

# The Implications of Choice

## Prescribing Generic or Preferred Pharmaceuticals Improves Medication Adherence for Chronic Conditions

William H. Shrank, MD, MSHS; Tuyen Hoang, PhD; Susan L. Ettner, PhD; Peter A. Glassman, MBBS, MSc; Kavita Nair, PhD; Dee DeLapp, RPh; June Dirstine; Jerry Avorn, MD; Steven M. Asch, MD, MPH

**Background:** A large proportion of Americans are enrolled in 3-tier pharmacy benefit plans. We studied whether patients enrolled in such plans who receive generic or preferred brand-name agents when initiating chronic therapy were more adherent to treatment than those who received nonpreferred brand-name medications.

**Methods:** We analyzed pharmacy claims filled between October 1, 2001, and October 1, 2003, from a large health plan for 6 classes of chronic medications: 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, calcium channel blockers, oral contraceptives, orally inhaled corticosteroids, angiotensin receptor blockers, and angiotensin-converting enzyme inhibitors. We measured adherence as the proportion of days covered (PDC) in each drug class during the first year of therapy. We evaluated how the formulary status of the initial prescription (generic, preferred, or nonpreferred) influenced PDC and adequate adherence, defined as PDC greater than 80%, over the subsequent year.

**Results:** A total of 7532 new prescriptions were filled in 1 of the classes evaluated: 1747 (23.2%) for nonpreferred medications, 4376 (58.1%) for preferred drugs, and 1409 (18.7%) for generic drugs. After controlling for patient sociodemographic characteristics and drug class, PDC was 12.6% greater for patients initiated on generic medications vs nonpreferred medications (58.8% vs 52.2%;  $P < .001$ ). The PDC was 8.8% greater for patients initiated on preferred vs nonpreferred medications (56.8% vs 52.2%;  $P < .001$ ). Patients initiated on generic and preferred medications had 62% and 30% greater odds, respectively, of achieving adequate adherence compared with those who received nonpreferred medications.

**Conclusion:** In 3-tier pharmacy benefit plans, prescribing generic or preferred medications within a therapeutic class is associated with improvements in adherence to therapy.

*Arch Intern Med.* 2006;166:332-337

**Author Affiliations:** Division of Pharmacoepidemiology and Pharmacoconomics, Brigham and Women's Hospital and Harvard Medical School, Boston, Mass (Drs Shrank and Avorn); VA Greater Los Angeles Healthcare System, Los Angeles, Calif (Drs Hoang, Glassman, and Asch); Department of Medicine, The David Geffen School of Medicine at UCLA, Los Angeles (Drs Ettner, Glassman, and Asch); RAND Health, Santa Monica, Calif (Drs Glassman and Asch); Department of Pharmacy, University of Colorado Health Sciences Center, Denver (Dr Nair); Anthem Blue Cross and Blue Shield, Denver (Mss DeLapp and Dirstine); and Anthem Prescription Management, Denver (Mss DeLapp and Dirstine).

**A** GROWING BODY OF RESEARCH has evaluated the relationship between pharmacy benefit design and prescription drug use. These studies have consistently found that increased copayment requirements are associated with decreased use of prescription drugs,<sup>1-7</sup> even for chronic medications to treat diabetes mellitus, hypertension, and hypercholesterolemia.<sup>7,8</sup> These studies have looked at populations, often cross-sectionally, and focused on how policy decisions made by health plans or state payers affect use.

The trend in pharmacy benefits is to offer physicians and patients substantial choice when prescribing, and out-of-pocket costs are often determined by decisions at the physician-patient encounter.<sup>9</sup> In 2004, approximately 65% of Americans with employer-based prescription drug coverage were enrolled in 3-tier pharmacy benefit structures.<sup>10</sup> In 3-tier plans, enrollees are re-

quired to pay highest copayments for nonpreferred brand-name medications (third tier), smaller copayments for preferred brand-name drugs (second tier), and smallest or no copayments for generic medications (first tier). Within these plans, physician and patient decisions to treat a medical condition with a generic rather than a nonpreferred medication can significantly affect the patient's out-of-pocket costs, with an average difference of \$23 a month in 2004.<sup>10</sup>

