

# Improving Drug Prescribing in Primary Care: A Critical Analysis of the Experimental Literature

STEPHEN B. SOUMERAI,  
THOMAS J. McLAUGHLIN, and  
JERRY AVORN

*Harvard Medical School*

**I**N RECENT YEARS, AN INCREASING NUMBER OF articles have been published describing programs designed to improve physician prescribing behavior. As powerful, costly new drugs and new clinical information about them become more available, the need for accurate prescribing decisions grows proportionately. In a time of constrained health care resources, and with increasing interest in expanding drug coverage in public and private insurance programs, the economic and clinical aspects of inappropriate prescribing becomes even more acute. We previously presented a critical review of interventions designed to improve prescribing in the hospital setting (Soumerai and Avorn 1984). This article focuses on studies of attempts to improve prescribing behavior in ambulatory settings.

The choice of an individual drug for a particular patient is one of the most important clinical decisions in office-based medical practice. Perhaps more than any other clinical judgment, the physician's prescribing decision is the result of input from the patient (Comaroff 1976; Marsh 1977); commercial sources (Avorn, Chen, and Hartley 1982); professional colleagues (Coleman, Katz, and Menzel 1966); the academic literature, and government regulators (Soumerai et al. 1987b). While these background factors have been reviewed previously (Miller

1973–74), there have not been any comprehensive reviews of attempts to improve prescribing practices in primary care settings. The stakes are high: in 1987 about \$33 billion, or 7 percent of all health care expenditures, were spent on medications in the United States (Pharmaceutical Manufacturers Association 1988; National Center for Health Statistics 1988). Approximately 75 percent of these expenditures occur in nonhospital settings (Pharmaceutical Manufacturers Association 1988). About 75 percent of all visits to office-based physicians result in at least one drug being prescribed (Cypress 1983); drug therapy is thus the most common form of treatment in medical practice. Because most insurance programs do not cover the cost of prescriptions, drugs comprise the third largest source of out-of-pocket health care expenses (National Center for Health Statistics 1978).

Drug use is highest among those aged 65 years and older. While representing only 12 percent of the population in 1986, those aged 65 years or older accounted for 32 percent of all drug mentions in the National Disease and Therapeutic Index (U.S. Department of Health and Human Services 1987). Based on estimates of the total number of prescriptions dispensed in the same year (1.56 billion) (IMS America 1986), the average number of prescriptions per elderly person per year was approximately 18. Since this estimate of 1.56 billion prescriptions is based on a survey of community pharmacies and excludes outlets such as mail order pharmacies, public clinics, Veterans Administration outpatient clinics, and outpatient hospital pharmacies, the number of prescriptions per elderly person could exceed 20 (based on estimated total national prescriptions of 1.9 billion [Dr. T. Donald Rucker, University of Illinois, personal communication]). This figure is even higher in chronically ill populations. For example, in a New Hampshire Medicaid population of chronically ill patients the average number of prescriptions per person per year was 52 (Soumerai et al. 1987b). While proposals to include drug coverage in other entitlement programs may reduce income barriers to the receipt of essential long-term medications among near-poor elderly, there is concern that this “catastrophic” coverage could also lead to excessive or extravagant prescribing as well.

Prescribing decisions are also important in terms of preventable morbidity and mortality. Monitoring of drug usage and quality assurance are more difficult and less widespread in ambulatory settings compared to the relatively more controlled inpatient environment. Yet, the risks of inappropriate drug use in these populations are high. Miller (1974)

has found that 3.7 percent of admissions to seven general acute care hospitals were the result of adverse drug reactions, according to the admitting physician; whether this is a result of unnecessary or inappropriate drug use is unclear. In a large, well-designed study, Ray, Federspiel, and Schaffner (1977) reported that over one-quarter of office-based Tennessee physicians misprescribed tetracycline to young children, in whom use of this antibiotic is associated with permanent discoloration of developing teeth. Rural family and general practitioners were found to be most at risk of prescribing these and other agents (e.g., chloramphenicol) (Ray, Federspiel, and Schaffner 1976) in a potentially unsafe manner. Ray, Griffin, et al. (1987) recently reported the results of a large population-based case-control study linking the inappropriate but common use of long-acting sedatives in elderly patients with falls and fractures of the hip. Based on these and other data, an expert consensus panel recently concluded that inappropriate medication use represented one of the five most important quality-of-care problems in the elderly in terms of avoidable morbidity (Fink et al. 1987).

