

# In Chronic Disease, Nationwide Data Show Poor Adherence by Patients to Medication And by Physicians to Guidelines

**A widespread approach that incorporates various stakeholders may be necessary to change adherence behavior**

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## ABSTRACT

**Purpose:** It is widely acknowledged in small studies that provider variation from evidence-based care guidelines and patient medication nonadherence lead to less than optimal health outcomes, increasing costs, and higher utilization. The research presented here aims to determine the prevalence of patient adherence to a medication regimen and provider adherence to guidelines for a variety of chronic conditions, using nationally representative data.

**Design:** A retrospective analysis of administrative claims data from a large national insurer was conducted.

**Methodology:** The study examined multiple quality indicators exemplifying evidence-based medicine and medication adherence for

several chronic conditions. Medication possession ratio (MPR) determined patient adherence. Using EBM Connect software created by Ingenix, we measured adherence to guidelines by applying a series of clinical rules and algorithms.

**Principal findings:** Adherence to the evidence-based practice guidelines examined in this study averaged approximately 59 percent, while patient medication nonadherence rates for all the conditions studied averaged 26.2 percent, with a range of 11 percent to 42 percent. Physician adherence to guidelines was highest in the prescribing of inhaled corticosteroids for persistent asthma. Ironically, medication adherence rates for inhaled corticosteroids were the worst identified. The best medication adherence rate was observed in patients with hypertension.

**Conclusion:** Like earlier studies, this analysis finds that poor adherence is common across the nation and across common chronic conditions.

## INTRODUCTION

It is widely acknowledged that variations in care and poor compliance with evidence-based care

guidelines lead to less than optimal health outcomes. McGlynn et al found that outpatients receive evidence-based care approximately 50 percent of the time (McGlynn 2003). More recent studies demon-

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strate similar problems in the pediatric and elderly populations (Mangione-Smith 2007, Jencks 2000, Schoen 2006). These striking and disturbing results continue to pave the way for the implementation and refinement of pay-for-performance initiatives and evolving physician-level measurement (Rosenthal 2005). Several studies have demonstrated that the implementation of evidenced-based, guideline-driven care results in improved clinical and economic outcomes (Peterson 2006, Walsh 2006, Yurk 2004).

Such strategies address physician performance, yet, even with half of patients with chronic conditions receiving appropriate evidence-based care, many still have poor outcomes. These outcomes are often related to patients' poor self-management, including nonadherence to medication.

Medication adherence, as used in this paper, is the extent to which a patient acts in accordance with the prescribed interval and dosage regimen as recommended by the health care provider (ISPOR). Nonadherence to medications may occur for a variety of reasons. One that is frequently discussed in the literature is cost. Patients who cannot afford the cost or even the copayments will frequently be nonadherent by not filling or not refilling prescriptions, by reducing doses to achieve longer supply, or by skipping doses (Kessler 2007, Tseng 2004).

There are many other concerns that can be linked to reduced medication adherence. A Boston Consulting Group/Harris Interactive survey found that 24 percent of nonadherence is related to forgetting to take or to refill prescriptions and that 20 percent is related to concern about side effects. Seventeen percent stated that cost was the primary issue, 14 percent didn't feel they needed the medication, and the remaining 21 percent stated a

variety of other reasons (BCG 2003).

In this paper, we present results from analyses of claims data from a national health plan. We sought to determine if findings from earlier studies, with study populations that were smaller than the present study, would be confirmed on a national scale and for multiple common primary care conditions. These results illustrate widespread medication adherence problems regardless of condition, and these problems contribute to higher health care utilization, increased costs, and poor outcomes. Finally, we compare our findings with current literature, offer suggestions for improving medication adherence, and discuss the results' implications on health care costs and outcomes.

## **METHODS**

### **Data**

A retrospective analysis was conducted based on claims data from a large national health plan (United-Healthcare) with more than 4 million members in regions across the United States. The data consist of pharmacy and medical claims as well as eligibility information and a subset of laboratory results. The data set does not contain any personal identifiers and is compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

### **Study population**

Study subjects were identified as having at least 2 medical claims during the period from Oct. 1, 2002 through Dec. 31, 2004 who had a diagnosis of asthma, chronic heart failure (CHF), coronary artery disease (CAD), depression, diabetes, hyperlipidemia, hypertension, or migraine, using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes.