Several studies have evaluated the effects of converting from a nontiered or 2-tiered pharmacy benefit system to a 3-tiered system. Three-tier plans steer patients toward preferred medications<sup>11-14</sup> and control health plan spending,<sup>14,15</sup> but also shift more of the costs of prescription drugs to patients.<sup>15</sup> Overall use of prescription drugs may also decrease when 3-tiered plans are instituted.<sup>6,15,16</sup> Little is known about the mechanism of this decrease in use, and some have speculated that more choice has led to increased confusion for patients and phy-

sicians who may not be aware of patients' out-of-pocket cost requirements at the time of prescribing.<sup>17</sup>

While previous studies have focused on the effects of insurers' decisions to increase copayments or implement tiered benefits, little is known about how decisions at the physician-patient level affect medication use. To our knowledge, no previous study has evaluated how prescribing decisions within a 3-tier framework affect patient adherence. We evaluate a specific but common clinical scenario, the initiation of a chronic medication. We examine whether the choice to initiate a generic medication, a preferred formulary medication, or a nonpreferred formulary medication influences patient adherence to chronic therapy.

## METHODS

### DATA SOURCE

Pharmacy data were supplied by Anthem Blue Cross and Blue Shield and Anthem Prescription Management. Anthem Blue Cross and Blue Shield is a large managed care plan providing health insurance coverage to patients in Colorado and Nevada. Large group, small group, individual, and state accounts were included in this analysis, while Medicare supplemental and national accounts were excluded because of difficulty accessing complete pharmacy records. The average enrolled membership of patients included in this study during the 2-year period was 270 137 members per month.

### IDENTIFICATION OF STUDY SUBJECTS

After excluding patients who were not continuously enrolled in the plan during the entire study period, we identified all patients who filled a new prescription in 1 of 6 drug classes: calcium channel blockers, 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins), oral contraceptives, orally inhaled corticosteroids, angiotensin receptor blockers, and angiotensin-converting enzyme inhibitors. These classes of medications were selected because they are all commonly prescribed, include multiple branded options with similar clinical efficacy,<sup>18</sup> and are typically prescribed for chronic use. Patients prescribed a medication in any of these classes would be expected to take the medication continually for the subsequent year. All but the angiotensin receptor blockers and inhaled corticosteroids included generic options during the study period.

New users were captured by identifying all prescriptions filled in the specified classes between October 1, 2001, and October 1, 2002. Index, or new, prescriptions were those filled by patients who had filled no prescriptions in the same class in the previous 6 months. We then captured all prescriptions filled in the same class in the 365 days following the index claim. If a patient initially filled a prescription for 1 statin and filled a prescription for a different statin later in the year, regardless of whether it was generic, preferred, or nonpreferred, we included all subsequent claims for drugs within the class when measuring adherence.

All patients in the study were enrolled in plans with at least 3 tiers. A small percentage of patients were enrolled in 4-tier plans (which charged greater copayments for high-expense or "lifestyle" drugs), but none of the drug classes evaluated in this study placed any brands into the fourth tier and only the first 3 tiers are evaluated herein. Copayments differed among insurance plans, and ranged from \$5 to \$20 for generics, \$15 to \$40 for preferred medications, and \$30 to \$60 for nonpreferred medications.

## OUTCOME MEASURES

### Switching Behavior

We grouped patients by the tier of initial prescription, and identified the frequency with which patients switched from the index prescription to a drug in a different tier within the same class. We compared switching rates by tier of initial prescription to assess how the decision to prescribe a generic, preferred, or nonpreferred medication affects the switching rates over the subsequent year.

### Adherence

Adherence was measured by using data on filled prescriptions to calculate the proportion of days that patients possessed a supply of any medication in the class of the index prescription in the year following the index prescription. The days' supply dispensed during the year was divided by 365 to calculate the proportion of days covered (PDC), a well-established measure of adherence.<sup>19</sup> Adherence, therefore, was measured on a scale of 0% to 100%. Patients who filled prescriptions for supplies greater than the number of days remaining in the year subsequent to the initial prescription were only given "credit" for the days remaining in the year. Patients achieved adequate adherence if the PDC was greater than 80%. While there are no data to suggest that 80% represents a clinically significant threshold, to our knowledge, this cutoff was used previously to differentiate levels of adherence.<sup>19-21</sup>

### PREDICTORS OF ADHERENCE

The predictor of interest was the tier of the initial prescription filled in a drug class: first-tier generics, second-tier preferred drugs, or third-tier nonpreferred drugs. Patients were categorized by the choice of tier of the index prescription, regardless of switches to lower- or higher-tier medications over the subsequent year. We selected the choice of tier of the initial prescription in a drug class (ie, generic, preferred, or nonpreferred) rather than the actual copayment amount as our predictor of interest because we believe that the tier of the drug is more relevant to the clinical encounter. Physicians and patients are more likely to be familiar with the tier of a prescription than the copayment, and identifying a patient's formulary is more straightforward than identifying the precise copayment that a patient will be charged.

