A Critical Analysis of Studies of State Drug Reimbursement Policies: Research in Need of Discipline

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PRESCRIPTION DRUGS ARE POWERFUL AGENTS FOR improving health outcomes for many somatic and psychiatric illnesses. About three out of four physician visits result in at least one drug prescription (Cypress 1983). Yet some medications also present significant risks of iatrogenic injury, especially when misused (Leape et al. 1991). In addition, increasingly prohibitive costs of newly developed drugs, both marginally and highly effective agents (e.g., clozapine), have caused concern among clinicians, economists, policy makers, and consumers because of growing problems of access to medications, and the economic, clinical, and social impact of gaps in drug coverage for the poor. A recent controlled study linking a drug payment cap in Medicaid to increased institutionalization among frail elderly persons underscores the importance of these issues (Soumerai et al. 1991).

In attempts to reduce expenditures during the last two decades, state governments, as the largest public insurers of prescription drugs for low-income, elderly, and disabled persons, have increased drug coverage restrictions and cost-sharing policies. Yet few investigations of the economic and health impact of these policies have been conducted, nor have available studies been evaluated systematically and rigorously. In this report we will analyze critically most published and unpublished

studies conducted over the last two decades that evaluate the effects of the two predominant types of state-level cost-containment policies: patient-level restrictions on access, such as cost-sharing or drug prescription limits; and administrative restrictions that limit clinicians' ability to prescribe particular medications, such as formularies, category exclusions, or prior authorization requirements.

The intended and beneficial effect of these policies is to reduce drug overutilization, expenditures, and iatrogenic risks. However, regulations that impede access may also produce unintended effects, including reduced use of cost-effective drug therapies; resulting declines in health status; substitution of less effective, more toxic, or more expensive medications for nonreimbursed agents; and increased utilization of costly physician or institutional care (e.g., hospitals and nursing homes). Among the hypothesized mechanisms for the increased medical and institutional care in low-income populations that has resulted from lack of access to effective drugs are objective declines in physical health status (Lurie et al. 1984); changes in patients' psychosocial health or perceptions of illness; increased ambulatory care visits to obtain medications; and the shifting of care to settings where reimbursement is available (Soumerai et al. 1991; Borus et al. 1985).

In this report, we investigate the background and intended objectives of the two types of cost-containment policy; examine 11-year trends in policy implementation in state programs; and describe what is known about policies' effects on utilization and expenditures for drugs and other health services. We will focus on studies that meet explicit research design criteria, but we will also discuss major sources of bias or imprecision in less well-controlled studies. We conclude by summarizing the findings relevant to Medicaid programs, important gaps in knowledge to be addressed in future research, and methods to evaluate policy effects more reliably.

Background to Medicaid Drug
Cost-containment Policies

Medicaid, the largest public payor of drug benefits in the United States, uses federal and state funds to cover inpatient and outpatient medical services for many poor elderly, permanently disabled persons and for recipients of Aid to Families with Dependent Children. In addition,

nine states operate publicly funded drug coverage programs for near-poor or moderate-income elderly people (Soumerai and Ross-Degnan 1990). Within these drug benefit programs, subgroups such as the chronically ill elderly, children, and adults with chronic disabilities (e.g., schizophrenia) are most dependent on access to essential medications. Their multiple illnesses and low incomes (often less than $400 per month in 1987 dollars) (Health Care Financing Administration 1987) make these groups very sensitive to the effects of restrictive drug policies. We will show that state legislatures and policy makers have often implemented cost-containment policies with little empirical evidence about their true impact. Four main factors help to explain the growth in the last decade of regulations restricting drug payments: rapid increases in public drug expenditures; overuse of medications; a desire to decrease iatrogenic illness; and the "optional" nature of Medicaid drug benefits.

The accelerated increase in both pharmaceutical prices and drug benefit expenditures has prompted many states to establish new cost-containment policies. Total U.S. expenditures on pharmaceuticals and sundries for ambulatory patients rose from $8.8 billion to $41.9 billion from 1970 to 1988, although these outlays as a percentage of total health system costs decreased from 11.8 to 7.8 percent (Schondelmeyer and Thomas 1990). In 1990, Medicaid pharmaceutical expenditures for ambulatory patients were $4.42 billion, almost double the 1985 level (Health Care Financing Administration 1991). Factors contributing to this growth in drug spending include a greater number of Medicaid recipients receiving drug benefits (18 percent more in 1990 than in 1986); a rise in the number of prescriptions per recipient per year (12.5 percent between 1982 and 1988); higher pharmaceutical prices (an average retail prescription price increase of 95 percent between 1982 and 1990) (Schondelmeyer and Thomas 1990; National Pharmaceutical Council 1980–91); and the introduction of new, more expensive drugs.

Drug payment regulations have also been motivated by the perception that medications are often overprescribed by physicians and abused by patients. Certainly, some drugs are prescribed for inappropriate indications (Beers et al. 1988; Soumerai, McLaughlin, and Avorn 1989; Kunin et al. 1990). On the other hand, well-designed studies have documented substantial underutilization of life-saving agents (e.g., cardiovascular agents) (Horwitz et al. 1990). Similarly, the popular perception of the Medicaid recipient as an abuser and supplier of psychoactive drugs may help to explain the existence of state triplicate prescription-monitor-

ing programs for benzodiazepines in three states (Weintraub et al. 1991). However, earlier findings that most Medicaid recipients who use multiple drugs chronically are elderly or disabled individuals with multiple illnesses (83 percent) suggest that the amount of abuse among multiple-drug recipients is small in relation to legitimate use (Soumerai et al. 1987).

Reducing overutilization of drugs is also commonly seen as a way to decrease the incidence of iatrogenic illness and associated expenditures for physician and hospital services (Ray et al. 1987). Clearly, some side effects of appropriately prescribed drugs are an unfortunate, but necessary, consequence of medication use. On the other hand, the risk of iatrogenesis is unnecessarily increased when drugs with no clear clinical indication, or with less toxic therapeutic alternatives, are prescribed. A key empirical question is whether drug reimbursement barriers reduce access to needed medications more than they decrease iatrogenic illness. The magnitude of risks due to specific agents is often not large, and some earlier epidemiologic estimates of risk (e.g., effects of beta-blockers on depression) have been reduced substantially following better controlled studies (Bright and Everitt 1992; Yudofsky 1992; Heidrich, Stergachis, and Gross 1991).

A final factor contributing to the increase in state drug benefit restrictions is that pharmaceutical benefits are considered "optional" services in Medicaid. Therefore, states have had considerable discretion about which and how many drugs to reimburse. Recent requirements to expand Medicaid coverage (e.g., to near-poor pregnant women and children) have increased the pressure on financially strapped Medicaid programs. Medicaid directors and state legislatures, desperate to identify cost-saving opportunities, have increasingly targeted optional coverages like drug benefits.

Provisions of the 1990 Omnibus Budget Reconciliation Act (OBRA) (known as the Pryor amendments) have introduced striking changes in the way pharmaceuticals are purchased by state Medicaid programs. If they wish to supply drugs under Medicaid, pharmaceutical companies are now required to provide rebates for drugs sold to Medicaid recipients in order to give the program discounts equal to those enjoyed by other large purchasers, such as the health maintenance organizations (HMOs). In return, Medicaid programs must guarantee that all drugs approved by the Food and Drug Administration (FDA) will be available, unless they are specifically put on prior authorization status for justifiable therapeu-

tic reasons; they must also ensure that Medicaid recipients can obtain all newly approved products during the first six months of their market life. The exceptions are certain classes of pharmaceuticals that can be disallowed in entirety, including fertility drugs, cough and cold medications, and benzodiazepines. One effect of these changes was to make obsolete the concept of a limited Medicaid formulary, which was implemented previously by many states to control costs and/or to improve the quality of product selection.

In the context of these dramatic changes in the strategies available to manage drug expenditures, we will seek to determine what is known about the actual impact of different historical cost-containment policies.

