal relationship with the primary care physician is associated with reduced likelihood of hospitalization, emergency room visits, lower healthcare expenses and greater satisfaction with care.^{74,75} In patients with diabetes, continuity of care is associated with higher adherence to medication as well as superior health outcomes.⁷⁶

Engage the Family

Self-care in diabetes is associated with improved glycemic control, reduction of complications, hospitalization and improvement in quality of life. Diabetes self-care activities include healthy eating, being physically active, monitoring of blood sugar, compliance with medications, good problem solving, healthy coping skills and risk-reduction behaviors.⁷⁷ However, some family members are nonsupportive and may sabotage patient's efforts to perform these healthy behaviors. Nonsupportive family members are associated with decline in adherence to the patient's diabetes medication regimen.⁷⁸ It is important to understand the role of the family

TABLE. Tools to improve medication adherence.

Self-reported medication measures	
Morisky Medication Adherence Scale	http://c.ymcdn.com/sites/www.aparx.org/resource/resmgr/Handouts/Morisky_Medication_Adherence.pdf
	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2562622/pdf/nihms52858.pdf
Adherence to Refills and Medication Scale to Diabetes Medicine (ARMDS-D)	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3915929/pdf/nihms534942.pdf
Summary of Diabetes Self-Care Activities Medications Subscale (SDSCA-MS)	http://care.diabetesjournals.org/content/23/7/943.full.pdf
Duke-UNC Functional Social Support Questionnaire	http://www.adultmeducation.com/AssessmentTools_4.html
Trust with Their Physicians Scale(TIPS)	http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3609434/pdf/nihms433915.pdf
Medication adherence challenges/solutions	
Pill appearance	https://www.acponline.org/multimedia/
Prescription drug label mistakes	https://www.acponline.org/multimedia/
Pill card	http://www.ahrq.gov/patients-consumers/diagnosis-treatment/treatments/pillcard/index.html
CardioSmart med reminder	https://www.cardiosmart.org/Tools/Med-Reminder?w_nav=Blog
Screen for health literacy	http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/literacy/index.html
Rapid estimate of adult health literacy	http://www.adultmeducation.com/AssessmentTools_1.html
Health literacy video of physician interviews with patients (AMA Health literacy video)	https://www.youtube.com/watch?v=BgTuD717LG8
	https://www.youtube.com/watch?v=cGTZ_vxjyA
Medication adherence resources for healthcare team	http://ndep.nih.gov/hcp-businesses-and-schools/HealthCareProfessionals/medication-adherence/
Medication adherence learning module	https://www.stepsforward.org/modules/medication-adherence
Prescription drug assistance	https://www.pparx.org/
	http://www.rxassist.org/
Communication	
Adherence to type 2 diabetes management plans: developing successful patient interactions	http://www.medscape.org/viewarticle/823213
Motivational interviewing	http://www.adultmeducation.com/FacilitatingBehaviorChange_2.html
Mayo Clinic shared decision-making aide	http://shareddecisions.mayoclinic.org/decision-aid-information/decision-aids-for-chronic-disease/diabetes-medication-management/
Patient-physician communication: empowering patients to ask questions	http://www.npsf.org/?page=askme3

support and identify nonsupportive family member behaviors.

SYSTEM SOLUTIONS

Many of the solutions have been discussed previously. In this section, we emphasize areas that were not discussed earlier (Table).

Lower Cost and Improve Access

Policy interventions to reduce co-payments or improve prescription drug coverage improve medication adherence. Thus, value-based insurance design with reduced co-payments for services and medications should result in improvements in medication adherence and disease control, and reductions in healthcare costs.⁷⁹ Sokol et al⁸⁰ in an observational study of greater than 130,000 patients found that with greater adherence there were higher medication costs, but also a net reduction in overall healthcare costs and an estimated return on investment of 7:1 for diabetes and 4:1 for hypertension.

Medication Reconciliation at Hospital Discharge

When preparing patients for discharge in the hospital, the plan for obtaining medications should be discussed. Insurance coverage or lack thereof and potential medication costs should be the information that patients are aware of before discharge. Balling et al⁸¹ found that using a transition of care pharmacist during hospital discharge, helped address insurance issues related to medication coverage. This pharmacist intervention appeared to result in reduced hospital readmission rates.