We also studied the effects of patient age, sex, and income on adherence. Income was estimated by linking median household income in ZIP code tabulation areas from the 2000 US census data with patient ZIP codes in the claims. Although this is an imperfect proxy for individual-level income,<sup>22,23</sup> its use is common in health services' research because of the lack of alternatives with claims data analyses. An average annual income of less than \$30 000 in the ZIP code of residence was considered low, annual income from \$30 000 to \$60 000 was categorized as middle, and annual income greater than \$60 000 was categorized as high. We included drug class as a predictor to control for different adherence patterns in different drug classes.

### STATISTICAL ANALYSIS

Multivariate linear regression was used to evaluate the relationship of our outcome variable, PDC, with the tier of the index prescription and all other predictors. Using a logistic transformation of the PDC as the dependent variable produced qualitatively similar results, so for ease of interpretation, we report the results for the untransformed version. We used logistic regression to model

the relationship between predictors and the likelihood that patients achieve adequate adherence, greater than 80% of days covered in the first year of therapy. Predictors were considered significant at  $P < .05$ . We used the generalized estimating equation to control for clustering at the physician level. All statistical procedures were performed using commercially available software.<sup>24</sup>

## RESULTS

### POPULATION CHARACTERISTICS

A total of 7532 new prescriptions were filled in the 6 drug classes analyzed between October 1, 2001, and October 1, 2002. These prescriptions were filled by 6755 patients, and written by 3110 physicians. Almost 90% of patients filled a new prescription in only 1 of the classes we studied, 9% filled prescriptions in 2 classes, and 1% filled a new prescription in 3 or 4 classes. Approximately 10% of patients lived in ZIP codes where the av-

**Table 1. Characteristics of the 6755 Patients**

Characteristic	Value*
Age, y†	42.2 (14.7)
Female sex	65.3
No. of prescriptions filled per month‡	2.7 (1.8)
Annual income in home ZIP code	
Low	10.3
Middle	68.9
High	21.8

\*Data are given as percentage of the sample unless otherwise indicated. Percentages may not total 100 because of rounding.

†Data are given as mean (SD).

‡The median was 2.3 (interquartile range, 1.6-3.2) prescriptions.

erage annual household income was less than \$30 000 (**Table 1**).

### MEDICATION CHOICES AND SWITCHING BEHAVIOR

Of the 7532 new prescriptions, 1747 (23.2%) were for nonpreferred third-tier medications, 4376 (58.1%) were for preferred second-tier medications, and 1409 (18.7%) were for generic first-tier medications (**Table 2**).

Of patients initially prescribed generic medications, 13.6% switched to a drug in a different tier within the class (**Table 3**). Of those initially prescribed preferred medications, 19.9% switched to a medication in a different tier within the class. Those prescribed nonpreferred medications were most likely to switch; 28.3% switched to a different tier, with 10.0% switching to generics and 18.3% switching to preferred brand-name medications. Patients initially prescribed nonpreferred medications were 2.1 times more likely to switch to a medication in another tier within the class than patients initially prescribed generic medications. Overall, patients who switched from their initial prescription were 2.8 times more likely to switch to a lower-tier medication (with a lower copayment) than to a higher-tier medication.

### MEDICATION ADHERENCE

Mean PDC was 54.8% for oral contraceptives, 56.5% for calcium channel blockers, 64.9% for ACE inhibitors, 60.7% for angiotensin receptor blockers, 62.1% for statins, and 20.6% for inhaled steroids (**Table 2**). Several patient characteristics significantly influenced adherence (**Table 4**). Older patients were more adherent; the PDC was 3 percentage points greater as patients aged 10 years ( $P < .001$ ). The PDC was

**Table 2. New Prescriptions by Tier and Adherence by Drug Class**

Drug Class	Total No. of Prescriptions	Generic, %*	Preferred, %*	Nonpreferred, %*	PDC (Adherence), Mean
Oral contraceptives	2407	34.2	38.2	27.5	54.8
Calcium channel blockers	633	41.1	42.8	16.1	56.5
ACE inhibitors	1852	16.4	61.9	21.8	64.9
Angiotensin receptor blockers	325	0	58.5	41.5	60.7
Statins	1641	1.4	73.9	24.7	62.1
Inhaled corticosteroids	674	0	94.5	5.5	20.6
Overall	7532	18.7	58.1	23.2	56.1

Abbreviations: ACE, angiotensin-converting enzyme; PDC, proportion of days covered.