Methods

All published and widely referenced unpublished U.S. reports evaluating the effects of specific drug cost-containment policies in state pharmaceutical programs were screened for inclusion in this review. We limited analysis to two broad classes of cost-containment policies. The first class included studies of the impact of patient cost sharing, including restrictions on the number or value of medications a recipient was eligible to receive. The second group included studies of all types of administrative restrictions on prescribing specific agents, from the imposition of a limited list of drugs eligible for reimbursement (a formulary), to withdrawal of certain classes of medication (a reduction in the scope of benefits), to requiring prior authorization to receive specific drugs (a procedural regulation). We used the computerized Medline system and a manual search of citations to identify studies of target drug cost-containment policies published in the medical, pharmacy, and social science literature between 1972 and 1992. To be included, studies were required to evaluate the impact of target policies in state-level programs on one or more of the following processes or outcomes:

1. overall or specific drug utilization/expenditures
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
5. clinical outcomes

We developed explicit criteria to rate the adequacy of study methodologies in the following areas: overall research design; appropriateness of study population; data quality and availability; reliability of measures of utilization; and adequacy of statistical analysis. The strength of overall research design is the most important criterion for evaluating a study's ability to suggest causal inferences. The strongest, least biased research design, the randomized controlled trial (RCT), is rarely feasible in the context of rapidly changing social policies, nor is it ethical to implement in vulnerable populations. As alternatives to the RCT, methodologists have described a continuum of quasi-experimental designs from well-controlled (e.g., time series with comparison series) to uncontrolled (e.g., post-only observation) (Campbell and Stanley 1963; Cook and Campbell 1979). Because changes in policies of interest are often concurrent with other changes in state and federal health policies (e.g., diagnosis-related groups, or DRGs), it is important to control for these threats to validity by using strong quasi-experimental designs. In a previous analysis of interventions to improve physician prescribing, we found that well-controlled, quasi-experimental studies reported effects of similar magnitude to estimates from RCTs, but that these effects tended to be more conservative than those found in less well-controlled, "pre-experimental" studies (Soumerai et al. 1989).

In this review, studies with strong quasi-experimental designs, such as time series with comparison series, are considered to be *well controlled* and are described in detail. Studies utilizing time series (without comparison series) or pre–post with comparison group designs are considered to be *partially controlled* and are also described. Studies with weak research designs, such as pre–post without a comparison group, or post-only observation (e.g., cross-sectional regressions), are considered likely to produce biased or unreliable assessments of the impact of target policies. We will briefly discuss the *inadequately controlled* studies in order to describe their methodological shortcomings. These ratings indicate varying levels of control of potential bias in results; they do not consider limitations in resources or settings that may have precluded the use of stronger designs.

Several other methodological characteristics were also assessed. For example, we determined whether studies appropriately followed a specific subgroup at risk (i.e., target drug recipients) rather than the entire Medicaid population. We also considered whether studies used patient-level claims data instead of less reliable, yearly aggregate Medicaid utilization

(HCFA-2082) reports. Finally, we considered the adequacy of statistical analysis based on the presence of an appropriate denominator to calculate utilization rates, and calculation of appropriate error variances for estimated effects on utilization and expenditures.

Results

Overview of Reviewed Studies

We identified a total of 19 studies that evaluated the effects of the target drug cost-containment policies. Seven studies examined the impact of patient cost sharing, whereas the other 12 evaluated effects of administrative restrictions on the prescribing of specific drugs. The distribution of the research designs employed in these studies is presented by type of policy in figure 1.
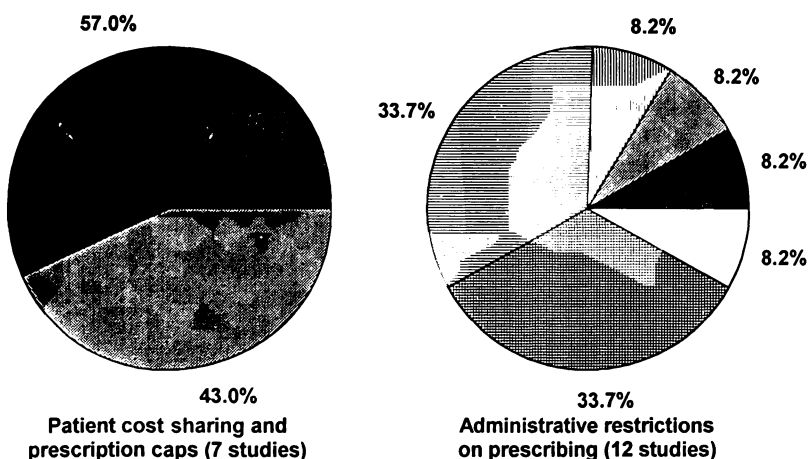
57.0%

33.7%

8.2%

8.2%

8.2%

8.2%

43.0%
**Patient cost sharing and
prescription caps (7 studies)**

33.7%
**Administrative restrictions
on prescribing (12 studies)**

FIG. 1. Research designs in reviewed studies by type of cost-containment policy. ■, time series with CS*†; ▨, pre–post with CG*; ▥, repeated measures‡; ▦, pre–post; ▨, post only with CG*§; □, post only.
* CS, CG indicate that design included an appropriate comparison series or comparison group.
† Time series are defined as analyses with six or more observations pre- and post-intervention.
‡ Repeated measures designs include two to five observations pre- and postintervention.
§ Category includes cross-sectional regression analyses.

All studies of cost sharing or prescription limits met minimum standards for adequacy of research design; four employed well-controlled designs (time series with comparison series); the remaining three used partially controlled pre–post with comparison group designs.

The studies of changes in administrative restrictions fare less well when judged by our design criteria. Only three of the twelve studies even partially controlled for possible exogenous influences on study results; four had no comparison group at all; and four additional studies with comparison groups only measured outcomes after formulary changes had already been introduced.

Descriptions of individual study findings that meet our minimum research design criteria, and further reflections on their methodological adequacy, are presented below.

Cost Sharing and Prescription Limits

Background. Cost sharing occurs when a health insurer does not cover the full cost of an item or service. Prescription drug cost sharing in state drug benefit programs can take several forms, including patient copayments (typically one to three dollars per prescription), or limits on the number or total value of prescriptions reimbursed. Prescription limits are the most severe form of cost sharing for low-income populations. In Medicaid, a prescription limit (or cap) may be as low as three prescriptions per recipient per month, and is often accompanied by strict one-month supply limits. A policy maker may not view a reimbursement cap as cost sharing; from the perspective of Medicaid recipients, however, caps require that they bear the full cost for any prescription over the limit.

The economic rationale for cost sharing is that increasing a medication's price to recipients will cause them to consider its necessity relative to the gain in marginal utility they would achieve by using the money to consume alternative products, thereby reducing their use of unnecessary or marginal drugs. This approach places the burden on patients to identify which medications are necessary, and to select some drugs while rejecting others. However, it is unlikely that most chronically ill, elderly patients are adequately informed about the efficacy of their medications and, in many cases, they may not be able to distinguish essential from less effective medications. Thus, for poor and chronically ill individuals who have few financial resources and multiple medical needs, there is a

risk that high levels of cost sharing will also reduce the use of effective and essential therapies.

Trends in Policy Implementation in Medicaid. Prescription drug cost-sharing requirements became a widespread Medicaid cost-containment strategy during the 1970s. Figure 2 indicates that prescription drug copayments had been adopted by 17 states by 1980. By 1991, this figure had increased to 22 states. Ten states also had patient-level caps on drug prescriptions or expenditures in effect in 1991 (fig. 3), although caps on the dollar level of reimbursement have almost disappeared while caps on the number of prescriptions have held constant.