A separate analyses for each dis-

ease condition was conducted; subjects were not mutually exclusive. The index date for all subjects was set as Sept. 30, 2004 to standardize the study follow-up period using the most currently available claims data.

Subjects were required to be age 18 or older for all conditions except pediatric asthma, to be continuously enrolled with medical benefits for at least 12 months before the index date, and to be continuously enrolled with pharmacy benefits for at least 6 months before the index date.

For asthma, additional eligibility criteria to stratify pediatric asthma (ages 5–17) versus adult asthma (age 18 or older) was applied and excluded subjects with chronic obstructive pulmonary disease (COPD). In addition, subjects were identified as having persistent asthma if they met any of the following criteria: at least 1 hospitalization for asthma as the principal diagnosis in the past 12 months, at least 1 emergency room visit for asthma as the principal diagnosis in the past 12 months, 6 or more outpatient visits for asthma in the past 12 months, 2 or more prescription fills for oral corticosteroids in the past 6 months, or 2 or more prescription fills for any asthma medications in the past 12 months.

EBM Connect software was used to select patients and to measure guideline and medication adherence. The software, used to measure guideline adherence through application of a series of clinical rules and algorithms, was developed through the review of published literature, review by clinicians, and validation analyses of claims data.

Utilizing national, peer-reviewed guidelines and expert coding, the rules and algorithms in the software are regularly updated to reflect the most current evidence.

## Outcome measures

The study examined multiple quality indicators exemplifying evidence-based medicine and medication adherence for nine chronic conditions that are prevalent and costly to society: pediatric asthma, adult asthma, CHF, CAD, depression, diabetes, hyperlipidemia, hypertension, and migraine.

Patients were identified by ICD-9 codes in claims incurred before the index date. Guideline adherence was estimated as the proportion of patients with at least one prescription fill of a recommended medication during the period 180 days before and 90 days after the index date. To calculate medication adherence, the medication possession ratio (MPR) was computed for study subjects with at least two fills for the identified medication during the period 180 days before and 90 days after the index date. MPR was defined as the ratio of days supplied of one or more medication refills, excluding the days supplied from the last prescription fill, divided by the time elapsed between the first and last fill date. The MPR threshold of 70 percent was used to classify adherent versus non-adherent subjects.

## RESULTS

Most (94 percent) enrollees were in the commercial segment of the health plan, 2 percent were under Medicaid, and 4 percent were under Medicare. Eight percent of enrollees were over age 65 years, and 24 percent were under age 18. While women constituted half of the enrollees in total and in the commercial plan, they made up nearly 60 percent of both the Medicaid and Medicare enrollee population (Table 1).

Adherence to evidence-based practice guidelines examined in this study averaged approximately 59 percent (Table 2). As found in other studies, levels of adherence to

guidelines varied across conditions and measures (BCG 2003). Use of angiotensin-converting enzyme (ACE) inhibitors was found in only 35 percent of patients with coronary artery disease, and just 36 percent of patients with hyperlipidemia had filled a prescription for a statin or appropriate alternative therapy.

Analyzing patient medication adherence, we found high rates in patients with diabetes, of whom 80 percent had filled at least one prescription for an oral antidiabetic medication.

Among patients with depression, 85 percent of patients had filled a prescription for an antidepressant and 56 percent had filled a prescription for either selective serotonin reuptake inhibitors (SSRIs) or serotonin & norepinephrine reuptake inhibitors (SNRIs).

For asthma, 78 percent of adult persistent asthma patients and nearly all of the pediatric persistent asthma patients (97 percent) filled a prescription for an inhaled corticosteroid.

Patient medication nonadherence rates across all the conditions studied averaged 26 percent, with a range of 11 percent to 42 percent. Nonadherence with a variety of hypertension medications was 11 percent. Patients with diabetes had nonadherence rates that ranged

from 16 percent to 25 percent. More than a quarter of patients with depression were non-adherent with their antidepressant, while 37 percent of adults and 42 percent of children with persistent asthma (high-utilizers of medical service) were not compliant with their inhaled corticosteroid therapy. Similar results were observed for patients with CHF, CAD, and hyperlipidemia (Table 3).