Medication reconciliation is a method of reducing medication discrepancies, which can potentially lead to adverse drug events. This process starts on admission. At discharge, changes to dosing, frequency or new medications should be clearly marked for patients, as should home medications that have been discontinued. Mueller et al⁸² conducted a systematic review in 2012 and found that various interventions involving pharmacy, information technology and multidisciplinary teams (such as hospital physician, emergency physician and

nurses), successfully decreased medication discrepancies and potential adverse drug events.

The medication reconciliation literature is most robust for pharmacist-led interventions. Using trained nurses or pharmacists to obtain preadmission medication histories improved the accuracy of admission medication reconciliation from 40–95%.^{83,84}

A total of 2 initiatives have synthesized best practices and offer toolkits for hospitals and clinicians to optimize the medication reconciliation process, the Medications at Transitions and Clinical Handoffs program and the Multi-Center Medication Reconciliation Quality Improvement Study.^{85,86} As lack of resources for medication reconciliation is a barrier for many institutions, Multi-Center Medication Reconciliation Quality Improvement Study investigators suggested focusing most on the admission history, where most errors occur, and directing resources to the patient population at highest risk for adverse drug events, such as the elderly, those with multiple comorbid conditions or those on numerous medications.

An emerging method for improving and increasing safety of admission medication reconciliation is the use of prescription drug monitoring databases. Many states currently have prescription drug monitoring databases of varying utility.⁸⁷

Evidence is emerging on the importance of engaging patients in medication reconciliation. Heyworth et al⁸⁸ found that engaging patients in a web-based medication reconciliation tool to verify their medication regimens and clarify inaccuracies identified 108 medication discrepancies and 23 potential adverse drug events, with nearly 50% of the potential adverse events classified as serious. Coleman et al⁸⁹ demonstrated that innovations such as a medical record owned and maintained by the patient, decreased hospitalization rates at 30 and 90 days (8.3% versus 11.9%, $P = 0.048$; 16.7% versus 22.5%, $P = 0.4$).

Many innovations are in the process of being trialed. At 1 center in the United States, discharge conversations are recorded and provided to the patient to listen to again once they are at home, to ensure important discharge points are not missed. This has resulted in a 56.9% improvement in Hospital Consumer Assessment of Healthcare Providers and Systems scores for the discharge communication domain.⁹⁰

Hospitals should provide in-house filling of prescriptions to avoid transportation issues and ensure compliance, if patients are amenable. Fischer et al⁹¹ also found reduced nonadherence to medications when e-prescriptions are utilized. Studies have shown that postdischarge phone calls can help detect and resolve medication issues early after discharge. Home healthcare nursing services for high-risk patients can also help ensure that medications are obtained and taken properly on discharge.⁹²

Improve Refill Efficiency

Improving refill consolidation works toward the goal of having all chronic medications filled for a patient at

one time. Mail order results in 100% refill consolidation. Policies to allow pharmacies to dispense a few additional pills (medication synchronization) to allow the medicines to come into “phase” so that all medications can be refilled on the same day decreases this barrier. Refilling medications for 15 months at one time or for even 365 days eases burden. Identifying who it is that picks up a family member’s prescriptions, and sending the order to a convenient location for that person may save caregiver time. Changing from routine 6-month refills to 1 year for most chronic medications can save significant time. In a study of over 100,000 patients by Curkendall et al,⁹³ more patients using mail order were adherent versus nonadherent, that is, 22.4% versus 13.5%, respectively. Indication-based prescribing that includes the reason for the medication with the directions increases patient understanding.

Provide the Necessary Time Required to Develop Trust

Uncovering true medication-taking behavior and relationship building requires time and institutional commitment to provide resources to achieve this goal. Escalating therapy in response to “resistant” hypertension or diabetes although being unaware that the patient is nonadherent, results in wasted time and potentially harmful therapy. A nonadherent patient with hypertension and diabetes, admitted to the hospital is likely to be prescribed their listed home medications along with new therapy, leading to patient harm such as hypotension or hypoglycemia or both several days later.