Study Results: Time Series with Comparison Series. As shown in figure 1, four cost-sharing studies used the strongest quasi-experimental design available, the time series with comparison series design. Nelson, Reeder, and Dickson (1984) used Medicaid claims data and a four-year time series to analyze the effects of small copayments among 17,800 Medicaid patients in South Carolina, of whom 67 percent were elderly and disabled. A small, but clearly observable and significant drop of 0.2 prescriptions per patient per month (−11 percent) followed the 1977 institution of a 50-cent per prescription copayment. The decline was sig-
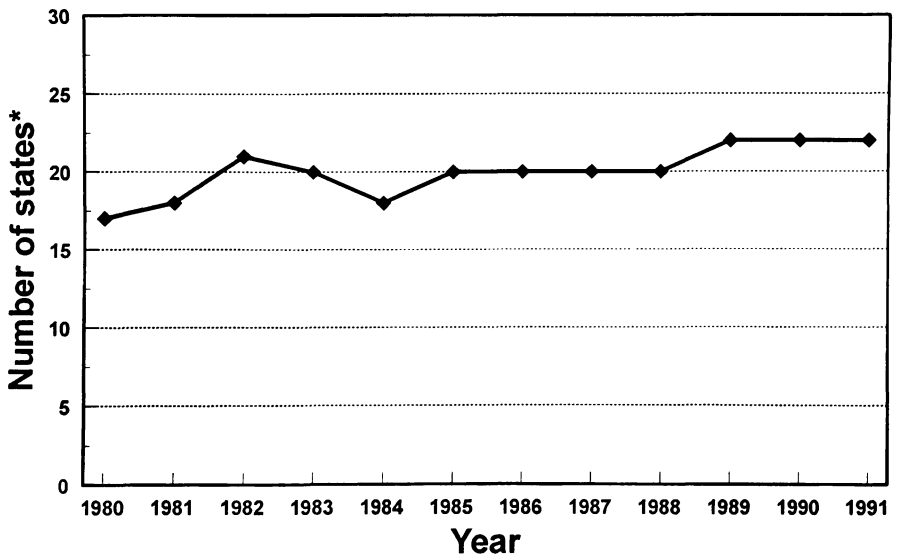

FIG. 2. Medicaid programs with copayment policies: fifty states and District of Columbia, 1980–91.
*Based on state program descriptions in NPC reports.

nificantly greater than in Tennessee, a comparison state with no drug cost-containment policy. The authors concluded that the policy was successful in achieving a small savings due to both reduced drug utilization and to revenues from the 50-cent copayment. Reeder and Nelson (1985) extended the analysis to determine variations in effect of cost sharing on ten classes of drugs. They observed a short-term drop in expenditures for all drug classes except analgesics and sedatives, and a long-term decline in the expenditure trends for cardiovascular, cholinergic, diuretic, and psychotherapeutic agents compared with the control state. Because cardiovascular and diuretic agents are sometimes prescribed for life-threatening conditions (e.g., congestive heart failure and hypertension), reduced use could potentially lead to increases in costly physician and hospital services, but these effects were not studied.

Only one paper has examined the effects of prescription reimbursement limits on use of medications. A quasi-experimental study of the New Hampshire Medicaid program analyzed the effect of a three-prescription-per-month payment limit that was replaced one year later by a one-dollar prescription copayment (Soumerai et al. 1987). Study
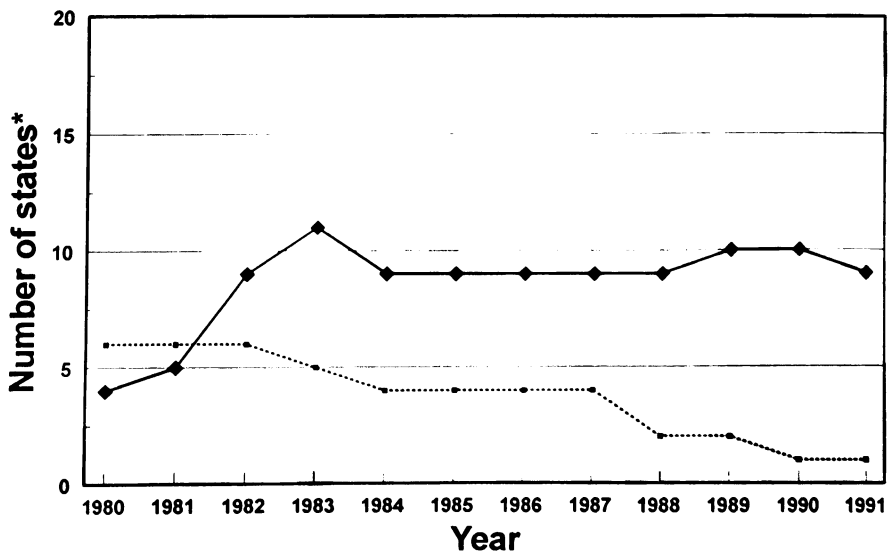

FIG. 3. Medicaid programs with reimbursement limits: fifty states and District of Columbia, 1980–91. ——◆——, limited number of prescriptions; ----■----, limited dollar value of drugs.
*Based on state program descriptions in NPC reports.

groups included nearly 11,000 continuously enrolled patients, and an at-risk cohort of 860 multiple-drug recipients who were predominantly elderly or disabled (83 percent) and female (81 percent). Analyses contrasted 48 months of data on overall drug use and on use of 16 medications that varied in clinical importance in the study state (New Hampshire) versus a comparison state (New Jersey) whose drug program differed only in the absence of these cost-sharing policies.

The results indicated that the three-drug cap caused a sudden, sustained reduction from 1.1 to 0.7 prescriptions per patient per month (−30 percent) in the overall cohort. Multiple-drug recipients were affected more severely by the cap, which reduced the number of reimbursed prescriptions in this group from 5.2 per person per month to 2.8 (−48 percent). The largest proportional reductions (−58 percent) were observed for "ineffective" drugs (e.g., propoxyphene, ergoloid mesylates); but there were also substantial decreases in "essential" medications such as insulin (−28 percent) and furosemide (−30 percent). Because of higher utilization rates for essential drugs, the largest decreases in the actual number of prescriptions occurred among essential medications. These reductions were minimally offset by out-of-pocket payments, which increased by only 10 percent in a subgroup of ten patients attending a computerized pharmacy. No changes were observed in the New Jersey comparison series. When a one dollar copayment replaced the cap, drug utilization rose to approximately 10 percent below precap levels. The authors estimated that Medicaid savings on drug costs resulting from both policies were comparable, at $0.4 to $0.8 million annually. However, because the copayment had less adverse impact than the cap on use of effective drugs among multiple-drug recipients, the authors viewed it as a safer and more equitable policy to reduce drug expenditures.

The observed reductions in essential drug use led the authors to conduct a follow-up study to examine whether such payment limitations may exacerbate preexisting chronic illnesses or increase admissions to hospitals and nursing homes (Soumerai et al. 1991). Study patients in New Hampshire (N = 411) and a New Jersey comparison cohort (N = 1,375) were matched on age (≥ 60 years), total baseline drug use (≥ three prescriptions per month), and chronic use of one or more of five maintenance drugs for specific major illnesses (e.g., heart and lung disease). Demographic characteristics of study and comparison groups were nearly identical at baseline. A sudden drop (−35 percent) in the use of study

drugs after the cap was associated with a significant increase in relative risk of admission to a nursing home compared with controls (relative risk = 1.8). Among recipients of three or more study medications, the relative risk of nursing-home admission during the cap was 2.2. A nonsignificant increased risk of hospitalization was also observed (relative risk = 1.2). Lack of access to Medicare data may have reduced statistical power to detect the latter effect.

After the cap was replaced by the copayment policy, medication use returned nearly to baseline, and the increased risk of nursing-home admission ceased. However, once admitted to a nursing home, most patients did not return to the community. The authors concluded that, even disregarding the negative impact on quality of life, increased institutional care expenditures resulting from the cap probably outweighed any economic savings achieved by decreased medication use.

Study Results: Pre–Post with Comparison Groups. Three partially controlled studies of copayments used a pre–post with nonrandomized comparison group design (Brian and Gibbens 1974; Roemer et al. 1975; Lingle, Kirk, and Kelley 1987). Nearly two decades ago, Brian and Gibbens (1974) reported the results of combined copayments for ambulatory providers (one dollar for each of the first two visits per month) and drug prescriptions (50 cents for each of the first two per month) on utilization of medications and other services in a large California Medicaid population. For ethical reasons, copayments were required only for the 30 percent of enrollees with cash or resources above a defined level, resulting in unknown selection bias. A stratified probability sample of patients was followed up one and a-half years after the start of the copayments, using Medicaid claims data and household surveys. Overall, the copayment was associated with a reduction of 7 to 11 percent in drug prescriptions obtained by different eligibility groups. However, it is impossible to disentangle the independent effects of the simultaneous provider and prescription copayments, and the further confounding effects of a prior authorization requirement (for more than two prescriptions or ambulatory visits per month) introduced two months before the copay. A later reanalysis of this study (Roemer et al. 1975) concluded that the cost savings associated with the one-time drop in medication use (again 5 to 10 percent) and other ambulatory care may have been offset by increases in more advanced services that perhaps were necessitated by failure to apply preventive care. Both studies used short-term follow-up periods, and

their results have been criticized for severe methodological problems (Chen 1976; Dyckman and McMenamin 1976).

