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**Benefits and Risks of Increasing Restrictions
on Access to Costly Drugs in Medicaid**

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FOREWORD

State Medicaid programs, like other third-party payers of prescription drugs, have a long history of adopting administrative mechanisms that are designed to reduce the costs of their pharmacy benefits. The recent proliferation of preferred drug lists (PDLs), limits on the number of prescriptions that Medicaid beneficiaries can obtain, and increases in cost sharing for Medicaid beneficiaries represent only the latest trend in such policies. Unfortunately, policymakers often lack a clear understanding of the impact of such cost-control mechanisms on health outcomes and access to appropriate care, particularly on vulnerable populations. Because Medicaid enrollees have low incomes and, in many cases, multiple chronic illnesses, the impact of such policies may be different from those applied to a higher-income or healthier population.

In this Issue Paper, Professor Stephen Soumerai, of the Harvard Medical School and Harvard Pilgrim Health Care, critically examines nearly four decades' worth of published evidence on the economic and clinical benefits and risks for vulnerable populations of policies that limit access to expensive drugs. This research represents a continuation of work that Professor Soumerai published in 1993. Unfortunately, his analysis shows that, as in 1993, there continues to be limited evidence for evaluating the impacts of pharmaceutical cost control policies. Professor Soumerai summarizes what adequate evidence does exist and combines this evidence with his own expertise to develop recommendations for both research and policy. His analysis provides an interesting perspective on the potential impact of pharmaceutical cost-control policies on vulnerable populations and suggests a useful agenda for policymakers and research.

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EXECUTIVE SUMMARY

States have responded to declining budgets and double-digit inflation in Medicaid drug expenditures by implementing a variety of cost-control policies aimed at limiting use of expensive or risky medications. These policies include preferred drug lists (PDLs), prior authorization before reimbursement for specific drugs, “fail first” requirements (that an alternative, inexpensive drug be tried before an expensive one), increased patient cost sharing for costly drugs, and drug category reimbursement exclusions.

This paper critically examines the evidence on the economic and clinical benefits and risks of such policies; identifies ways to reduce clinical risks and maximize savings; and recommends research and policy at the state and federal levels.

Methodology

All published studies of the above Medicaid policies were identified through computerized searches of the medical and social science literature from 1965 to 2003. Comparable studies in non-U.S. government insurance programs serving elderly and low-income beneficiaries were also reviewed. To be included, studies had to evaluate the impact of *prior authorization, drug category exclusions, or increased patient cost sharing* for expensive drugs. In addition, studies had to have minimally adequate research designs, such as interrupted time-series with or without comparison series, and before-and-after comparison group designs.

Findings

Although several hundred candidate studies were identified through the computerized search, only 13 were identified that evaluated the impact of prior authorization, drug category exclusions, or increased patient cost sharing for expensive drugs, and only eight of the 13 studies used an adequate research design that could control for threats to internal validity, such as preexisting changes in pharmaceutical marketing, the presence of insurance coverage, and other pharmaceutical policies.

Prior Authorization. Three adequate studies that examined the impact of prior authorization were reviewed. One of these studies demonstrated that prior authorization of effective, high-cost drugs (e.g., cimetidine) almost eliminated use of the restricted agent and, because few alternative choices were available, probably reduced appropriate care. The effect of such policies on overall health care costs was not well studied.

The other two prior authorization studies examined use of nongeneric medications for symptomatic illness (e.g., nonsteroidal anti-inflammatory drugs, or NSAIDs), when equally effective, inexpensive alternatives existed. In both of these studies, the findings showed substantial reductions in drug expenditures without increased use and attendant costs of physician or hospital services. However, the effects on patient symptoms and quality of life were not studied.

Drug Category Exclusions. A large study found that withdrawing coverage for scientifically unsubstantiated therapies and irrational combination products resulted in widespread substitution of both improved and unimproved therapies and did not reduce overall use of medications or expenditures.

Increased Patient Charges for Costly Drugs. Four well-controlled studies found that reference pricing policies that charge patients for the extra cost of higher-priced drugs in a class, but allow generous exemptions for high-risk patients, substantially reduced government expenditures for ACE inhibitors, nitrates, and H₂ blockers. No increases in use of acute health care services followed reference pricing of ACE inhibitors and H₂ blockers. Not studied, however, were changes in patient-reported symptoms, quality of life, or long-term health outcomes.

Discussion

Solid data on the risks and benefits of Medicaid drug cost-containment policies are generally insufficient to document their safety and effectiveness. Research is sorely needed on the economic and clinical consequences of prior authorization (PA) and differential cost-sharing policies that promote use of lower-cost, preferred drugs for major medical illnesses (e.g., cardiovascular disease, chronic mental illnesses, and neurologic disorders), especially in low-income Medicaid populations. Data are especially needed on patient-reported symptoms and longer-term health outcomes or the effects of such policies on use of physician, other outpatient, and hospital services.