Develop Team-Based Care

The current emphasis on population health, outcomes, healthcare reform and system evolution makes it essential that future models of care take full advantage of the growing number of nurse practitioners, physician assistants, pharmacists and medical assistants all contributing to improving patient understanding, engagement and adherence, as well as community educators. Centers for Medicare & Medicaid Services reimburses 10 program hours of initial diabetes education followed by 2 hours in each subsequent year.⁹⁴ Only if every member of the team thoughtfully evaluates the medication-taking behavior and in a blame-free setting, obstacles to adherence would be addressed. Just as we move to assume that poor health literacy is present, adjusting our approach to assuming that nonadherence is present would lead to improved recognition.

Effectively Use Technology

Innovative methods are needed to assist with non-adherence. Effective use of the EHR enables providers to define alerts for primary nonadherence of critical medications such as antiplatelet therapy following implantation of a drug-eluting stent. This allows for an

intervention to a specific patient, improving adherence and averting a stent thrombosis that may result in myocardial infarction and rehospitalization. More than 90% of adults in the United States are mobile phone owners and more than half of smartphone owners have used their phone to get health information.^{95,96} Mobile phones are the most commonly used form of technology worldwide and have the potential to influence large populations. Thus, a movement to use mobile health to enhance self-management of chronic disease, to deliver health education and to assist patients to improve medication adherence may be practical. Mobile phone text messages may promote adherence to antiplatelet therapy within 30 days after myocardial infarction or percutaneous coronary artery intervention or after both.⁹⁷ In patients with diabetes after the emergency room visit, daily health text messages to promote knowledge, healthy eating, exercise, self-efficacy and medication-taking reminders have improved medication adherence.⁹⁸ The use of mobile health technology may provide an innovative, practical and inexpensive means to promote medication adherence.

CONCLUSIONS

Improving medication adherence may have a greater influence on the health of the population than any new medical discovery. Adherence to prescribed therapies for patients with chronic diseases can prevent or delay the onset of complications, reduce hospitalization risks and decrease healthcare costs. As Director of the Agency for Healthcare Research and Quality, Carolyn Clancy, MD, declared, "Medication adherence is America's new drug problem."⁹⁹

Medication adherence is influenced by numerous variables. Trust, communication and empathy are not easily measured by current administrative databases but are associated with medication adherence. These factors may have a far greater influence on the medication behaviors of patients and explain the elusive challenge of improving adherence. Efforts to improve patients' understanding of medication benefits, access and trust in their provider and health system need to be included in the multifactorial solutions to improve medication adherence. Efforts to improve providers' recognition and understanding patients' beliefs, fears and values, as well as their own biases need to be addressed simultaneously if improvements in medication adherence and ultimately population health are to be achieved.

ACKNOWLEDGMENTS

The authors would like to thank Ted E. Feldman, MD, Northshore University for his editorial support and comments.