## DISCUSSION

These data offer another look at the prevalent medication adherence problem that exists throughout our health care system. Past research has demonstrated similar findings at a more condition-specific level.

A recent study of diabetic patients found nonadherence rates ranging from 13 percent to 64 percent (Lee 2006). Patients with major depression were discovered to have nonadherence rates around 50 percent after three months (Vergouwen 2002). An examination of patients with at least one of four cardiovascular-related conditions (coronary heart disease, hypertension, diabetes, and hyperlipidemia) found an overall nonadherence rate of 40 percent (Gazmararian 2006).

Also, a study of six classes of chronic medications revealed nonadherence rates of 43 percent for calcium channel blockers, 35 per-

**TABLE 1**  
**Member age and gender by insurance type**

**Members between Oct. 1, 2002 and Dec. 31, 2004**

Age group	Total members: (N=4,330,240)	Commercial (n=4,070,426)	Medicaid (n=86,605)	Medicare (n=173,210)
0-17	24%	92%	8%	0%
18-34	20%	98%	2%	0%
35-49	28%	99%	1%	0%
50-64	20%	98%	1%	1%
65+	8%	56%	1%	43%
Female	51%	51%	58%	58%

**TABLE 2****Evidence-based guideline adherence, by chronic conditions**

Quality Indicators	# of eligible patients	% of patients receiving recommended care		
		All	Commercially insured	Medicare
Coronary artery disease (CAD) patients with ACE inhibitor	26,220	35%	36%	29%
Hyperlipidemia patients with statin or acceptable alternative	622,110	36%	38%	27%
Congestive heart failure (CHF) patients with beta blocker	5,883	50%	53%	39%
Congestive heart failure (CHF) patients with ACE inhibitor	5,883	55%	58%	44%
Depression patients with SSRIs or SNRIs	26,068	56%	56%	45%
Depression patients with any antidepressants	26,068	85%	85%	72%
Migraine patients with narcotics	33,984	57%	57%	66%
Adult persistent asthma patients with ICS	53,470	78%	79%	58%
Diabetes patients with oral diabetes therapy	162,394	80%	81%	74%
Pediatric persistent asthma patients with ICS	8,378	97%	97%	96%*

\*Medicaid pediatric population data

cent for ACE inhibitors, and 38 percent for statins (Shrank 2006). These studies generally find non-adherence to be even more prevalent than we did, and this may reflect the lack of standardization of study design and/or the effect of insurance coverage on our population.

Other studies demonstrate that those covered under Medicaid and Medicare may have more medication adherence problems, particularly related to cost barriers (Mojtabai 2003). Nevertheless, it is clear that even patients who have commercial insurance are frequently non-adherent with their medications.

This study's results show that adherence to guidelines as well as patient adherence to medication is a cross-cutting issue, irrespective of socioeconomic status and level of insurance coverage. The differences in the rates of the commercial and Medicare populations raise interesting questions about the effects of insurance coverage on quality of care.

Past research has focused mainly on individual conditions, types of providers or patients, local regions,

and methods for improving adherence. The data presented here, representing a national commercially insured population, illustrate the need for a widespread approach to address problems with medication adherence.

It is necessary but not sufficient to say that providers and patients must comply. The issue of medication adherence is far from new, and not restricted to the United States (WHO 2003). This may be the ideal time to tackle these problems again as health care costs continue to rise and poor outcomes, some perhaps resulting from nonadherence, assist in strangling an already flailing system. Along with costs, the advent of consumer-directed health care and the growth of consumer-directed health information has primed this key target audience. Now may be the ideal time to reach out to consumers on the importance of medication adherence, by implementing a variety of strategies.

#### **Clinical and economic problems**

Studies have demonstrated that nonadherence to medication is a costly problem because of poor out-

comes. Sokol et al found that annual medical costs for patients with high cholesterol fell from \$6,810 to \$3,124 as medication adherence improved from the lowest range studied (less than 20 percent) to the highest range (80 percent and greater) (Sokol 2005).

Similarly, they found that costs for diabetic patients dropped from \$8,812 to \$3,808. Hepke et al, also studying a diabetic population, showed a consistent decrease in costs from a peak of approximately \$6,200 as compliance rose above 40 percent (Hepke 2004).