\*Percentages may not total 100 because of rounding.

**Table 3. Switching Behavior: Patients Prescribed a Medication in 1 Tier Who Switched to a Medication in Another Tier Within the Same Class in the Subsequent Year\***

Initial Prescription	Patients Who Switched to a Medication in a Different Tier, %			Total Switches
	Generic	Preferred Drug	Nonpreferred Drug	
Generic	0	7.5	6.1	13.6
Preferred drug	14.9	0	5.0	19.9
Nonpreferred drug	10.0	18.3	0	28.3

\*Generic medications fell in the first tier, preferred drugs in the second tier, and nonpreferred drugs in the third tier.

**Table 4. Linear Regression Evaluating Predictors of Adherence, Measured as PDC\***

Predictor†	Variable Estimate	SE	P Value
Generic	6.6‡	1.3	<.001
Preferred formulary agent	4.6‡	1.0	<.001
Annual income			
Middle	2.2	1.5	.15
High	3.9‡	1.6	.02
Male sex	3.1‡	1.0	.001
Age	0.3‡	0.0	<.001
Oral contraceptives	-0.2	1.5	.91
CCBs	-5.5‡	1.7	.001
ACE inhibitors	1.9	1.1	.09
ARBs	0.6	2.1	.76
Inhaled corticosteroids	-37.3‡	1.3	<.001

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; PDC, proportion of days covered.

\*Adjusted for clustering as the physician level using generalized estimating equations.

†Referent categories were as follows: nonpreferred formulary agents, low income, female sex, and statins.

‡Statistically significant ( $P < .05$ ).

4 percentage points greater for patients who resided in high-income ZIP codes compared with those residing in low-income ZIP codes ( $P = .008$ ). The PDC was 3 percentage points greater for males than females ( $P < .001$ ).

After controlling for demographic variables and drug class, we found that the formulary status of the index prescription significantly affected patient adherence to chronic medications. The PDC was 6.6 percentage points greater for patients who filled prescriptions for generic medications compared with patients who received nonpreferred medications, corresponding to a 12.6% increase in adherence (58.8% vs 52.2%;  $P < .001$ ). Similarly, the PDC was 4.6 percentage points greater for patients who filled prescriptions for preferred branded medications compared with patients who received nonpreferred medications, corresponding to an 8.8% increase in adherence (56.8% vs 52.2%;  $P < .001$ ).

#### ADEQUATE ADHERENCE

Patients who received generic medications had 62% greater odds (OR, 1.62, 95% confidence interval, 1.39-1.89) of achieving adequate adherence (>80% of days covered), and patients who received preferred branded medications had 30% greater odds (OR, 1.30, 95% confidence interval, 1.15-1.47) of achieving adequate adherence, than those who received nonpreferred branded medications (**Table 5**). Income in ZIP code of residence did not affect the likelihood that patients achieved adequate adherence, while males had 16% greater odds of achieving adequate adherence. We calculated relative risks for variables in the model and found the estimates to be similar to the reported odds ratios.

#### COMMENT

We found that in 3-tier pharmacy benefit plans, the prescription choice made when initiating chronic therapy

**Table 5. Logistic Regression Evaluating Predictors of Adequate Adherence\***

Predictor†	Odds Ratio	95% CI
Generic	1.62‡	1.39-1.89
Preferred formulary agent	1.30‡	1.15-1.47
Annual income		
Middle	1.10	0.95-1.28
High	1.17	0.98-1.39
Male sex	1.16‡	1.03-1.31

Abbreviation: CI, confidence interval.

\*Controlling for drug class and age. Adequate adherence is defined as proportion of days covered >80%.

†The referent categories were as follows: nonpreferred formulary agents, low income, and female sex.