Finally, a partially controlled study by Lingle, Kirk, and Kelley (1987) attempted to evaluate whether the availability of the New Jersey Pharmaceutical Assistance Program for the Aged (PAAD) reduced Medicare utilization and expenditures. The PAAD program provides coverage for medications with a two-dollar per prescription copayment for near-poor to moderate-income elderly enrollees. Medicare data for a year before and a year following intervention were obtained from New Jersey and an eastern Pennsylvania comparison group. Different pre- and poststudy samples (N = 9,966) were drawn randomly from the two states' Medicare recipients who were 65 years old and over and not eligible for Medicaid. Overall, no differences in Medicare service utilization were observed between the two states. However, because only 28 percent of the New Jersey cohort participated in the drug benefit program (≥ one prescription), and because pre–post changes in key outcome variables were not measured, this study was severely limited in its power to detect potentially important effects.

Administrative Restrictions on Prescribing of Specific Drugs

Background. For many years, administrative mechanisms have been employed in hospitals, HMOs, and Medicaid programs to control costs and assure quality of medication use. Central to these administrative restrictions are institutional decisions about which medications represent clinically effective and cost-effective therapies whose use should be unrestricted in drug benefit plans. In addition, formulary processes and other administrative restrictions can sometimes be used as powerful tools for controlling costs by requiring suppliers to submit lower bids (prices) for therapeutically equivalent drugs as a condition of coverage. However, the ideal of maintaining quality of care and efficiency through administrative actions may be more achievable in an organized setting like a hospital or HMO than in large, public insurance programs because of better communication with prescribers and more elaborate interpersonal mechanisms for influencing their choice of therapies.

In Medicaid programs, administrative restrictions on specific drugs have been used increasingly as a cost-containment tool. These policies

can be generally classified into three main categories: formularies, category exclusions, and prior authorization programs.

Formularies.   Formularies "provide the foundation for guiding clinicians in choosing the safest, most effective agents for treating particular medical problems" (Rucker and Schiff 1990). Most "restrictive formularies," a term often used pejoratively, are essentially limited lists of reimbursable pharmaceutical agents. "Positive" formularies have been described as the creation of a list of reimbursable agents based on the superior safety, efficacy, or "cost-effectiveness" of included drugs. In contrast, "negative" formularies reimburse all marketed drugs, except those singled out for nonpayment (Schweitzer and Shiota 1992). We do not distinguish between "positive" and "negative" formularies in this analysis because neither the reviewed studies nor the annual National Pharmaceutical Council (NPC) reports provide the basis to make the distinction. Most formularies reviewed in this article limit reimbursement for substantial numbers of drugs within and across many therapeutic categories, often excluding payment for 20 to 40 of the 100 most prescribed drugs (Sloan 1989).

Drug Category Exclusions.   Many states withdraw entire classes of medications from Medicaid reimbursement because of concerns about cost, safety, or efficacy. For example, concern about potential abuse or overuse led five states in 1990 to stop reimbursing for benzodiazepine sedatives/hypnotics, or to do so only with prior authorization. However, these states did pay for more potent and potentially toxic sedatives such as barbiturates, presenting potential problems of inappropriate drug substitution. Current federal regulations promulgated as part of the 1990 Pryor amendments allow states to eliminate reimbursement for categories of products used for anorexia, weight gain, fertility, hair growth, cosmetic effect, symptomatic relief of cough or colds, and smoking cessation; all vitamins except for prenatal use; barbiturates; benzodiazepines; drugs approved for sale before the 1962 Kefauver amendments to the Food and Drug Act that were found to lack proof of efficacy; and drugs linked with the sale of monitoring equipment. The impact of such categorical payment restrictions depends on volume of use and the clinical importance of the affected medications, the cost and clinical rationality of potential substitute products, and whether patients pay out of pocket for withdrawn drugs.

Prior Authorization.   Prior authorization is an administrative mechanism by which preapproval is required for reimbursement of prescriptions

for particular drugs or drug categories. On a continuum of restrictiveness, prior authorization lies conceptually between the open formulary and the more restrictive category, exclusion. In theory, prior authorization provides a method to target costly, newly introduced, and/or potentially toxic drugs only to recipients who truly need them, while eliminating their use in cases where less expensive or safer alternatives could be used; however, this hypothesis has unknown validity.

As an example of a prior authorization program, the California Medicaid (MediCal) prior authorization process is initiated when a provider telephones or writes to one of the two Treatment Authorization Request (TAR) field offices in Los Angeles and San Francisco (SysteMetrics 1991). The program received nearly 140,000 requests in 1986–87 (about 60 percent by telephone); overall, 29 percent were disapproved. Average processing time was three days, with a mean of one day for telephoned requests and four days for mailed requests. Administrative costs of such systems are not well documented.

Under provisions of the 1990 Omnibus Budget Reconciliation Act, states may no longer maintain a restricted formulary without offering prior authorization for drugs not included on the formulary, although they can restrict categories of medications. Such prior authorization must give 24-hour turnaround on provider requests and provide a 72-hour emergency drug supply.

Key Issues in Evaluating Administrative Restrictions. Because administrative restrictions, such as formularies, frequently deny Medicaid patients access to newer, more expensive, and possibly more effective single-source agents, they have become increasingly controversial during the last 20 years. Proponents of administrative restrictions cite drug savings due to utilization of more established, cost-effective products. On the other hand, opponents argue that failure to reimburse effective drugs causes unintended reductions in quality of care and *increased* costs due to use of suboptimal substitute products, exacerbation of disease, or substitution of expensive physician and hospital services (Moore and Newman 1989).

Much of this controversy is based more on an ideological position regarding the need for pharmaceutical regulation than on scientific findings. The potential for administrative controls on prescribing to produce unintended consequences depends on many factors, including their restrictiveness, efficacy and substitutability of affected drugs, potential for irrational drug substitution effects, and perceived need for a particular

drug by patient or physician. Clearly, restrictions on highly effective and nonsubstitutable agents could potentially result in increased physician visits or hospitalizations to gain access to treatments or to manage the sequelae of untreated disease (Fineberg and Pearlman 1981). On the other hand, withdrawing reimbursement for irrational drug combinations (e.g., sedatives and theophylline) has been found to improve drug therapy for asthmatics (Soumerai et al. 1990).

To understand the impact of administrative restrictions, there is a need to study trade-offs between restricted drugs and (1) substituted medications (first-order effects), and (2) substitution of other health services (second-order effects). To be complete, first-order effects should include changes in utilization of all plausible substitute therapies (e.g., narcotic analgesics for nonsteroidal anti-inflammatory agents). Because Medicaid drug claims data are reliable, complete, and specific for individual medications, carefully designed quasi-experimental studies can estimate the magnitude and costs of increased prescribing of both rational and irrational substitute agents.

Second-order effects include increased physician and emergency-room visits, hospitalizations, and nursing-home admissions that may result from changes in drug therapy. Demonstrating a causal link between an administrative restriction and any second-order effect is more difficult for several reasons. Restrictions in access to individual drugs constitute only one of many factors influencing the likelihood of physician or hospital visits. For example, states with strict formularies may have more severe cost constraints, and may simultaneously apply a variety of other cost controls on hospital or physician visits. In addition to changes in other policies, variations in the population of Medicaid recipients over time (e.g., through eligibility changes) can also seriously confound effects.

The presence of these known and unknown factors, which can lead to incorrect inference about the cause of changes in drug and service utilization, emphasizes the importance of using the strong research designs in studies of administrative restrictions. However, as we have seen in figure 1, only three of the twelve studies on this topic used even partially controlled research designs and multiple time points to demonstrate the effects of changes in policy.