Another study observed a decrease of \$685–\$950 in 1997 dollars per diabetic patient as glycemic control improved, while two recent studies discovered that adherence reduced diabetic costs by somewhere between 4 percent and 29 percent, respectively, due mainly to substantial decreases in hospitalizations (Wagner 2001, Shenolikar 2006, Lee 2006).

Hospital admissions and emergency department utilization are also expensive and preventable for patients with asthma. One study showed that increased use of inhaled corticosteroids contributed

**TABLE 3****Nonadherence with prescription medications, by chronic conditions**

<b>Chronic Condition</b>	<b>% of Patients not adherent with medications (MPR&lt;70%)</b>
Pediatric persistent asthma: ICS	42%
Adult persistent asthma: ICS	37%
Chronic heart failure:	
ACE inhibitor	19%
Beta blockers	25%
Coronary artery disease: ACE inhibitor	15%
Depression: SSRIs or SNRIs	26%
Diabetes:	
Sulfonylurea	22%
Biguanides	25%
Thiazolidinedione	20%
Any oral therapies	16%
Hyperlipidemia: Statins or other alternatives	21%
Hypertension: Any acceptable therapies	11%

**Drug and drug classes reviewed by condition**

Asthma: inhaled corticosteroids (ICS)

Chronic heart failure: angiotensin-converting enzyme (ACE) inhibitors, beta-blockers

Coronary artery disease: ACE-inhibitors

Depression: selective serotonin reuptake inhibitors (SSRIs), serotonin &amp; norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, monoamine oxidase inhibitors (MAOI), bupropion, nefazodone, mirtazapine

Diabetes: Biguanides, thiazolidinediones, alpha-glucosidase inhibitor, sulfonylurea, meglitinide, D-phenylalanine

Hyperlipidemia: statins, niacin, fibric acid derivatives

Hypertension: ACE-inhibitors, angiotensin receptor blockers (ARBs), diuretics, calcium-channel blockers, alpha-adrenergic blockers, central alpha-adrenergic agonists, vasodilators, peripheral adrenergic antagonists, selective aldosterone receptor antagonists

to a 35 percent decrease in pediatric hospitalizations and a 27 percent decrease in emergency department visits, while another also demonstrated an association between non-adherence to asthma medications and increased risk of hospitalization (Cloutier 2005, Piccoro 2001). Chronic heart failure patients have been shown to cost nearly \$8,000 per hospitalization, leading to aggregate costs in the millions of dollars that can be reduced by greater adherence to beta-blockers and ACE inhibitors (Xuan 2000). Fi-

nally, patients with depression have lower costs for both primary depression care and care associated with comorbid conditions (Eaddy 2005, Katon 2005).

Costs for primary care of depression run more than \$6,000 and potentially could be reduced by one sixth, while charges for three common comorbidities have been determined to range from \$400 to more than \$1,100, with a possible 6 percent to 20 percent reduction in these charges with adequate medication adherence.

Concerns remain about how well physicians and others assess patients' medication adherence, and further, what they are doing to improve poor rates (Shrank 2006). Yet as we noted earlier, it is not the sole responsibility of the provider and/or the patient to take on the challenge of improving medication adherence, as others' policies and practices also influence adherence rates.

Studies find that in patients with diabetes and high cholesterol, high levels of medication adherence correlate with subsequent lower disease-related medical costs, and these savings more than compensate for the increase in medication costs, often borne by companies offering employer-based insurance (Epstein 2004). Several studies find that medical care utilization rates for various conditions, including diabetes, high cholesterol, hypertension and chronic heart failure, were significantly lower for patients with high levels of medication adherence (Rosenthal 2004, Stuart 2005).

**Improving medication adherence**

Patients carry the primary responsibility of being adherent to their medication regime. Still, the fact that patients aren't receiving prescriptions for appropriate medication, or are receiving multiple, possibly contraindicated, prescriptions from one or more providers, necessitates strategies that go beyond the individual patient.

Another approach to improving medication adherence encourages the delivery of evidence-based care. Literature continues to emphasize the poor level of evidence-based care delivered to patients with chronic conditions. McGlynn et al found that for the conditions we reviewed (hypertension, CAD, CHF, diabetes, depression, hyperlipidemia, and asthma), the percent-

age of recommended care received ranged from a high of 68 percent (CAD) to a low of 45.4 percent (diabetes), with the mean percentage across these seven conditions being 57.4 percent (McGlynn 2003).