‡Statistically significant ( $P < .05$ ).

significantly affected patient medication adherence. First, a surprisingly high percentage of initial prescriptions were filled for nonpreferred drugs, approximately 23% of all initial prescriptions in the classes we evaluated. Patients initiated on generic medications had 12.6% greater adherence than those who received nonpreferred brand-name formulary agents. Likewise, patients who received preferred brand-name prescriptions had 8.8% greater adherence than patients who received nonpreferred prescriptions. Although the absolute differences in PDC between groups were modest (6.6 percentage points and 4.6 percentage points for generic and preferred medications, respectively, vs nonpreferred medications), these findings demonstrate a relationship between formulary compliance and patient adherence to therapy. For patients enrolled in tiered pharmacy benefit systems, clinicians can influence long-term adherence by choosing wisely within a drug class and prescribing generic or preferred formulary agents when initiating chronic therapy.

In addition, patients initially prescribed generic medications were least likely to switch to a medication in a different tier within the same class. Those who received generics switched at less than half the rate of patients who received nonpreferred medications. Patients who received preferred brand-name drugs were 30% less likely to switch to a medication in another tier than patients who received nonpreferred drugs, and were almost 3 times more likely to switch to a generic than to a nonpreferred drug. These findings suggest that physician workload may decrease when more generics are prescribed, because physicians would likely receive fewer telephone calls from patients, pharmacists, or pharmacy benefits managers to change prescriptions. These findings also suggest that pharmacists may play an important role in educating patients about less expensive medications and facilitating switches.

We would expect that if a physician prescribes and a patient fills a prescription for a more expensive medication, the physician or patient may believe that it is either more effective or associated with less adverse effects than less expensive medication alternatives. We could not control for physicians' or patients' perceived efficacy of generic or brand-name medications, but the evidence for large differentials in adverse effects or efficacy in the classes

of drugs we evaluated is sparse.<sup>18</sup> If we had been able to control for perceived efficacy, we likely would have observed larger adherence differences between patients who initially received generic and nonpreferred medications, if patients who perceive higher efficacy of branded drugs have a greater likelihood of adhering to that drug. For this reason, our results represent a conservative estimate of the relationship between choice of generic medications and adherence to those medications for patients and physicians without strong preferences.

The limitations inherent in using claims data also lead to a conservative estimate of the effect of initial prescription choice in a drug class on adherence. By using pharmacy claims to measure adherence, we are unable to identify patients who never filled the initial prescription. It is likely that some patients, when informed of a high copayment at the pharmacy, may experience “sticker shock” and choose not to fill the initial prescription. As a result, we underestimate nonadherence in this study and likely present a conservative estimate of the effect of the tier of the initial prescription on adherence. We would expect that patients initially prescribed nonpreferred medications would be most likely to decide not to fill the first prescription. In addition, our measure of adherence measures only prescription filling, but cannot definitively measure whether patients took the prescribed medication. Nevertheless, this method is used commonly in health services’ research and is unlikely to bias the comparative findings in this study.

We found that adherence (PDC) in the 6 classes of medications ranged from 20.6% to 64.9%. These findings are within the range of previous research<sup>25-31</sup> using pharmacy claims to evaluate adherence for each of these classes of medications. Our findings that older patients and wealthier patients are more likely to be adherent are consistent with prior research<sup>32-35</sup> on adherence, while previous research<sup>35,36</sup> evaluating the relationship between sex and adherence has been mixed.

Our study is limited by the fact that our patient sample is relatively young, most were employed, and all reside in 1 of 2 Western states. Yet, the pharmacy benefit structures used in this study are representative of typical benefit structures nationwide, and there is little reason to believe that patients from other parts of the country would respond differently. Also, the odds ratios used to present the differences in adequate adherence are somewhat larger than the relative risks (not shown) because of the frequency that patients were adequately adherent.

For patients enrolled in 3-tier pharmacy benefit plans and for physicians who prescribe medications to them, these findings ought to stimulate awareness of the importance of the choice of prescription when initiating therapy. Physicians are often unaware of patients’ formularies and out-of-pocket costs,<sup>37</sup> and rarely discuss out-of-pocket expenses with their patients.<sup>38</sup> This study suggests that patients and physicians need to pay close attention to the formulary status of medications when prescribing to improve adherence. The use of information technology to provide additional decision support for physicians and/or patients at the time of prescribing could help them identify the availability of generic or preferred formulary agents in the therapeutic class prescribed.