Based on the extant evidence, seven tentative principles (or prerequisite conditions) based on the extant evidence were identified to guide policymakers in developing drug cost-containment policies that can maximize benefits and minimize risks to patients:

1. Solid pharmacoepidemiological evidence should exist that a very high proportion of patients receiving high-cost medications in a class could be treated successfully with much lower-cost drugs in the same class (e.g., NSAIDs, H₂ blockers, or ACE inhibitors).
2. Drug classes considered for PA should have low heterogeneity in patient response (efficacy or side effects) within a drug class (e.g., H₂ blockers).
3. Exclusions from reimbursement of entire categories of effective drugs (e.g., benzodiazepines) are likely to reduce the quality of care and should be avoided.
4. Financial or procedural barriers to medication access should be avoided in the most vulnerable, high-risk populations for whom careful selection of medications can prevent severe illness, hospitalization, or death (e.g., acutely ill patients with unipolar depression, bipolar illness, or schizophrenia or patients with AIDS, seizure disorder, osteoporosis, and physical disabilities).

5. Enforced drug switching in patients with major chronic illnesses should be applied judiciously unless evidence exists that such switches are safe and effective and that simple mechanisms exist for switching back to previous therapies in case of treatment failure.
6. If possible, multiple preferred agents should be provided to reduce the likelihood of limited access to an effective treatment.
7. The process for prior authorization should be automated and/or rapid.

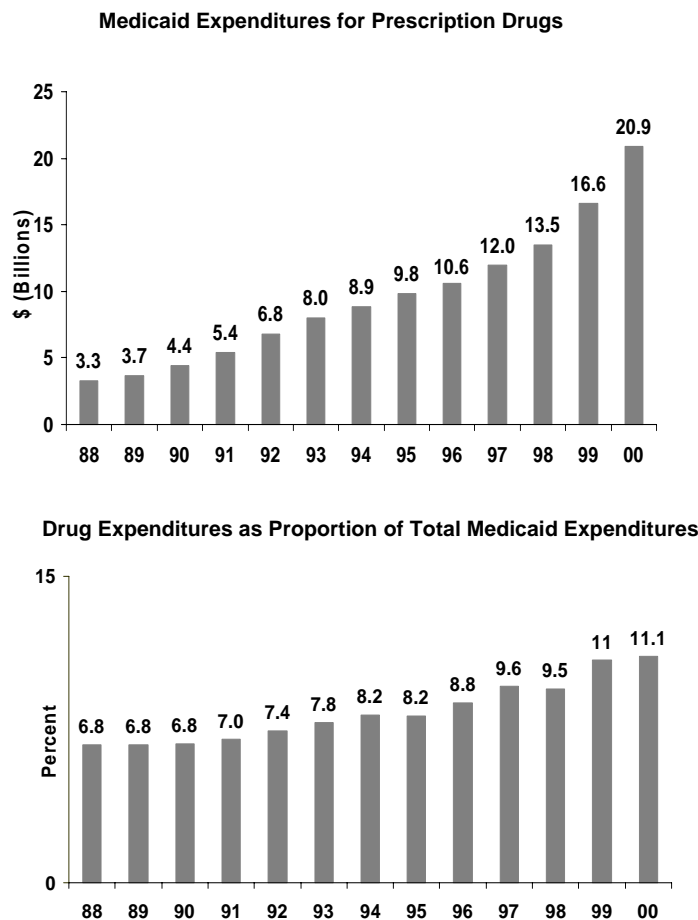
Conclusion

In summary, increasingly popular cost-containment policies promoting the use of inexpensive, “preferred drugs” have risks as well as benefits. Under certain circumstances, rigid policies that target essential classes of medications with heterogeneous patient responses and side effects can reduce appropriate care, adversely affect health status, and shift costs to other drugs or more expensive types of care. However, careful consideration of the degree of inappropriate use of specific high-cost drugs before implementing regulations and institution of simple and rapid mechanisms to exempt high-risk patients may minimize harm. The current exponential growth in such cost-containment policies throughout the United States and the limited evidence base justifies a substantial investment in research to identify which policies can achieve savings without shifting costs or adversely affecting the health of our nation’s most vulnerable populations.

Introduction

Fueled in part by growing use of costly new drugs, Medicaid drug expenditures have increased by more than 18 percent per year since 1997 (Kaiser Family Foundation, 2002) and exceeded \$20 billion in 2000 (see Figure 1). Some of this growth is likely attributable to physicians prescribing expensive new drugs when older, inexpensive agents would be equally effective (Soumerai, et al., 2000), a trend supported to some extent by pharmaceutical manufacturers' high spending on direct marketing to physicians (estimated at \$5.5 billion in 2001) (United States General Accounting Office, 2002). Despite this high rate of growth, and the fact that medications often represent the most cost-effective technologies for treating chronic illnesses (Scandinavian Simvastatin Survival Study Group, 1994; Soumerai, et al., 1997), prescription drugs accounted for only 11.1 percent of Medicaid expenditures in 2000 (Centers for Medicare and Medicaid Services, 2002).