REFERENCES

1. **Ward BW, Schiller JS, Goodman RA.** Multiple chronic conditions among US adults: a 2012 update. *Prev Chronic Dis* 2014;11:130389.
2. **Chan DC, Shrank WH, Cutler DP, et al.** Patient, physician, and payment predictors of statin adherence. *Med Care* 2010;48(3):196–202.
3. **Heidenreich PA.** Patient adherence: the next frontier in quality improvement. *Am J Med* 2004;117(2):130–2.
4. **Ho PM, Bryson CL, Rumsfeld JS.** Medication adherence: its importance in cardiovascular outcomes. *Circulation* 2009;119(23):3028–35.
5. **De Geest S, Sabaté E.** Adherence to long-term therapies: evidence for action. *Eur J Cardiovasc Nurs* 2003;2(4):323 [WHO (2003) WHO, editor. Geneva, Switzerland: World Health Organization (WHO)].
6. **Cramer JA, Roy A, Burrell A, et al.** Medication compliance and persistence: terminology and definitions. *Value Health* 2008;11(1):44–7.
7. **Fischer MA, Choudhry NK, Brill G, et al.** Trouble getting started: predictors of primary medication nonadherence. *Am J Med* 2011;124:1081.e9–22.
8. **Shah NR, Hirsch AG, Zacker C, et al.** Factors associated with first-fill adherence rates for diabetic medications: a cohort study. *J Gen Intern Med* 2009;24(2):233–7.
9. **Shah NR, Hirsch AG, Zacker C, et al.** Predictors of first-fill adherence for patients with hypertension. *Am J Hypertens* 2009;22(4):392–6.
10. **Ho PM, Magid DJ, Shetterly SM, et al.** Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. *Am Heart J* 2008;155(4):772–9.
11. **Rasmussen JN, Chong A, Alter DA.** Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *J Am Med Assoc* 2007;297(2):177–86.
12. **Gurwitz JH, Field TS, Harrold LR.** Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *J Am Med Assoc* 2003;289(9):1107–16.
13. **IMS Institute for Healthcare Informatics.** Avoidable costs in US health care. 2013. Available from: http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/IMS%20Institute/RUOM-2013/IHIL_Responsible_Use_Medicines_2013.pdf. Accessed May, 2015.
14. **Loepke R, Taitel M, Haufle V, et al.** Health and productivity as a business strategy: a multiemployer study. *J Occup Environ Med* 2009;51(4):411–28.
15. **Roebuck MC, Liberman JN, Gemmill-Toyama M, et al.** Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Aff (Millwood)* 2011;30(1):91–9.
16. **Jha AK, Aubert RE, Yao J, et al.** Greater adherence to diabetes drugs is linked to less hospital use and could save nearly \$5 billion annually. *Health Aff (Millwood)* 2012;31(8):1836–46.
17. **Lapane KL, Dubé CE, Schneider KL, et al.** Misperceptions of patients vs providers regarding medication-related communication issues. *Am J Manag Care* 2007;13(11):613–8.
18. **Açıköz SK, Açıköz E, Topal S, et al.** Effect of herbal medicine use on medication adherence of cardiology patients. *Complement Ther Med* 2014;22(4):648–54.
19. **Krueger KP, Berger BA, Felkey B.** Medication adherence and persistence: a comprehensive review. *Adv Ther* 2005;22(4):313–56.
20. **Hong JS, Kang HC.** Relationship between continuity of ambulatory care and medication adherence in adult patients with type 2 diabetes in Korea: a longitudinal analysis. *Med Care* 2014;52(5):446–53.
21. **Marcum ZA, Gellad WF.** Medication adherence to multidrug regimens. *Clin Geriatr Med* 2012;28(2):287–300.
22. **Unni EJ, Olson JL, Farris KB.** Revision and validation of Medication Adherence Reasons Scale (MAR-Scale). *Curr Med Res Opin* 2014;30(2):211–21.
23. **Stewart K, Mc Namara KP, George J.** Challenges in measuring medication adherence: experiences from a controlled trial. *Int J Clin Pharm* 2014;36(1):15–9.
24. **Gonzalez JS, Schneider HE, Wexler DJ, et al.** Validity of medication adherence self-reports in adults with type 2 diabetes. *Diabetes Care* 2013;36(4):831–7.
25. **Rose A, Peters N, Shea JA, et al.** Development and testing of the health care system distrust scale. *J Gen Intern Med* 2004;19(1):57–63.
26. **LaVeist TA, Isaac LA, Williams KP.** Mistrust of health care organizations is associated with underutilization of health services. *Health Serv Res* 2009;44(6):2093–105.
27. **Cobb WMJ.** The Tuskegee syphilis study. *Natl Med Assoc* 1973;65(4):345–8.