The next two sections will document trends in the use of administrative restrictions in Medicaid during the 1980s, and will attempt to answer one fundamental question: does the existing evidence support
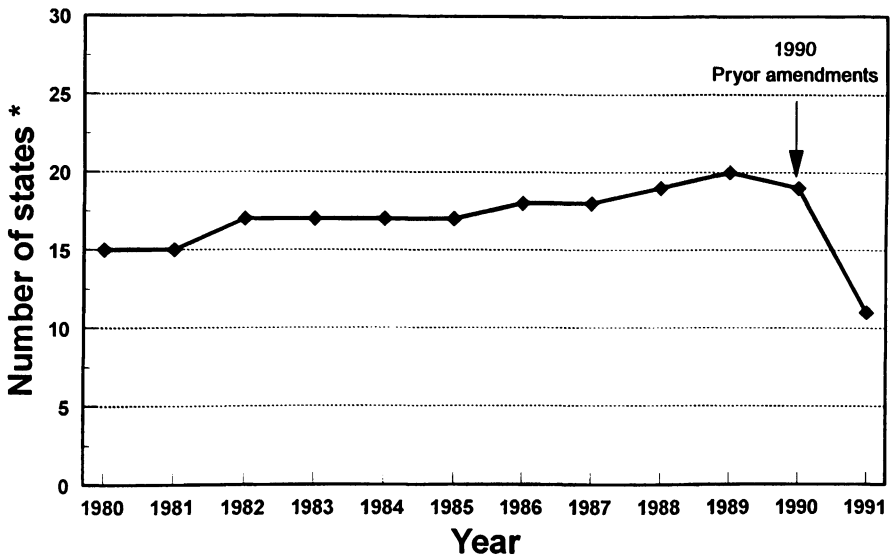
FIG. 4. Medicaid programs with "restrictive" formularies: fifty states and District of Columbia, 1980–91.
*Based on state program descriptions in NPC reports.

the argument that restrictions on prescribing specific drugs cause substitution of inappropriate drugs, increase utilization of more intensive medical services, and increase total Medicaid costs? Our analysis will also identify and describe the methodological flaws that are widespread in this literature, casting doubt on many of the published conclusions.

Trends in Implementation of Administrative Restrictions on Specific Drugs. Figures 4–6 display the number of Medicaid programs operating "restrictive" formularies, excluding particular categories of drugs, or administering prior authorization programs from 1980 through 1991, based on data reported yearly by the NPC (National Pharmaceutical Council 1980–91).

In 1980, only 15 states had restrictive formularies, compared with 19 states in 1990; this figure dropped abruptly to 11 states in 1991 (fig. 4), presumably as a result of the 1990 Pryor amendments.[1] It is unclear to what extent states are maintaining formulary restrictions by limiting access to specific drugs using prior authorization. Before the 1990 Pryor amendments, uncertainty about the effectiveness of formularies, com-
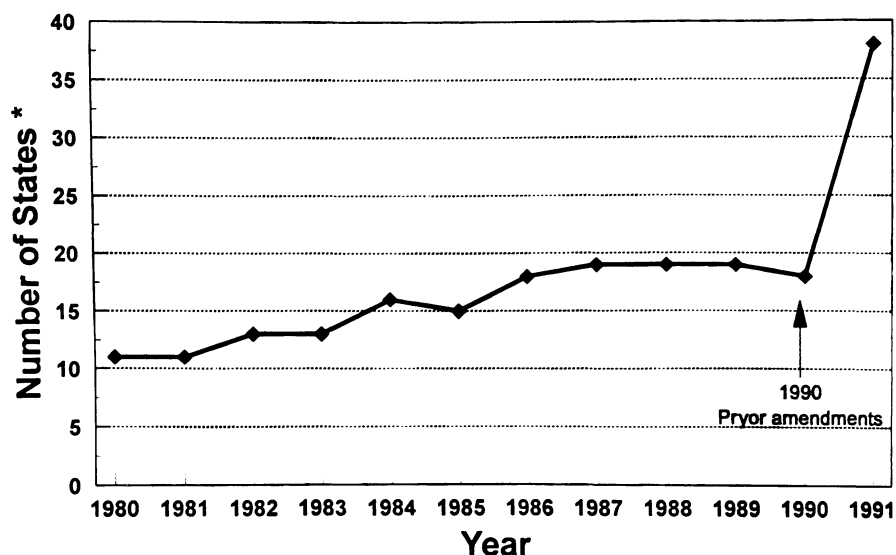
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[1] PL 101-508.

FIG. 5.   Medicaid programs with some prior authorization: fifty states and District of Columbia, 1980–91.
*Based on state program descriptions in NPC reports.

bined with unpredictable political and budgetary pressures, resulted in contrary trends in formulary use across states. For example, whereas six states dropped restrictive formularies between 1980 and 1990, ten states instituted them.

Prior authorization programs were in effect in 18 states by 1990, an increase of 64 percent since 1980 (fig. 5). This number more than doubled to 38 Medicaid programs in 1991, the year following the enactment of the Pryor amendments, which permit prior authorization as a mechanism to control access to medications, although it is unclear how fully operational or extensive these programs were. Because state Medicaid programs must reimburse for all new drugs for a six-month period after introduction, they may find it more difficult to place popular drugs on prior authorization status after prescribers and recipients have had six months of unrestricted use.

As shown in figure 6, use of category exclusions has remained stable or increased slowly over time in many of the currently allowed categories. Most notable is the recent growth in limits on drugs used to stimulate fertility during the same years that these drugs have gained in importance; however, these products would not be expected to have a large market among Medicaid recipients.
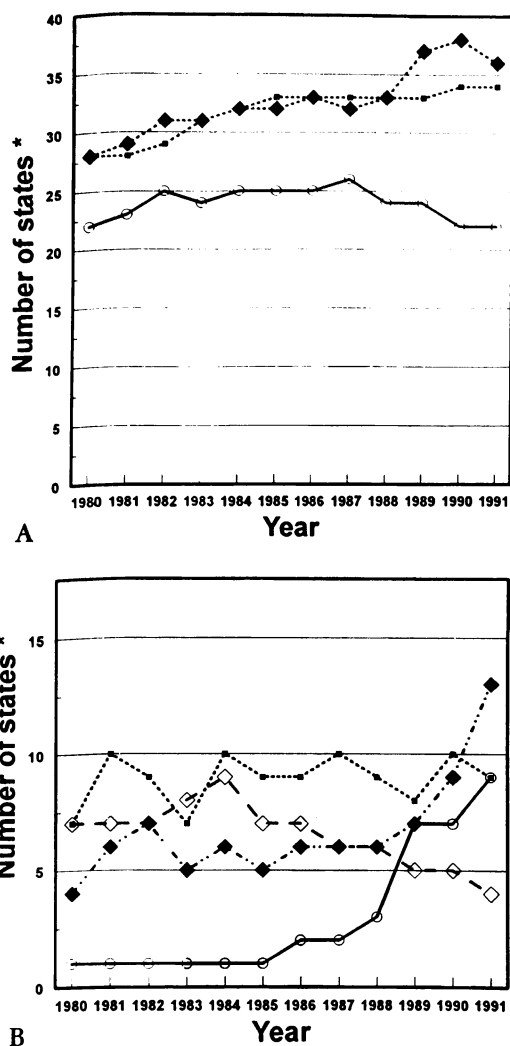
FIG. 6.   Medicaid program drug category restrictions: fifty states and District of Columbia, 1980–91. A: —⊖—, vitamins; ----■----, amphetamines and anorectics; ----◆----, over-the-counter products. B: —⊖—, fertility drugs; ----■----, cough and cold products; - · · ◆ · · -, cosmetics and dermatologics; —◇—, benzodiazepine sedatives.
*Based on state program descriptions in NPC reports.