Figure 1. Trends in Medicaid Drug Expenditures, 1988-2000



Source: "Medicaid Payments, All Eligibility Groups, by Type of Service: Fiscal Years 1975-1998," *Health Care Financing Review, Medicare and Medicaid Statistical Supplement, 2000*, (Baltimore: U.S. DHHS), p. 304; and Centers for Medicare and Medicaid Services, "CMS Benefit Payments by Major Personal Health Expenditure Service Categories Calendar Year 2000," and "Medicaid Payments by Type of Service in Selected Fiscal Years," in *2002 Data Compendium* (September, 2002), <http://cms.hhs.gov/researchers/pubs/datacompendium/>, (April 11, 2003)

States have responded to declining overall budgets and Medicaid drug cost increases by implementing a variety of policies aimed at limiting use of expensive or risky medications. These include adoption of preferred drug lists (PDLs), prior authorization before reimbursement of specific drugs, increased cost sharing, limits on the number of prescriptions that can be filled without prior authorization (National Conference of State Legislatures, 2003), “fail first” requirements (that an alternative, inexpensive drug be tried before an expensive one), and drug category reimbursement exclusions (Kaiser Family Foundation, 2002). Such policies would most likely have an impact on drug use by elderly and disabled Medicaid beneficiaries, who represent 27 percent of Medicaid enrollees and account for 80 percent of Medicaid drug expenditures (Bruen, 2000; Bruen and Holahan, 2001).

While the goal of these policies is to reduce costs without reducing appropriate care, there are concerns that, when used inappropriately, they could also result in unintended outcomes, including less use of essential therapies; declines in health; substitution of less effective, more toxic, or more expensive medications for nonreimbursed agents; or increased use of more expensive physician or institutional care (Soumerai, et al., 1987; Soumerai, et al., 1991; Soumerai, et al., 1994; Tamblyn, et al., 2001). For example, well-controlled studies demonstrate that arbitrary limits on the number of Medicaid prescriptions reimbursed for chronically ill elderly and disabled resulted in a dramatic 35 percent reduction in the use of clinically essential drugs (e.g., insulin), particularly among those with mental health problems or chronic pain; increased exacerbation of chronic illness; and a 200 percent increase in the use of more expensive services (e.g., nursing homes and emergency mental health services) that exceeded the cost of drugs (Soumerai, et al., 1987; Fortess, et al., 2001). In one study, increases in use of emergency services among schizophrenic patients for whom the number of prescriptions was capped outweighed drug savings by a factor of 17 to 1 (Soumerai, et al., 1994). Even moderate drug cost sharing has been found to reduce use of essential medications among low-income and elderly populations, increase hospitalization and nursing home admissions, and increase mortality in a recent well-controlled study (Tamblyn, et al., 2001).

This paper assesses the implications of the more recent, widespread adoption of policies encouraging use of less costly drugs within a therapeutic class (e.g., cholesterol-lowering medications) by critically examining evidence on the economic and clinical risks and benefits of such policies. It also identifies ways to reduce clinical risks and maximize savings and concludes with recommendations for research and policy.

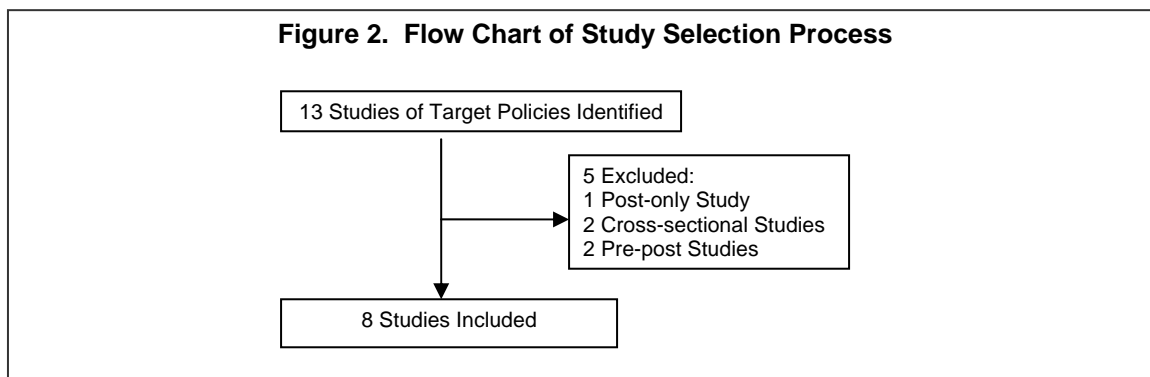
Methods for Systematic Review of the Evidence

Computerized searches of the Medline system as well as manual searches of medical, pharmacy, and social science literature from 1965 to March 2003 were conducted to identify all published reports evaluating the effects of prevalent administrative restrictions on prescribing specific drugs in state Medicaid programs or other government programs providing drug benefits to low-income and elderly beneficiaries. To be included, studies were required to evaluate the impact of *prior authorization* and “*fail first*” requirements, *drug category exclusions*, or *increased patient cost sharing for expensive drugs* on one or more of the following outcomes:

1. use of, or expenditures for, medications targeted by the policy;

2. frequency, cost, or efficacy of drug substitutions in place of restricted drugs;
3. underuse of effective medications;
4. substitution of other health services for drugs; or
5. clinical outcomes.