While we cannot be sure that the findings from our study generalize to an older population, this study may raise important concerns as the nation prepares for the implementation of the Medicare Modernization Act. The Medicare Modernization Act has endorsed the role of private health plans in the delivery of medications to seniors, likely leading to increased enrollment in tiered pharmacy benefit systems and “assur[ing] that drug costs and formularies will vary from plan to plan and locality to locality.”<sup>39(p391)</sup> Medicare beneficiaries disproportionately use prescription drugs,<sup>40</sup> and many seniors may have difficulty with the cognitive task of navigating tiered formularies and advocating for themselves. As a result, seniors who are unable to identify generic or preferred options within therapeutic classes prescribed may face unnecessarily high out-of-pocket expenses. Careful evaluation of patient populations that have difficulty identifying preferred formulary options, combined with efforts to improve patient and physician awareness of cost requirements at the time of prescribing, could have an important effect on seniors’ adherence to chronic medications.

**Accepted for Publication:** September 3, 2005.

**Correspondence:** William H. Shrank, MD, MSHS, Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women’s Hospital and Harvard Medical School, 1620 Tremont St, Suite 3030, Boston, MA 02120 (wshrank@partners.org).

**Author Contributions:** Dr Shrank had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Financial Disclosure:** None.

**Funding/Support:** This study was supported by a “Locally-Initiated Project” Award from the Veterans Affairs Center for the Study of Healthcare Provider Behavior, a Veterans Affairs Health Services Research and Development Center of Excellence, located within the VA Greater Los Angeles Healthcare System, at Sepulveda Ambulatory Care Center, Sepulveda, Calif. Dr Shrank received a Veterans Affairs Health Services Research and Development fellowship.

**Role of the Sponsor:** The funding bodies had no role in data extraction and analyses, in the writing of the manuscript, or in the decision to submit the manuscript for publication.

**Additional Information:** This project was approved by the VA Greater Los Angeles Healthcare System Institutional Review Board.

## REFERENCES

1. Hillman AL, Pauly MV, Escarce JJ, et al. Financial incentives and drug spending in managed care. *Health Aff (Millwood)*. 1999;18:189-200.
2. Stuart B, Zacker C. Who bears the burden of Medicaid drug copayment policies? *Health Aff (Millwood)*. 1999;18:201-212.
3. Smith DG. The effects of copayments and generic substitution on the use and costs of prescription drugs. *Inquiry*. 1993;30:189-198.
4. Reeder CE, Nelson AA. The differential impact of copayment on drug use in a Medicaid population. *Inquiry*. 1985;22:396-403.
5. Schneeweiss S, Walker AM, Glynn RJ, Maclure M, Dormuth C, Soumerai SB. Outcomes of reference pricing for angiotensin-converting-enzyme inhibitors. *N Engl J Med*. 2002;346:822-829.
6. Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG. The effect of incentive-based formularies on prescription-drug utilization and spending. *N Engl J Med*. 2003;349:2224-2232.