Study Results: Time Series with Comparison Series.   In the largest study of category exclusions to date, Soumerai et al. (1990) used an interrupted time series with comparison series design to evaluate the effect of withdrawing 12 categories of questionably effective or irrational (Drug Efficacy Study Implementation, or DESI) drugs on the quality and cost

of substitute agents among 390,465 New Jersey Medicaid patients, using 42 months of claims data. Although withdrawn drugs accounted for 7 percent of baseline utilization, the reimbursement restriction did not produce measurable reductions in overall medication use or expenditures. In addition, reduced use of DESI medications (−22 prescriptions per 1,000 enrollees per month) was offset by equal or greater increases in use of substitute drugs (34 prescriptions per 1,000 enrollees per month), which varied substantially in cost and efficacy. For example, patients regularly receiving irrational combination products containing asthma drugs and barbiturates prior to the policy were more likely to receive more therapeutically appropriate prescriptions for bronchodilators without sedatives after the reimbursement cut-off. On the other hand, patients who received ineffective peripheral and cerebral "vasodilators" for senile dementia and claudication were often switched to equally ineffective and sometimes more costly drugs. The results suggest that eliminating reimbursement of even irrational agents does not address the perceived need for drugs by patients and physicians, and can result in both appropriate and inappropriate substitution effects.

Study Results: Pre–Post with Comparison Group.   In a widely referenced unpublished report for the NPC. Hefner (1980) examined the effects of withdrawing reimbursement for cough and cold preparations. minor tranquilizers, combination antianemia preparations, certain gastrointestinal remedies, vitamins, enzymes, and anorexics in the Louisiana Medicaid program. The study utilized a partially controlled pre–post, comparison group design, with matched samples of over 10.000 Medicaid recipients per year in Louisiana and Texas, the comparison state. Overall. prescription drug expenditures declined by 14 percent. Although only a small proportion of medications and patients were affected. and the unreimbursed drugs generally were used to treat minor. symptomatic illnesses, results suggested a 108 percent increase in hospital days among elderly and disabled recipients in Louisiana compared with Texas, and a 248 percent increase in hospital admissions related to heart disease (a diagnosis that had no direct relation to the withdrawn drugs). Thus. a modest reduction in medication use was credited with a more than fivefold rise in hospitalization, an implausible finding given that the hospitalization effects were observed for the entire population. even those never affected by the drug payment restriction. These results suggest that important, unmeasured, nonformulary factors were responsible for the changes in hospitalization rates.

Study Results: Repeated Measures.   Kozma, Reeder, and Lingle

(1990) took advantage of a natural experiment in the South Carolina Medicaid program, which switched from a "restrictive" to a "nonrestrictive" formulary affecting a large number of therapeutic agents. Although this study used more reliable patient-level drug claims, a large and continuously enrolled population of nonelderly (N = 12,139), and a partially controlled repeated measures design, the lack of a sufficient preintervention period to model baseline utilization trends resulted in uninterpretable findings. For example, although the authors reported decreases in inpatient hospitalizations, no estimates are provided of either the magnitude of these decreases or of the reported "increases" in outpatient hospital visits, physician visits, and drugs.

Study Results: Inadequately Controlled Designs. Nine of the twelve studies of administrative changes used research designs that fail to meet our criteria for adequately controlling possible sources of internal and external bias. The results of these studies, and their methodological problems, are reviewed briefly below. Dranove (1989) evaluated the effects of adding several newer anti-infective agents to the Illinois Medicaid formulary. The study population included nonelderly patients with specific infectious disease diagnoses in the year before and after the policy change. Using claims data, the author examined changes in ambulatory visits and an ambulatory variable that included both visits and antibiotic costs; no data were reported for changes in medication cost alone or inpatient care. Regression analyses comparing postformulary and during-formulary periods suggested a slight, nonsignificant (-4 percent) decline in outpatient visits, which were attributed to "faster cures." However, Dranove also observed a 6 percent increase in ambulatory costs ($p<0.05$) due to the added cost of the new medications. Unfortunately, the absence of either adequate controls or preintervention trend data makes it impossible to determine whether the modest changes were not simply the continuation of historical trends.

A pre–post study using three-month observation periods one year apart examined the effect of withdrawing reimbursement for propoxyphene napsylate, a marginally effective and abusable analgesic, from the Wisconsin Medicaid program (Kreling, Knocke, and Hammel 1989). Prescribing of the alternative propoxyphene formulation on the formulary (propoxyphene hydrochloride) increased, as did use of nonsteroidal anti-inflammatory drugs (NSAIDs), judged to be safer and more effective agents. The lack of control for prior trends is especially problematic given the rapid growth in NSAID use during the 1980s.

Smith and MacLayton (1977) used a pre–post design to examine the

impact of withdrawing reimbursement for nonnarcotic analgesics in the Mississippi Medicaid program. Their nonstatistical analysis of a stratified sample of 20 pharmacies in northern Mississippi reported a 76 percent increase in narcotic analgesic prescriptions, as well as increases in analgesic expenditures and pill supply per prescription after the policy change. However, the analysis did not control for the likelihood of differential prior trends in drug utilization across analgesic categories. Nevertheless, the large reported increase in use of narcotic analgesics suggests the possibility of inappropriate substitution for less toxic, nonreimbursed agents.

Bloom and Jacobs (1985) used a pre–post design to study the "withdrawal" of cimetidine due to imposition of a closed formulary with prior authorization in the West Virginia Medicaid program. Because of the established cost-effectiveness of this agent in preventing inpatient surgery for peptic ulcer disease, severe restrictions on access by low-income patients might have increased hospital service use, especially when no other H-2 receptor antagonists existed at the time of the formulary change (1982). The study contrasted a nine-month open formulary observation period with the same nine-month period a year later, during which West Virginia covered without prior authorization only a very restricted formulary of 66 products. Cimetidine use declined by 84 percent among patients with peptic ulcer diagnosis at the same time that its use was increasing nationwide (*Statistical Bulletin* 1990). Medicaid costs to treat peptic ulcer were 15 percent lower during the closed formulary period. The percentage of patients hospitalized for ulcer disease did not vary significantly, although inpatient costs per patient-month rose somewhat. Methodological problems make it difficult to be confident in the observed effects. No comparison group was available at a time when other cost-containment procedures (e.g., DRGs) were being implemented: the open formulary period excluded the medically needy for one-third of the period; and diagnostic ascertainment bias may have resulted in a comparatively sicker population during the closed formulary period because patients were likely to receive diagnosis later in their illness. Despite these problems, it is a cause for concern when a policy makes a cost-effective medication like cimetidine more difficult to obtain at a time when few alternative therapies existed.

Moore and Newman's unpublished report (1989) for the Pharmaceutical Manufacturers' Association (PMA) was cited as "the strongest study of the effects of restrictive formularies on Medicaid expenditures" (Sloan 1989, 8), and has been used extensively by the PMA to lobby against the

implementation of restrictive drug formularies. The study was based largely on a post-only, cross-sectional regression analysis of four years of aggregate Medicaid expenditure data by state ($N = 47$). No adjustments were made for preexisting differences in Medicaid program characteristics between formulary and nonformulary states (e.g., other drug cost-control policies, differences in patient characteristics, and other health care reimbursement policies). The analysis did not include sufficient time points (e.g., monthly or quarterly) to adjust for differential prior trends in expenditures among states with and without formularies. Although a second analysis purported to estimate changes associated with "switches" between formulary and nonformulary status between 1985 and 1988 — a potentially adequate research design — the small number of observation periods and states affected precluded the use of more powerful time-series models. In addition, most states made changes in the first year of observation, resulting again in a weak post-only design.

Smith and Simmons (1982) examined the effect of reimbursement restrictions on 24 categories of medications in cross-sectional regression analyses, as well as two-group comparisons, using eight years of aggregate Medicaid expenditure data obtained from the NPC. No consistent relationship was found between formulary controls and drug expenditures, and the validity of the reported findings is limited.

Several other cross-sectional regression analyses of the effects of formulary restrictions have also yielded uncertain results. In a study of 30 state Medicaid programs, Schweitzer, Salehi, and Boling (1985) constructed an index of formulary "restrictiveness," which they found to be negatively associated with state-level aggregate Medicaid expenditures, but unassociated with actual drug expenditures. The post-only design severely limits the scientific or policy significance of these surprising findings. Hammel (1972) compared (without statistical analyses) four years of Medicaid expenditures in states with and without formularies, and suggested that states with closed formularies had higher health care expenditures per recipient. However, trend data from the two states that shifted from open to closed formularies showed no change from preexisting expenditure trends.