Studies with minimally adequate research designs,¹ such as interrupted time-series with or without comparison series, and before-and-after comparison group designs, were reviewed. Studies that used uncontrolled pre-post and post-only designs were excluded because they have been shown to yield invalid results (see Figure 2).



This review includes 10 years of additional research not analyzed in an earlier report on cost-containment policies in Medicaid (Soumerai, et al., 1993) as well as recent well-controlled studies of innovative policies in provincial drug benefit programs in Canada that cover elderly and low-income populations and that have been considered for adoption by Medicaid programs (Santa, 2002).

It should be noted that the evidence base on the risks and benefits of such policies, while improved somewhat over the last decade, remains weak. Despite the extensive literature review, only 13 studies were identified that evaluated the impact of the above policies. Only eight of these 13 studies used an adequate research design that can control for threats to internal validity, such as preexisting changes in pharmaceutical marketing, the presence of insurance coverage, and other pharmaceutical policies.² Adequately controlled studies are described below; the administrative cost-control mechanisms that they address include: (1) prior authorization, (2) drug category exclusions, and (3) increased patient cost sharing for expensive drugs (see Table 1).

¹ These methods are based on the methodology described in Soumerai, et al. (1993).

² Our computerized search of papers containing the key words, *Medicaid*, and one of the following: *cost containment; formularies; prior authorization; fail first; drug category exclusion; cost sharing; copayment; or reference pricing*. Although several hundred candidate studies were identified using these search criteria, few of them were studies of cause and effect.

Table 1 Description of Included Studies

Article	Research Design	Study Sample	Policy	Follow-up Period	Reported Results
Prior Authorization (PA)					
Bloom and Jacobs (1985)	Pre-post, supplemented by national comparison group	2,658 WV Medicaid enrollees with diagnosis of peptic ulcer disease before and after policy	PA of cimetidine, the only H ₂ antagonistic available for peptic ulcer disease	~1 year	84% decrease in cimetidine use, while use increased nationally.
Smalley et al. (1995)	Time-series	495,821 TN Medicaid enrollees	PA of single-source NSAIDs	7 months	53% decrease in NSAID expenditures, \$12.8 M savings over 2 years, 26% reduction in NSAID use, no observed increase in nondrug expenditures
Kotzan et al. (1993)	Time-series	80,064 continuously enrolled GA Medicaid enrollees receiving NSAIDs, 39,604 receiving H ₂ antagonists	PA of single-source NSAIDs and of long-term single source H ₂ antagonists	2 years	Decrease in costs of \$3M for NSAIDs, \$1.4M for H ₂ antagonists. No observed increase in use of medical services
Drug Category Exclusions					
Soumerai et al. (1990)	Time-series	390,465 NJ Medicaid enrollees	Withdrawal of reimbursement of 12 categories of questionably effective or irrational combination agents	~2 years	No cost savings, decrease in use of targeted drugs offset by greater increase in use of substitute drugs (both appropriate and inappropriate)
Increased Cost Sharing for Expensive Drugs					
Schneeweiss et al. (2002)	Time-series with comparison series	37,362 elderly enrollees in British Columbia's Pharmacare program receiving high-cost ACE inhibitors	Reference pricing: Required enrollees to pay "extra" costs of higher-priced ACE inhibitors (above reference price of lower-cost agents in class)	~1 year	11% decrease in use of all ACE inhibitors, 29% decline in high-price agents, savings of \$6.7M in drug expenditures, temporary increase in physician visits but no change in ER or hospital use
Grootendorst et al. (2001)	Time-series	All elderly enrollees in British Columbia's Pharmacare program	As above for high-cost nitrates	3½ years	\$14.9M savings in nitrates, no data on health services
Hazlet & Blaugh (2002)	Time-series	Two cohorts of 10,000 British Columbia Pharmacare enrollees receiving H ₂ antagonists	As above for high-cost H ₂ antagonists	~2 years	No observed change in health services use
Marshall et al. (2002)	Time-series	All elderly enrollees in British Columbia's Pharmacare program	As above (H ₂ antagonists)	~3½ years	4-fold increase in use of cimetidine, more than 50% decrease in use of restricted H ₂ antagonists, drug cost savings of \$2-3M, but increased cost sharing of 16% of drug expenditures