28. **LaVeist TA, Nickerson KJ, Bowie JV.** Attitudes about racism, medical mistrust, and satisfaction with care among African American and white cardiac patients. *Med Care Res Rev* 2000;57(suppl 1):146–61.
29. **Grande D, Shea JA, Armstrong K.** Pharmaceutical industry gifts to physicians: patient beliefs and trust in physicians and the health care system. *J Gen Intern Med* 2012;27(3):274–9.
30. **Sansbury B, Dasgupta A, Guthrie L, et al.** Time perspective and medication adherence among individuals with hypertension or diabetes mellitus. *Patient Educ Couns* 2014;95(1):104–10.
31. **Reach G.** Is there an impatience genotype leading to non-adherence to long-term therapies? *Diabetologia* 2010;53(8):1562–7.
32. **Galvan FH, Bogart LM, Wagner GJ, et al.** Conceptualisations of masculinity and self-reported medication adherence among HIV-positive Latino men in Los Angeles, California, USA. *Cult Health Sex* 2014;16(6):697–709.
33. **Ahmedani BK, Peterson EL, Wells KE.** Asthma medication adherence: the role of God and other health locus of control factors. *Ann Allergy Asthma Immunol* 2013;110(2): [75-9.e2].
34. **Parikh NS, Parker RM, Nurss JR.** Shame and health literacy: the unspoken connection. *Patient Educ Couns* 1996;27(1):33–9.
35. **Kutner National Assessment of Adult Literacy U.S.** Department of Education NCES 2006–483.
36. **Sheridan SL, Pignone M.** Numeracy and the medical student's ability to interpret data. *Eff Clin Pract* 2002;5(1):35–40.
37. **Peters E, Hibbard J, Slovic P, et al.** Numeracy skill and the communication, comprehension, and use of risk-benefit information. *Health Aff (Millwood)* 2007;26(3):741–8.
38. **Carpenter DM, Elstad EA, Blalock SJ.** Conflicting medication information: prevalence, sources, and relationship to medication adherence. *J Health Commun* 2014;19(1):67–81.
39. **Kata A.** A postmodern Pandora's box: anti-vaccination misinformation on the Internet. *Vaccine* 2010;28(7):1709–16.
40. **De Geest S, Sabaté E.** Adherence to long-term therapies: evidence for action. *Eur J Cardiovasc Nurs* 2003;2(4): [323WHO (2003) WHO, editor. Geneva, Switzerland: World Health Organization (WHO)].
41. **Paling J.** Strategies to help patients understand risks. *Br Med J* 2003;327(7417):745–8.
42. **DiMatteo MR, Lepper HS, Croghan TW.** Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000; 160(14):2101–7.
43. **Gonzalez JS, Peyrot M, McCarl LA, et al.** Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes Care* 2008;31(12): 2398–403.
44. **Koopmans B, Pouwer F, de Bie RA, et al.** Depressive symptoms are associated with physical inactivity in patients with type 2 diabetes. The DIAZOB Primary Care Diabetes study. *Fam Pract* 2009;26(3):171–3.
45. **Dirmaier J, Watzke B, Koch U, et al.** Diabetes in primary care: prospective associations between depression, nonadherence and glycaemic control. *Psychother Psychosom* 2010;79(3):172–8.
46. **Ciechanowski PS, Katon WJ, Russo JE.** Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med* 2000;160(21):3278–85.
47. **Katon WJ, Von Korff M, Lin EH, et al.** The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry* 2004;61(10):1042–9.
48. **Diabetes Care.** 2015 Jan;38 Suppl: S4. <http://dx.doi.org/10.2337/dc15-S003>. Standards of medical care in diabetes—2015: summary of revisions. [No authors listed].
49. **Katon WJ, Simon G, Russo J, et al.** Quality of depression care in a population-based sample of patients with diabetes and major depression. *Med Care* 2004;42(12):1222–9.
50. **Serna MC, Cruz I, Real J, et al.** Duration and adherence of antidepressant treatment (2003 to 2007) based on prescription database. *Eur Psychiatry* 2010;25(4):206–13.
51. **Osterberg L, Blaschke T.** Adherence to medication. *N Engl J Med* 2005;353:487–97.
52. **Schoenthaler A, Allegrante JP, Chaplin W, et al.** The effect of patient-provider communication on medication adherence in hypertensive black patients: does race concordance matter? *Ann Behav Med* 2012;43(3): 372–82.