Smith and McKercher (1984) examined the effects of withdrawing reimbursement for laxatives, antacids, vitamins and nutritional supplements, cough and cold preparations, antivertigo medications, and selected DESI drugs in the Michigan Medicaid program by conducting a post-only evaluation of 137 patients with prescriptions for one or more

of the eliminated drugs. The small sample, lack of control group, and danger of regression to the mean when following a cohort identified by previous use reduce confidence in the estimates of drug substitution effects.

Discussion

Overall Research Design

Strength of research design is a key determinant of the extent to which a study of the impact of drug reimbursement policies can control for threats to internal validity, such as changing trends in use of medications due to new products and pharmaceutical promotion; changes in insurance coverage, eligibility, and other health-service-related regulations; and shifting demographics (e.g., aging of the study population). It has been established previously that uncontrolled studies produce misleading estimates of the effects of a variety of social programs (Gilbert, Light, and Mosteller 1975).

The potential bias that may result from inadequate control for preexisting differences and trends can be understood by examining preintervention changes in drug use documented in the more rigorous time-series studies. For example, Nelson, Reeder, and Dickson (1984) observed a 12 to 15 percent increase in average number of prescriptions per Medicaid recipient *before* the policy intervention in both study (South Carolina) and comparison states (Tennessee). Similarly, in unpublished data from their study of reimbursement withdrawal for scientifically unsubstantiated drugs in New Jersey Medicaid, Soumerai and Ross-Degnan (1990) found that in the 23 categories of possible substitute medications whose utilization among 390,000 enrollees averaged one prescription per 1,000 enrollees per month or more, the median increase in use was 3.6 percent in the 12 months prior to the policy. However, the changes in utilization ranged from −83.3 to 67.9 percent (interquartile range −10.8 to 20.3 percent), indicating the high frequency of "naturally occurring" fluctuations in these types of measures.

Most single-group pre–post studies in this review report "effects" of formulary restrictions similar to these natural fluctuations. Therefore, changes in drug use attributed to the intervention could be due entirely to previous underlying trends. This provides strong support for wider

application of time-series designs. Because policies are almost always implemented suddenly, and many individual drug utilization trends can be modeled with reasonable precision, time series provide ideal models for observing whether changes cause abrupt, visible, and measurable interruptions in underlying trends. Hypothesized cause-and-effect relationships can be more convincingly demonstrated than in weaker pre-post designs. The clear and abrupt changes in utilization levels observed in several of the reviewed time-series studies (Nelson, Reeder, and Dickson 1984; Soumerai et al. 1987; 1990) provide further evidence for the advantages of this approach.

The high prevalence of inadequate designs (pre–post or post only) among studies of administrative restrictions (83 percent) is striking. Possible explanations are that most studies were privately funded, had fewer resources, and did not undergo formal peer review at the proposal stage or during publication. In contrast, the cost-sharing studies were funded predominantly by federal government agencies and research programs, and results were published only after competitive peer review. Finally, administrative restrictions may be inherently more difficult to evaluate using available databases and methodologies (e.g., lack of precise definitions of formulary restrictiveness).

Other Threats to Validity

Adequate research design is necessary but not sufficient to ensure validity. Other important characteristics of study design and analysis are displayed in table 1, together with the performance of the reviewed studies.

Data Sources. Reliable and complete data are necessary to estimate policy effects precisely. Medicaid data on reimbursed claims provide reliable information on patient-level acquisitions of medications and other Medicaid-reimbursed health services, but no data on out-of-pocket purchases. All of the cost-sharing studies utilized claims data, whereas just 58 percent of the studies of administrative limits used patient-level information. Three post-only analyses used state-level aggregate expenditure data (e.g., HCFA 2082 data) to estimate effects on drug and non-drug expenditures. Aggregate data have unproven reliability for this purpose. They do not allow analysis of either subpopulations at risk or monthly changes in utilization, nor do they control for patient-level differences between states. In addition, such key independent variables as formulary "restrictiveness" are measured imprecisely in such state-level

TABLE 1
Distribution of Selected Design and Analysis Characteristics
in Reviewed Studies

Characteristic	Cost-sharing/caps (n = 7) (%)	Formulary (n = 12) (%)
Data sources		
Direct patient-level outcomes	1 (14)	0 (0)
Medicaid drug claims[a]	7 (100)	7 (58)
Nondrug claims (Medicaid or Medicare)	4 (57)	5 (42)
Individual pharmacy data	0 (0)	2 (17)
State-level aggregate (annual) (e.g.,		
HCFA 2082 reports)	0 (0)	3 (25)
Other design features		
Analyses of predefined subgroups at risk[b]	4 (57)	4 (33)
Follow-up observation period > 6 mos.[c]	7 (100)	6 (50)
Statistics		
Utilization rates adjusted for changes in		
denominator	7 (100)	7 (58)
Acceptable statistical tests[d]	4 (57)	3 (25)

[a] Includes state drug benefit programs for the elderly, in addition to Medicaid.
[b] Higher-than-average baseline use of all or targeted drugs.
[c] Does not include post-only studies.
[d] CI, SE, or p-value, using appropriate statistical tests.

datasets. Therefore, studies relying on aggregate data may produce biased or unreliable results.

Some Medicaid recipients (e.g., elderly and disabled) are dually entitled Medicaid/Medicare "crossover" patients. For these individuals, Medicare is the primary payor of physician and hospital services; thus, use of these services may not be reliably recorded in Medicaid claims data. In particular, hospitalizations may be undercounted in studies on elderly and disabled Medicare patients when using Medicaid data (Bloom and Jacobs 1985; Soumerai et al. 1991). Finally, few studies have measured out-of-pocket purchases, which may be an unintended cost-shifting effect of some administrative restrictions.

Subgroups at Risk. A small proportion of chronically ill individuals consume disproportionate amounts of medication. For example, 8 percent of continuously enrolled Medicaid patients in one state consumed 47 percent of prescriptions (Soumerai et al. 1987). Such subgroups are

likely to be most sensitive to the impact of reimbursement restrictions. Yet only a small proportion of studies (57 percent of cost sharing, 33 percent of administrative restrictions) followed high-risk subgroups. For example, one study using person-level data followed chronically ill elderly persons with high use of medication for serious conditions (e.g., congestive heart failure) in order to demonstrate a significant link between drug reimbursement and nursing-home admissions (Soumerai et al. 1991). This effect might not have been detected in a random sample drawn from the overall Medicaid population.

Follow-up Period. Reimbursement policy changes typically introduce a period of instability into established patterns of service utilization as providers and patients adjust their behavior to the new context. Because patients and providers may learn to circumvent reimbursement regulations over time (e.g., by increasing prescription size in the face of copayments or caps), it is important to examine the "durability" and long-term stability of changes in utilization. Ideally, follow-up observation periods should include two or more years of data; however, only 50 percent of formulary studies achieved a more modest criterion of six months' follow-up. In contrast, all seven cost-sharing quasi-experiments followed patients for more than six months beyond the start of the intervention.

Analysis. Although a comprehensive critique of the statistical methodologies of the reviewed studies is beyond the scope of this article, compliance with several *minimal* analytic criteria was assessed. For example, aggregate utilization of drugs or other health services among specific populations is a dependent variable in many studies. Because of changes in the number of Medicaid enrollees over time (especially in AFDC during the 1980s), utilization over time must be expressed as rates per person-month (or year) so that any observed shifts in expenditures do not merely reflect eligibility changes. Five studies of administrative restrictions on specific drugs failed to satisfy this basic requirement for study validity.

Only 25 percent of formulary studies and 57 percent of copayment studies used appropriate statistical tests to examine the precision of estimated policy "effects," even with the modest requirement of an appropriate calculation of confidence intervals, standard errors, or p-values. Other common analysis problems were no adjustments for multiple comparisons, and the use of unconventional cut-off values for statistical significance (e.g., two-tailed, .20). For example, one unpublished study

reported significance tests on 624 comparisons between states with a given drug category restriction and states without such a policy (Smith and Simmons 1982). The authors found 14 significant (one-tailed) "effects"; this is about half the number expected owing to chance alone.

Conclusions and Recommendations

If adequacy of design increases confidence in the validity of findings, then our synthesis of what is known about the impact of drug reimbursement policies must be based mainly on the small number of well-controlled studies (5 of 19 reviewed). Therefore, gaps in understanding, particularly of the impact of changes in formularies, greatly exceed our current knowledge base.