Prior Authorization for Nonpreferred Drugs

The 1990 Omnibus Budget Reconciliation Act (OBRA 90) disallowed use of closed formularies (i.e., limited lists of reimbursed drugs) in Medicaid; the effects of such restrictive formularies have been evaluated in an earlier review (Lexchin, 2001). Recently, however, there has been a rapid growth in the use of prior authorization (PA), which is allowed under OBRA 90, to limit use of particular medications. Many states have established preferred drug lists (PDLs) that generally promote use of lower-cost drugs within classes of medications considered to have equivalent efficacy, but they may also discourage use of less effective drugs. Under PA, preapproval is required for reimbursement of drugs not on PDLs. According to OBRA 90, states must respond to clinician requests for prior authorization within 24 hours and provide a 72-hour emergency drug supply while the request is processed. While some states use evidence-based criteria to establish their preferred drug list, some Medicaid programs are placing large numbers of medications on prior authorization lists primarily on the basis of price or provision of supplemental rebates (National Conference of State Legislatures, 2003). For example, the Michigan Medicaid program requires prior authorization for nonpreferred drugs in 40 medication categories. Between 2000 and 2003, the number of states with PDLs has grown from three to 22 (Perez-Pena, 2003). About 40 states have some form of prior authorization program (Gencarelli, 2003).

“Fail first” policies refer to prior authorization mechanisms that require patients to have failed a lower-cost treatment (e.g., trial of a generic nonsteroidal anti-inflammatory drug (NSAID), such as ibuprofen, for treatment of arthritis) before approving use of a more expensive agent (such as a Cox-2 inhibitor).

In theory, prior authorization and other policies promoting substitution of preferred agents can be used to encourage more judicious use of costly, new, and/or potentially toxic drugs. However, some PA programs may induce physicians to avoid the hassle of seeking preauthorization of appropriate medications. Further, low-income patients who do not discover that their prescription requires prior authorization until they arrive at the pharmacy may give up on trying to fill the prescription rather than seek PA. In addition, for certain therapies (e.g., selective serotonin reuptake inhibitors (SSRI) antidepressants), differences in chemical composition or pharmacologic properties of individual drugs within a class may result in poorer treatment response among recipients of preferred drugs (Bagby, et al., 2002). Many pharmacy and therapeutics committees base formulary inclusion decisions on group comparisons of drugs in randomized clinical trials. However, results for such therapies may be inappropriate for individual treatment decisions because nonresponders to one drug are likely to respond to another drug in the same class (Glick, 2001). (Indeed, some states ban some of these types of drugs from their PA programs (National Conference of State Legislatures, 2003).

Studies of Prior Authorization in Medicaid

Three studies provide useful evidence on the effects of PA in Medicaid. Bloom and Jacobs (1985) used a pre-post design to study the effects of prior authorization of cimetidine in the West Virginia Medicaid program (see Table 1)(Bloom and Jacobs, 1985; Soumerai, et al., 1993). Cimetidine is a highly cost-effective drug for peptic ulcer disease because it can prevent inpatient surgery (Fineberg and Pearlman, 1981). The data indicated a striking 84 percent decline in use of cimetidine after implementation of the PA policy among Medicaid patients with peptic ulcer diagnosis at a time when its use was increasing nationwide (Metropolitan Insurance Companies, 1990). Hospitalizations for peptic ulcer disease rose somewhat after policy implementation. While it is possible that other cost-containment regulations affected use of hospital services, the policy probably reduced quality of care for peptic ulcer disease given the magnitude of the reduction in use of the medication, its established cost-effectiveness, and the few alternative therapies that existed at the time (Fineberg and Pearlman, 1981; Soumerai, et al., 1993).

Smalley et al. (1995) used a strong time-series design to evaluate the effects of a PA policy targeting nongeneric NSAIDs in the Tennessee Medicaid program. A large number of low-cost generic NSAIDs existed at the time of the policy that could provide effective alternatives to the brand-name agents. The policy resulted in an immediate, 53 percent decline in expenditures for NSAIDs, primarily through increased use of generic drugs, and saved an estimated \$12.8 million over two years without any simultaneous effect on use of other drugs, physician visits, or hospital admissions. While this study provides some encouragement regarding the cost-effectiveness of this policy, some caution is warranted. There was a 26 percent reduction in overall use of NSAIDs, raising the question—not addressed by the study—of how much of the reduction could be attributed to reducing inappropriate or duplicative use of NSAID versus how much to unintended reductions in medically appropriate treatment of pain (Soumerai and Lipton, 1995). This latter point is difficult to assess, since the study did not include any measures of changes in levels of pain or inflammation, both of which are affected by NSAID treatment.

Kotzan et al. (1993) used a time-series design to examine changes in the use of H₂ blockers and NSAIDs after a prior authorization policy was initiated in the Georgia Medicaid program. Their findings indicate that the decrease in medication costs (\$1.4 million per year for H₂ blockers, \$3 million in NSAIDs costs) was not offset by increases in the use of other health care services.