7. Goldman DP, Joyce GF, Escarce JJ, et al. Pharmacy benefits and the use of drugs by the chronically ill. *JAMA*. 2004;291:2344-2350.
8. Ellis JJ, Erickson SR, Stevenson JG, Bernstein SJ, Stiles RA, Fendrick AM. Suboptimal statin adherence and discontinuation in primary and secondary prevention populations. *J Gen Intern Med*. 2004;19:638-645.
9. Avorn J. *Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs*. New York, NY: Random House Publishers; 2004.
10. Kaiser Family Foundation and Health Research and Educational Trust. Employer health benefits: 2004 summary of findings. Available at: <http://www.kff.org/insurance/7148/loader.cfm?url=/commonspot/security/getfile.cfm&PageID=46206>. Accessed October 12, 2004.
11. Rector TS, Finch MD, Danzon PM, Pauly MV, Manda BS. Effect of tiered prescription copayments on the use of preferred brand medications. *Med Care*. 2003;41:398-406.
12. Nair KV, Wolfe P, Valuck RJ, McCollum MM, Ganther JM, Lewis SJ. Effects of a 3-tier pharmacy benefit design on the prescription purchasing behavior of individuals with chronic disease. *J Manag Care Pharm*. 2003;9:123-133.
13. Briesacher B, Kamal-Bahl S, Hochberg M, Orwig D, Kahler KH. Three-tiered copayment drug coverage and use of nonsteroidal anti-inflammatory drugs. *Arch Intern Med*. 2004;164:1679-1684.
14. Motheral B, Fairman KA. Effect of a three-tier prescription copay on pharmaceutical and other medical utilization. *Med Care*. 2001;39:1293-1304.
15. Joyce GF, Escarce JJ, Solomon MD, Goldman DP. Employer drug benefit plans and spending on prescription drugs. *JAMA*. 2002;288:1733-1739.
16. Gleason PP, Gunderson BW, Gericke KR. Are incentive-based formularies inversely associated with drug utilization in managed care? *Ann Pharmacother*. 2005;39:339-345.
17. Shrank WH. Effect of incentive-based formularies on drug utilization and spending. *N Engl J Med*. 2004;350:1057.
18. Oregon Health Sciences University. Drug evaluation review project. Available at: <http://www.ohsu.edu/drugeffectiveness/reports/index.htm>. Accessed August 12, 2004.
19. Avorn J, Monette J, Lacour A, et al. Persistence of use of lipid-lowering medications: a cross-national study. *JAMA*. 1998;279:1458-1462.
20. Gurwitz JH, Yeomans SM, Glynn RJ, Lewis BE, Levin R, Avorn J. Patient non-compliance in the managed care setting: the case of medical therapy for glaucoma. *Med Care*. 1998;36:357-369.
21. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effects of initial drug choice and comorbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. *Am J Hypertens*. 1997;10:697-704.
22. Soobader M, LeClere FB, Hadden W, Maury B. Using aggregate geographic data to proxy individual socioeconomic status: does size matter? *Am J Public Health*. 2001;91:632-636.
23. Geronimus AT, Bound J. Use of census-based aggregate variables to proxy for socioeconomic group: evidence from national samples. *Am J Epidemiol*. 1998;148:475-486.
24. SAS statistical software, version 8.2. Cary, NC: SAS Institute Inc; 2001.
25. Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. *JAMA*. 2002;288:455-461.
26. Rudd P. Compliance with antihypertensive therapy: raising the bar of expectations. *Am J Manag Care*. 1998;4:957-966.
27. Insull W. The problem of compliance to cholesterol altering therapy. *J Intern Med*. 1997;241:317-325.
28. Chmelik F, Doughty A. Objective measurements of compliance in asthma treatment. *Ann Allergy*. 1994;73:527-532.
29. Yeung M, O'Connor SA, Parry DT, Cochrane GM. Compliance with prescribed drug therapy in asthma. *Respir Med*. 1994;88:31-35.
30. Rand CS, Wise RA, Nides M, et al. Metered-dose inhaler adherence in a clinical trial. *Am Rev Respir Dis*. 1992;146:1559-1564.
31. Rosenberg MJ, Waugh MS. Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons. *Am J Obstet Gynecol*. 1998;179:577-582.
32. Apter AJ, Reisine ST, Affleck G, Barrows E, ZuWallack RL. Adherence with twice-daily dosing of inhaled steroids: socioeconomic and health-belief differences. *Am J Respir Crit Care Med*. 1998;157:1810-1817.
33. Apter AJ, Boston RC, George M, et al. Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol*. 2003;111:1219-1226.
34. Hinkin CH, Hardy DJ, Mason KI, et al. Medication adherence in HIV-infected adults: effect of patient age, cognitive status, and substance abuse. *AIDS*. 2004;18 (suppl 1):S19-S25.
35. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care*. 2004;42:200-209.
36. Berg KM, Demas PA, Howard AA, Schoenbaum EE, Gourevitch MN, Arnsten JH. Gender differences in factors associated with adherence to antiretroviral therapy. *J Gen Intern Med*. 2004;19:1111-1117.
37. Shrank WH, Young H, Ettner SL, Glassman P, Asch SM, Kravitz R. Do the incentives in three-tier, incentive-based pharmaceutical benefit plans operate as intended? results from a physician leadership survey. *Am J Manag Care*. 2005;11:16-22.
38. Alexander GC, Casalino LP, Meltzer DO. Patient-physician communication about out-of-pocket costs. *JAMA*. 2003;290:953-958.
39. Doherty RB. Assessing the new Medicare prescription drug law. *Ann Intern Med*. 2004;141:391-395.
40. *Medical Expenditure Panel Survey Highlights: Distribution of Healthcare Expenses, 1996*. Rockville, Md: AHRQ; 2000. Publication 00-0024.