Cost Sharing and Prescription Limits

Based largely on the results of studies utilizing time-series designs, the following conclusions can be drawn about the impact of cost sharing in state programs:

- Medicaid enrollees and other low-income populations appear to be sensitive to copayments as low as 50 cents to one dollar per prescription (or about 10 to 15 percent of average prescription costs). Three studies of similar copayments in three different Medicaid programs all observed declines ranging from 5 to 10 percent in overall drug utilization (Roemer et al. 1975; Nelson, Reeder, and Dickson 1984; Soumerai et al. 1987).
- Some evidence exists that even modest cost sharing can reduce the use of essential agents as well as less essential drugs (Reeder and Nelson 1985).
- Prescription limits, such as three-drug-per-patient caps, have been shown to have a sizable impact on the use of both "essential" medications (e.g., insulin and furosemide) and ineffective drugs (Soumerai et al. 1987). Prescriptions filled by chronically ill elderly and disabled recipients decreased by 48 percent overall; these reductions were only minimally offset by out-of-pocket payments.
- Information on changes in patient outcomes following changes in

drug use is limited. However, absolute restrictions on reimbursement (e.g., three-drug limits) have been found to increase costs and nursing-home admissions significantly among elderly persons with chronic illnesses (Soumerai et al. 1991). The mechanism of effect (e.g., exacerbation of preexisting illness, or admission to gain access to medications) is unknown. Because of these observed adverse effects, it is recommended that state and federal drug benefit programs eliminate the use of arbitrary prescription limits as cost-containment strategies.

These findings from state Medicaid programs are also supported by a quasi-experiment in a large HMO population in which a $1.50 copayment was associated with an 11 percent decline in overall medication use (Harris, Stergachis, and Ried 1990). Similarly, the Rand health insurance experiment found that a much higher 95 percent coinsurance reduced the use of over 20 categories of medications by 50 to 70 percent, compared with plans that had no cost sharing (Lohr et al. 1986). Lower income was associated with greater reductions in utilization.

Although the impact of modest copayments has been studied in Medicaid populations as a whole, little is known about the relative effects of copayments on groups that vary according to medical needs, income, or sensitivity to such interventions (e.g., chronically ill elderly, disabled adults, chronically ill children, etc.). In addition, more data are needed to assess clearly whether modest cost sharing reduces the use of less essential therapies in preference to essential or life-sustaining drugs. More precise estimates of the size of effects on effective medications would help to determine whether specific copayment levels adversely affect health status.

Almost no data exist on medication substitution effects at different levels of cost sharing, and the clinical and economic appropriateness of such substitutions. Combined with better understanding of the response of different recipient subgroups, this knowledge could lead to more clinically rational and equitable policies involving copayments and exemptions of different products or recipient subgroups.

An important research priority is to examine the second-order effects of interventions in carefully defined populations at risk of adverse outcomes, including use of more intensive and expensive services (e.g., nursing homes and hospitals), physician visits, and, if feasible, direct measures of health status. In addition, data are needed on the economic

effects of cost shifting to other types of Medicaid and non-Medicaid ser-
vices (e.g., increased costs of Medicare hospitalization, state-funded
mental health centers, psychiatric hospitals, nursing homes, and emer-
gency rooms).

Administrative Restrictions on Prescribing

In comparison to the cost-sharing literature, the available empirical
research on how administrative limits have affected prescribing is of poor
methodological quality. Only one of 12 studies used the strongest avail-
able quasi-experimental research design, while another two investiga-
tions were partially controlled. Nevertheless, the adequate studies,
combined with other investigations conducted outside of state drug-benefit
programs, provide evidence of both positive and negative effects, depend-
ing on the types of drugs involved.

- One reviewed study (Soumerai et al. 1990) observed widespread
  drug substitutions following withdrawal of irrational combination
  products and scientifically unsubstantiated therapies. In part
  because of these substitutions, the policies did not reduce overall
  pharmaceutical use or expenditures.
- Drug substitutions following product withdrawals can result in
  both improved and unimproved therapies, depending upon the
  specific characteristics of the drugs, the conditions for which they
  were prescribed, the availability of therapeutic substitute therapies,
  and physician motivations for use.
- In many cases, specific substitutions can be predicted in advance,
  offering an opportunity to carry out guideline implementation and
  education programs to encourage use of appropriate replacement
  therapies.

The findings related to therapeutic substitution following product
removal from a Medicaid formulary were mirrored in a similar study con-
ducted at a national level in Ireland (Ferrando, Henman, and Corrigan
1987). In this repeated measures study, the removal of reimbursement
for cough and cold preparations, antihistamines, antacids, and mild
analgesics (most of which were over-the-counter products) resulted in

observable increases in more expensive and sometimes more toxic prescription-only medications that remained on the national formulary. However, no statistical analyses were reported to support the data presented. The authors argue, in the context of a national health system, for complementing formulary changes with physician and patient education to encourage desired therapeutic substitutions.

Given the historical popularity of various administrative restrictions on prescribing in state drug benefit programs, combined with the recent congressional decision to abandon the concept of a limited list of reimbursed drugs in Medicaid programs, it is remarkable how few data are available to answer important questions concerning the impact of such restrictions on utilization, expenditures, and health outcomes.

Almost no data from well-controlled studies exist on the impact of formulary restrictions targeting effective medications that are perceived to be overused. Does limiting prescriber choice to lower-cost products from within a therapeutic class of effective drugs help to contain costs and, if so, at what risk to quality of care? What are the unintended effects of withdrawing an entire category of effective medications like benzodiazepines because of concerns about perceived overuse?

Reliable data are especially needed on the impact of restrictions that target clinically and economically important classes of drugs, such as anti-ulcer agents, antihypertensives and other cardiovascular agents, new antidepressant and antipsychotic agents, and antibiotics used in ambulatory care. Studies should address the difficult issue of defining inappropriate versus appropriate utilization of restricted and substitute therapies, and second-order effects on utilization of physician, other outpatient, and hospital services.

Prior authorization is one type of administrative restriction specifically allowed under OBRA 1990, although *no* data from well-controlled studies exist to determine the impact of this policy. The preliminary finding from West Virginia (Bloom and Jacobs 1985) that a prior authorization program was associated with an 84 percent decline in cimetidine use at a time when no other H-2 antagonists were marketed is cause for concern that, under some circumstances, such policies may reduce quality of care and increase hospital admissions. There is a pressing need for studies to examine the dynamics of clinical decision making and medication dispensing when prior authorization is required, and to determine the degree to which such policies can selectively preserve or inappropriately reduce essential care.

Recommendations to Increase
Study Validity

The most important conclusion to be drawn from this review is that great improvements in research methodology are needed before definitive recommendations are possible about how to implement cost-control policies without compromising quality. In light of the existing studies' major methodological failings, it is important for future research to take these steps:

- Follow the basic principles of design needed to minimize internal and external threats to validity, including *measurement before and after policy changes*, and appropriate, *well-chosen comparison populations*.
- Incorporate *multiple measurement points* to better control for underlying trends in the use of drugs and other health services.
- Utilize *patient-level data* and *appropriate denominators* in outcome measures, so that changes in the size and mix of recipient populations do not bias analyses.
- Investigate *specific changes in health service use and clinical outcomes* for *well-defined populations at risk* of these outcomes in order to build the chain of logic necessary to suggest causal relationships from nonexperimental data.
- Measure the independent variable (e.g., formulary restrictiveness) more precisely.
- Apply *appropriate statistical techniques* to reduce the likelihood that observed differences are due to chance fluctuations, taking care to account for multiple comparisons and to aggregate data at the appropriate unit of analysis.

These methodological issues are of more than academic importance. Inadequate research methods reduce the scientific validity and reliability of study results, cast doubt on the conclusions drawn, and perpetuate the dissemination of inaccurate information about health care policies. If federal and state decision makers continue to base pharmaceutical policies on unproven assumptions about their economic and clinical impact, there will remain a disturbing potential not only to waste increasingly scarce public health care resources, but also to further endanger the health of many of the most vulnerable members of society.

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