Drug Category Exclusions

Current federal regulations also allow Medicaid programs to eliminate reimbursement for entire categories of drugs. Examples of categories commonly excluded are medications used in the treatment of anorexia, weight gain, fertility, hair growth, and symptomatic treatment of coughs or colds; smoking cessation products; barbiturate sedatives; benzodiazepines; and drugs approved for sale before the 1962 Food and Drug Act requiring proof of drug efficacy (Drug Efficacy Study Implementation [DESI] drugs).

Studies of Drug Category Exclusions in Medicaid

Soumerai et al. (1990) used 42 months of claims data (i.e., time-series data) to measure the effects of withdrawing reimbursement for 12 categories of older, questionably effective Drug Efficacy Study Implementation (DESI) drugs or irrational combination products in almost 400,000 New Jersey Medicaid patients in 1981. The policy reduced neither overall drug use nor expenditures, because reduced use of DESI drugs (22 fewer prescriptions per 1,000 enrollees per month) was offset by equal or greater increases in use of generally newer and more costly substitute drugs (34 more prescriptions per 1,000 enrollees per month). The appropriateness of substitute drugs varied substantially. For example, patients receiving irrational combination products containing asthma drugs and potent sedatives (barbiturates) before the policy were more likely to receive more therapeutically appropriate prescriptions for bronchodilators without sedatives after the coverage change. However, patients who received ineffective peripheral and cerebral “vasodilators” for senile dementia and claudication were often switched to equally ineffective drugs (e.g., ergot alkaloids). The results suggest that simply stopping payment for even irrational therapies does not address patients’ and physicians need for drugs, and it can result in both appropriate and inappropriate substitution effects.

Increasing Patient Cost Sharing for Expensive Drugs

An increasingly popular approach to contain drug costs is to impose economic disincentives on patients to reduce their use of specific high-cost drugs. Sometimes called differential cost sharing, these policies differ from prior authorization due to their reliance on economic rather than procedural barriers to use of nonpreferred medications. These policies are less common in the Medicaid context than in the private sector because federal regulations limit Medicaid cost sharing for prescription drugs to nominal amounts. However, some Medicaid programs already charge higher copayments for brand-name drugs when generic equivalents exist. Programs targeted toward lower-income populations in other industrialized countries can also shed light on how cost sharing affects lower-income populations. In particular, reference drug pricing, as implemented in public drug benefit programs in the Canadian province of British Columbia (Schneeweiss, et al., 2002a), completely covers the cost of several lower-price drugs in a therapeutic class (i.e., those drugs priced below a “reference price”), but charges patients the extra cost above the reference price for higher-priced products (Schneeweiss, et al., 2002a; Kanavos and Reinhardt, 2003).

The efficacy of such strategies relies on the ability of expert advisory panels to identify drug classes that are “therapeutically equivalent.” However, as in the case of PA, several key issues may affect the degree to which such incentives to patients affect quality of care. This includes the degree to which there is heterogeneity in clinical responses or risks of side effects that could make a more expensive agent the only effective drug for a given patient (Glick, 2001), and nonselective effects of cost sharing on appropriate and inappropriate care (Soumerai, et al., 1987) .

Studies of Increased Cost Sharing for Expensive Drugs

Four well-controlled studies examined the effects of several incentive-based reference pricing (RP) policies. Schneeweiss et al. (2002a; 2002b) reported the results of RP for ACE inhibitors (antihypertensive agents) among more than 120,000 elderly patients in British Columbia's Pharmacare program. Use of higher-priced agents declined by 29 percent immediately after the policy was instituted, and use of low-cost reference drugs increased by similar amounts. The policy saved \$6.7 million per year in drug expenditures (Schneeweiss et al. 2002c). Due to generous exemptions for high-risk patients (e.g., those with cardiovascular disease and diabetes), only 18 percent of patients previously receiving high-priced ACE inhibitors switched to low-cost agents. There were no increases in use of emergency rooms or hospitalization among patients switching from high- to low-cost drugs. However, there was a temporary six-month increase in physician visits following switching, presumably to switch and monitor therapy, which increased expenditures on physician services by \$700,000.

The overall results suggest that the policy did not increase use of acute care services. However, some important potential effects were not addressed in the study. For example, because no blood pressure data were collected, it is not possible to determine whether patients developed higher blood pressure that would be associated with long-term health risks that the study did not capture. Such effects could occur if a patient is controlled on one agent, but fails to respond to a different antihypertensive. Second, reference pricing was associated with an 11 percent reduction in use of all ACE inhibitors; it is not possible to determine how much of this reduction was due to inappropriate or duplicate use of antihypertensives and how much represents policy-related underuse.