53. **Linzer M, Manwell LB, Williams ES, et al.** Working conditions in primary care: physician reactions and care quality. MEMO (Minimizing Error, Maximizing Outcome) investigators. *Ann Intern Med* 2009;151(1): 28–36.
54. **Bodenheimer T, Sinsky C.** From triple to quadruple aim: care of the patient requires care of the provider. *Ann Fam Med* 2014;12(6):573–6.
55. **Patterson SM, Cadogan CA, Kerse N.** Interventions to improve the appropriate use of polypharmacy for older people (Review). The Cochrane Collaboration and published in The Cochrane Library 2014, Issue 10.
56. **Barnett K, Mercer SW, Norbury M, et al.** Epidemiology of multi-morbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37–43.
57. **Gurwitz JH, Field TS, Judge J, et al.** The incidence of adverse drug events in two large academic long-term care facilities. *Am J Med* 2005;118 (3):251–8.
58. **Fu AZ, Jiang JZ, Reeves JH, et al.** Potentially inappropriate medication use and healthcare expenditures in the US community-dwelling elderly. *Med Care* 2007;45(5):472–6.
59. **Campanelli CM.** American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. *J Am Geriatr Soc* 2012;60(4):616–31.
60. **Tarn DM, Heritage J, Paterniti DA, et al.** Physician communication when prescribing new medications. *Arch Intern Med* 2006;166(17):1855–62.
61. **Chan DC, Shrank WH, Cutler D, et al.** Patient, physician, and payment predictors of statin adherence. *Med Care* 2010;48(3):196–202.
62. **Alexander GC, Casalino LP, Meltzer DO.** Patient-physician communication about out-of-pocket costs. *J Am Med Assoc* 2003;290(7):953–8.
63. **Zhang Y, Baik SH, Chang CC, et al.** Disability, race/ethnicity, and medication adherence among Medicare myocardial infarction survivors. *Am Heart J* 2012;164(3):425–33.
64. **Curao G, Zambon A, Parodi A, et al.** Do socioeconomic disparities affect accessing and keeping antihypertensive drug therapy? Evidence from an Italian population-based study. *J Hum Hypertens* 2009;23: 238–44.
65. **Cua YM1, Kripalani S.** Medication use in the transition from hospital to home. *Ann Acad Med Singapore* 2008;37(2):136.
66. **Cohen MJ, Shaykevich S, Cawthon C, et al.** Predictors of medication adherence postdischarge. *J Hosp Med* 2012;7(6):470–5.
67. **Block L, Hutzler L, Habicht R, et al.** Do internal medicine interns practice etiquette-based communication? A critical look at the inpatient encounter. *J Hosp Med* 2013;8(11):631–4.
68. **Schillinger D, Piette J, Grumbach K, et al.** Closing the loop: physician communication with diabetic patients who have low health literacy. *Arch Intern Med* 2003;163(1):83–90.
69. **Kripalani S, LeFevre F, Phillips CO, et al.** Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. *J Am Med Assoc* 2007;297(8):831–41.
70. **Haynes RB, Ackloo E, Sahota N, et al.** Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2008(2): CD000011.
71. **Brown MT, Bussell JK.** Medication adherence: WHO cares? *Mayo Clin Proc* 2011;86(4):304–14.
72. **Ratanawongsa N, Karter AJ, Parker MM, et al.** Communication and medication refill adherence: the Diabetes Study of Northern California. *JAMA Intern Med* 2013;173(3):210–8.
73. **Schoenthaler A, Montague E, Baier Manwell L, et al.** Patient-physician racial/ethnic concordance and blood pressure control: the role of trust and medication adherence. *Ethn Health* 2014;19(5):565–78.
74. **Knight JC, Dowden JJ, Worrall GJ, et al.** Does higher continuity of family physician care reduce hospitalizations in elderly people with diabetes? *Popul Health Manag* 2009;12(2):81–6.
75. **Chen CC, Cheng SH.** Better continuity of care reduces costs for diabetic patients. *Am J Manag Care* 2011;17:420–7.
76. **Chen CC, Tseng CH, Cheng SH.** Continuity of care, medication adherence, and health care outcomes among patients with newly diagnosed type 2 diabetes: a longitudinal analysis. *Med Care* 2013;51(3):231–7.