Building on the literature regarding the challenges of promoting clinical practice guidelines, and the groundswell of work to promote patient-centered care and participatory decision making, it behooves quality improvement experts to take advantage of the tools and knowledge to access and reduce barriers to medication adherence. Some strategies include the use of opinion leaders to champion the use of practice guidelines and the use of quality improvement activities, such as pay for performance (Doumit 1997).

Medicare's pilot pay-for-performance program, which pays physicians on the basis of a set of evidence-based care measures (e.g., annual eye exams for diabetes, appropriate asthma medication) promises to improve quality by giving providers an incentive to follow evidence-based guidelines (Sokol 2005, Hepke 2004).

While these payment models stand to influence provider behaviors, medication coverage policies more often create barriers to patient medication adherence. Coverage caps and gaps, copayments, and premiums all put financial strains on low-income patients.

The "doughnut hole" in Medicare Part D design is a prime example of a coverage gap that has the potential to deter patients from being compliant with their medication to avoid an abrupt jump in out-of-pocket costs (Stuart 2005).

All health care providers — physicians, nurses, pharmacists and others — have a key role in improving medication adherence, including promoting the importance of adherence to their patients. Involving their patients in medica-

tion decisions and ensuring that these decisions fit within their lifestyle and budget will increase the probability of adherence.

Providers can also encourage appropriate medication use by discussing adherence problems at follow-up visits and by working collaboratively with patients to overcome identified barriers (Hesler 2004).

Education, information, and access to medications are three important factors in medication adherence. Understanding the purpose of a medication, its possible side effects, and its health benefits will require education and information from providers, health plans, employers, and others. Tools such as automated pill cases and care management call can facilitate the timely and appropriate use of medications (Haynes 2005).

### **Limitations**

It is widely acknowledged that the use of claims data for various analyses can be a limitation in the generalization and application of results (Motheral 1997). Problems with data entry, coding, and completeness all create challenges with analysis and the relative significance of findings.

While these are examples of claims data limitation, it must also be recognized that until electronic medical records are more readily available, claims data constitute the most comprehensive form of information available for utilization research. Finally, the comprehensiveness of the database used for these analyses allows for assurance that findings are relatively generalizable.

While MPR may not be an exact tool, it is widely used and accepted as a measure of adherence and persistence. As with clinical claims data, usage of pharmacy data has limitations, but again, pharmacy data are often used to assess fill-rates; it is the most efficient way to

obtain medication dispensing information.

The authors acknowledge that the inclusion criteria of limiting medication adherence analyses to only those patients filling at least two prescriptions potentially underestimates the medication non-adherence rates; however, when using claims data, two medications are required to calculate a time-to-refill ratio.

Similarly, other inclusion criteria, such as those for persistent asthma, based on emergency room visits, hospitalization, and other health care service utilization measures, also serve to underestimate medication adherence. It is understood that a more restrictive inclusion rule requiring more claims for a condition would reduce possible biases and reduces the number of false positives — those that appear to meet the criteria but may have been misdiagnosed or miscoded.

### **Considerations for research**

As this area of research matures, numerous questions must be addressed. Are patients simply not filling the prescriptions they receive, and therefore the rates of medication adherence are grossly underestimated? Are provider-prescribed changes in dose and/or medication types leading to alteration in fill rates that may be misinterpreted as poor adherence? Are patients getting medications from other sources, creating the impression of nonadherence?

What role could and should health care providers play in enabling patients to adhere to their medication regimens? What role can health plans play in improving medication adherence?

With nearly one-fifth of patients noncompliant with their medication regimen, it is imperative that these questions be considered as the field of health services research continues to evaluate medication ad-

herence behaviors and improvement strategies.

## CONCLUSION

Past research has already demonstrated on a smaller scale the extent of medication adherence problems. The causes of medication nonadherence have been delineated and some strategies for improving medication adherence have been implemented in small target populations. Adherence problems stem from both patient and provider behaviors and require that both are invested in making improvements.

This study demonstrates that the problems seen in other disease- and site-specific research studies are similar across conditions and across the country. While targeted activities to improve adherence have proven successful, a more widespread approach with a variety of key stakeholders may be necessary to truly change adherence behaviors.

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