Three other studies evaluated the effects of British Columbia's policy on other drug classes. Grootendorst et al. (2001) found that reference pricing of nitrates, used for angina, resulted in a \$15 million savings for nitroglycerin, a larger savings than for ACE inhibitors due to the large price differences between low-cost and higher-priced nitroglycerin products. However, 8 percent of this \$15 million represented cost shifting to elderly patients who continued to use partly reimbursed medications. No data were reported on the policy's effects on patient health or overall health care costs.

Marshall et al. (2002) also studied reference pricing of H₂ blockers in British Columbia elderly and observed a four-fold increase in use of low-priced cimetidine; use of high-priced agents declined by more than 50 percent. Cost savings were estimated at about \$2-\$3 million. However, cost shifting to patients was substantial, representing 16 percent of drug expenditures on H₂ blockers. In a time-series study of random samples of British Columbia Pharmacare beneficiaries, Hazlet and Blaug (2002) concluded that reference pricing of H₂ blockers was not associated with any increased use of health services, and reported that the policy did not have any severe, negative effects on patient health.

Discussion

Given the rapid increase in the use of prior authorization policies and other cost-control mechanisms in Medicaid, the relative lack of data on their risks and benefits is cause for concern. These policies can be viewed as massive experiments on vulnerable populations. It is sobering to realize that, if such policies were considered for a clinical study, the possible risks of reduced access to essential medications would likely result in failure to obtain human subjects approval from most Institutional Review Boards (IRBs). Nevertheless, the adequate studies reviewed above provide some evidence of both intended and unintended effects on costs and quality of care that vary according to the types of illnesses, drug categories, and methods of implementation. This evidence is summarized below.

Prior Authorization

- One study found that prior authorization of an effective, high-cost drug, *when few alternative choices were available*, almost eliminated use of the restricted agent and probably reduced appropriate care (Bloom and Jacobs, 1985). The effects of such policies on overall health care costs are still unknown.
- Two other studies of prior authorization applied when equally effective, inexpensive alternatives exist—one examining prior authorization of nongeneric NSAIDs (Smalley, et al., 1995) and the other of higher-cost H₂ blockers (Kotzan, et al., 1993)—found that each policy reduced drug expenditures substantially without increasing use and costs of physician or hospital services. However, the effects on patient symptoms and quality of life are still unknown.

Drug Category Exclusions

- One large study found that withdrawal of scientifically unsubstantiated therapies and irrational combination products resulted in widespread substitution of both improved and unimproved therapies, and did not reduce overall use of medications or expenditures (Soumerai, et al., 1990).

Increased Cost Sharing for Costly Drugs

- Four well-controlled studies found that reference pricing policies that charge patients for the extra cost of higher-priced drugs in a class, but allow generous exemptions for high-risk patients, substantially reduced government expenditures for ACE inhibitors, nitrates, and H₂ blockers (Schneeweis, et al., 2002a; Schneeweis, et al., 2002b; Grootendorst, 2001; Hazlet and Blough, 2002). No increases in use of acute health care services followed reference pricing of ACE inhibitors and H₂ blockers (Schneeweiss, et al., 2002b; Hazlet and Blough, 2002). No data exist, however, on changes in patient-reported symptoms, quality of life, or long-term health outcomes.

Implications for Research

Medicaid programs, reeling from budgetary crises, are increasingly engaged in policies designed to alter the drugs prescribed to vulnerable populations of chronically ill elderly and disabled. Research on the policy impact of such experiments has not kept pace with policy implementation. While some policies can reduce drug expenditures, their effects on health status and costs remain largely unknown. Addressing the following research questions is a necessary first step in improving our understanding of the impact of increasingly greater restrictions on access to expensive agents. Such information is especially critical, given the recent passage of Medicare drug coverage legislation and accompanying cost controls in the future, and the likely increased sensitivity to national policy effects on patient outcomes. It may also represent a high-priority research agenda for the National Institutes of Health, the U.S. Agency for Healthcare Research and Quality, and state governments.

1. What are the economic and clinical consequences of PA and differential cost-sharing policies affecting drugs for major medical illnesses (e.g., cardiovascular disease, chronic mental illnesses, and neurological disorders) on the use of physician, other outpatient, and hospital services?
2. Which policies can selectively reduce inappropriate use of costly medications while preserving appropriate drug use?
3. What are the effects on costs and quality of care of exclusions of entire categories of effective medications, such as benzodiazepines and smoking-cessation products?
4. What are the effects of pharmaceutical cost-control policies on direct measures of patient symptoms and health status?

Studies of these issues should include drug classes with high patient heterogeneity in response to treatment.

Implications for Policy

Given the pressing need to restrain Medicaid spending, policymakers often will not want to wait for good evidence in designing drug cost-containment policies. Thus, the following are some tentative principles (or prerequisite conditions) based on the extant evidence to guide policymakers in developing policies that can maximize benefits and minimize risks to patients.