77. **Austin MM.** AADE7 Self-Care Behaviors. AADE. *Diabetes Educ* 2008; 34(3):445–9.
78. **Mayberry LS, Osborn CY.** Family support, medication adherence, and glycemic control among adults with type 2 diabetes. *Diabetes Care* 2012; 35(6):1239–45.
79. **Kulik A, Desai NR, Shrank WH.** Full prescription coverage versus usual prescription coverage after coronary artery bypass graft surgery: analysis from the post-myocardial infarction free Rx event and economic evaluation (FREEE) randomized trial. *Circulation* 2013;128(11 suppl 1):S219–25.
80. **Sokol MC, McGuigan KA, Verbrugge RR, et al.** Impact of medication adherence on hospitalization. *Med Care* 2005;43(6):521–30.
81. **Balling L, Erstad BL, Weibel K.** Impact of a transition-of-care pharmacist during hospital discharge. *J Am Pharm Assoc* 2003;55(4):443–8.
82. **Mueller SK, Sponsler KC, Kripalani S, et al.** Hospital-based medication reconciliation practices: a systematic review. *Arch Intern Med* 2012;172(14):1057–69.
83. **Whittington J, Cohen H.** OSF healthcare's journey in patient safety. *Qual Manag Health Care* 2004;13(1):53–9.
84. **Haynes KT, Oberne A, Cawthon C, et al.** Pharmacists' recommendations to improve care transitions. *Ann Pharmacother* 2012;46(9):1152–9.
85. **Gleason KM, McDaniel MR, Feinglass J, et al.** Results of the Medications at Transitions and Clinical Handoffs (MATCH) study: an analysis of medication reconciliation errors and risk factors at hospital admission. *J Gen Intern Med* 2010;25(5):441–7.
86. **Mueller SK, Kripalani S, Stein J, et al.** A toolkit to disseminate best practices in inpatient medication reconciliation: multi-center medication reconciliation quality improvement study (MARQUIS). *Jt Comm J Qual Patient Saf* 2013;39(8):371–82.
87. **Perrone J, Nelson LS.** Medication reconciliation for controlled substances—an “ideal” prescription-drug monitoring program. *N Engl J Med* 2012;366(25):2341–3.
88. **Heyworth L, Paquin AM, Clark J, et al.** Engaging patients in medication reconciliation via a patient portal following hospital discharge. *J Am Med Inform Assoc* 2014;21(e1):e157–62.
89. **Coleman EA, Parry C, Chalmers S, et al.** The care transitions intervention: results of a randomized controlled trial. *Arch Intern Med* 2006;166(17):1822–8.
90. **Patient experience case study—CRMC.** Available from: <http://www.theberylinstitute.org/default.asp?page=CASE0812>. The Beryl Institute. Patient experience case study—CRMC; Accessed March 15, 2015.
91. **Fischer MA, Choudhry NK, Brill G, et al.** Trouble getting started: predictors of primary medication nonadherence. *Am J Med* 2011;124(11):1081.
92. **Stewart S, Pearson S.** Uncovering a multitude of sins: medication management in the home post acute hospitalisation among the chronically ill. *Aust N Z J Med* 1999;29(2):220–7.
93. **Curkendall SM, Thomas N, Bell KF.** Predictors of medication adherence in patients with type 2 diabetes mellitus. *Curr Med Res Opin* 2013; 29(10):1275–86.
94. **Powers MA, Bardsley J, Cypress M.** Diabetes self-management education and support in type 2 diabetes: a joint position statement of the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics. *Diabetes Care* 2015;38(7):1372–82.
95. <http://www.pewresearch.org/fact-tank/2013/06/06/cell-phone-ownership-hits-91-of-adults/>.
96. <http://www.pewinternet.org/2015/04/01/us-smartphone-use-in-2015/>.
97. **Park LG, Howie-Esquivel J, Chung ML.** A text messaging intervention to promote medication adherence for patients with coronary heart disease: a randomized controlled trial. *Patient Educ Couns* 2014;94(2): 261–8.
98. **Arora S, Peters AL, Agy C.** A mobile health intervention for inner city patients with poorly controlled diabetes: proof-of-concept of the TEXT-MED program. *Diabetes Technol Ther* 2012;14(6):492–6.
99. **Ostrowski M.** Report takes aim at America's other drug problem: poor adherence. [editorial]. *J Fam Pract* 2007;56:734.

From the Department of Medicine (MTB, SD), Rush Medical College, Chicago, Illinois; Department of Medicine (CJB), Clinical Faculty Feinberg School of Medicine, Northwestern University, Evanston, Illinois; Vizient Inc. (KD), Irving, Texas; Fantus General Medicine Clinic (SS), John H. Stroger Jr Hospital, Chicago, Illinois; Department of Internal Medicine (SM), Cook County Health and Hospital System, Chicago, Illinois.

Submitted October 29, 2015; accepted January 25, 2016.

The authors have no financial or other conflicts of interest to disclose.

Correspondence: Marie T. Brown, MD, Department of Medicine, Rush Medical College, 251 Longcommon Road, Chicago, IL 60612. (E-mail: mbrown@mbrownmd.net).