1. *Solid pharmacoepidemiological evidence or expert consensus should exist that a very high proportion of patients receiving high-cost medications in a class could be treated successfully with much lower-cost drugs in the same class (e.g., NSAIDs, H₂ blockers, or ACE inhibitors) (Smalley, et al., 1995; Schneewiess, et al., 2002b; Schneewiess, et al., 2002c). To achieve this goal, Medicaid pharmacy and therapeutic committees should: (a) include specialists knowledgeable about the specific drug categories, e.g., primary care physicians, pharmacists, and other health care professionals; (b) consider safety, efficacy, and therapeutic need before economic*

- factors; and (c) review PDLs regularly.
2. *Drug classes considered for PA should have low heterogeneity in patient response (e.g., H₂ blockers).* For example, the recent decision by the Michigan Medicaid program to require prior authorization for newly treated patients prescribed all but the two oldest SSRI antidepressant agents may expose patients to unnecessary risks of treatment failure because the older drugs have higher rates of side effects (agitation and sedation) and drug interactions that raise the blood levels of cardiovascular agents; the policy could inhibit use of effective, “nonpreferred” drugs. Several examples of drug classes to avoid (with high heterogeneity in patient response) include antipsychotic agents, antidepressants, medications for bipolar illness and other chronic mental illnesses, and drugs for seizure disorder (Hardman, Limbird and Gilman, 2001; Somers and Perkins, 2003).
 3. *Exclusions from reimbursement of entire categories of effective drugs that are made on the basis of cost, rather than on patient safety, are likely to reduce the quality of care and should be avoided.*
 4. *Financial or procedural barriers to medication access should be avoided in the most vulnerable, high-risk populations for whom careful selection of medications can prevent severe illness, hospitalization, or death.* For example, acutely ill patients with unipolar depression, bipolar illness, or schizophrenia often do not respond to the first or second psychoactive medication regimen tried due to idiosyncratic differences among patients, and it is often impossible to predict which drugs will ultimately be effective. Similarly, patients with these conditions have notoriously poor compliance to medication regimens; any changes in medications are likely to disturb fragile social and biologic equilibriums, resulting in expensive exacerbations of illness (Soumerai, et al., 1994). Patients with AIDS, seizure disorder, osteoporosis, and physical disabilities experience similar problems. The practice of some states (e.g., Indiana) to exclude drugs used to treat mental illness from PA is more consistent with protection of the most vulnerable, high-cost patients.
 5. *Among patients with major chronic illnesses, enforced drug switching as a result of cost-containment policies should be applied judiciously until evidence exists that such switches are safe and effective and that simple mechanisms exist for returning to previous therapies in case of treatment failure.*
 6. *If possible, multiple preferred agents should be provided to reduce the likelihood of limited access to an effective treatment.* Excellent applications of this principle include the availability of a large number of preferred generic NSAIDs in Tennessee Medicaid (Smalley, et al., 1995) and several effective ACE inhibitors in British Columbia’s reference-pricing program (Schneeweiss, et al., 2002b).
 7. *The process for prior authorization should be automated and/or rapid.* Rigid, time-consuming barriers to appropriate medications will cause physicians and patients to avoid nonpreferred drugs altogether. Some physicians refuse to fill out any prior

authorization forms because of the time burden, thus “capitulating” by prescribing only preferred agents (Bloom and Jacobs, 1985). While many states attempt to minimize delays by reducing turnaround time and written justifications for authorizations of nonpreferred drugs, the existence of any formal preapproval process (and the tendency for physicians to follow the path of least resistance) may extinguish many requests for nonpreferred drugs (Soumerai, et al., 1993). Alternatively, the program of reference pricing of ACE inhibitors in British Columbia used the computerized claims data to automatically exempt vulnerable populations, such as those with diabetes or congestive heart failure (CHF), without requiring any paperwork by patients or physicians. To our knowledge, most Medicaid and managed care plans in the United States do not allow such exemptions for high-risk patients.

Conclusion

In summary, medications may represent the most comprehensive and cost-effective treatments in the medical arsenal, but they are not always used judiciously. Increasingly popular cost-containment policies promoting the use of inexpensive, “preferred drugs” have risks as well as benefits. The belief that such policies generally have isolated effects on medication use is not always borne out by the evidence. Rigid policies targeting essential classes of medications with heterogeneous patient responses and side effects may reduce appropriate care, adversely affect health status, and shift costs to other drugs or more expensive types of care. However, careful consideration of the degree of inappropriate use of specific high-cost drugs before implementing regulations and the institution of simple and rapid mechanisms to exempt high-risk patients may minimize harm. Such principles may, at times, raise drug expenditures, but they can also reduce nondrug costs. At the same time, the current exponential growth in such cost-containment policies throughout the United States and the limited evidence base justifies a substantial investment in research to identify which policies can achieve savings without shifting costs or adversely affecting the health of our nation’s most vulnerable populations.

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