Much less documented, but possibly of greater consequence, is the preventable morbidity and mortality caused by the underuse of effective agents for treatable diseases. For example, a study conducted in a large health maintenance organization found that nearly two-thirds of newly diagnosed hypertensive patients were not followed up for treatments six to 12 months after diagnosis, despite the clear link between uncontrolled hypertension and the risk of myocardial infarctions and strokes (Barnett et al. 1983).

Many interacting factors contribute to inappropriate prescribing decisions. These include: failure of physicians to keep abreast of developments in pharmacology; overpromotion of drugs by pharmaceutical sales representatives or "detailers" (Avorn, Chen, and Hartley 1982); simple errors of oversight or omission (McDonald 1976); physician ignorance of (or apathy toward) cost issues; insulation of physician and patient from cost considerations because of third-party coverage; pressure from patients or families for a particular drug, regardless of indications (Schwartz, Soumerai, and Avorn 1989); overreliance on clinical experience versus scientific data; physicians' needs to provide some treatment for problems with no clear medical solution (e.g., dementia); pressure from other health workers (e.g., standing order psychoactive drug use in nursing homes); and high-volume practices requiring use of the prescription as a "termination strategy" to keep visits short.

These factors can result in a wide variety of prescribing errors. Among these are the use of toxic or addictive drugs (e.g., barbiturates) when safer agents are available; use of drug therapy when no therapy is required (e.g., antibiotics for viral respiratory infections); use of an ineffective drug for a given indication; use of a costly drug when a less-expensive preparation would be just as effective (e.g., new broad-spectrum antibiotics for uncomplicated infections); under- or excessive use of effective agents; and the failure to introduce new and effective drugs into practice (e.g., new chemotherapeutic agents and cholesterol-lowering medications).

In this report, we review studies of nonregulatory measures to improve physician prescribing, such as printed educational materials, government warnings, prescription audits plus feedback, reminders at the time of prescribing, public-interest face-to-face "detailing," and physician counselor approaches. Only those programs which attempted some evaluation of their impact will be described. The objectives of this article are to review critically what is known about the effectiveness and efficiency of these approaches to improving prescribing practices in office settings, and to suggest the most promising methods for adoption and further research.

## Methods

All published studies describing nonregulatory, noncommercial programs aimed at improving physician drug prescribing in primary care settings were initially examined for inclusion in this review. The medical, public health, and social sciences literature was screened for studies of interest from 1970 through 1988 with the assistance of computerized retrieval systems such as Medline, Paperchase, and Toxline. Non-English language studies, reports of pure regulatory actions, and changes in financial incentives to patients were considered beyond the scope of this review and were excluded. Numerous descriptive studies of educational programs without measures of behavior were also not considered. Occasionally, studies reporting patient outcomes which might be associated with changed prescribing patterns were included. Forty-four studies met our inclusion criteria and are discussed below.

The reviewed programs were divided into seven categories, based on their dominant approach:

1. dissemination of printed educational materials;
2. reports of patient-specific lists of prescribed medications;
3. group education, including rounds, conferences, lectures, seminars, and tutorials;
4. feedback of physician-specific prescribing patterns;
5. reminders at the time of prescribing;
6. one-to-one education;
7. ongoing clinical pharmacy services.

Some previous reviews of the continuing medical education literature (Haynes et al. 1984) utilized a "two-tier system" for study inclusion which effectively discarded most studies which were not true experiments. While conservative, this approach excludes from consideration many strong quasi-experimental studies (e.g., interrupted time-series) which can sometimes indicate cause and effect relationships in settings in which randomized clinical trials are not feasible or ethical (Soumerai et al. 1987b; Rubenstein 1973). In this review good quasi-experimental designs, such as time-series designs and pretest-posttest comparison group designs, are described in addition to true experiments.

Within any of the seven intervention categories, the best controlled studies are described in more detail than less well-controlled studies. As in our review of inpatient studies (Soumerai and Avorn 1984), the classification schemes of Campbell and Stanley (1963) were used to describe and rate the research designs of the reviewed studies into three groups. The adequacy of the design to make causal inferences between the observed effects and the described intervention ranged from large well-controlled trials with random assignment to experimental groups (+); to pretest-posttest comparison groups ( $\pm$ ) and interrupted time-series designs ( $\pm$ ); and to inadequate single-group pretest-posttest or posttest-only designs (-) (see ratings in table 1\*). Table 1 also presents a summary of the main features and findings of the well-controlled (+) ( $n = 9$ ) or partially-controlled studies ( $\pm$ ) ( $n = 15$ ). An additional 20 descriptions of inadequately designed studies are described briefly in the text but not in the table.

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\* Table 1 is presented on pp. 306-317.

## Studies Reviewed

The studies described below encompassed several kinds of settings, including private office practices, health maintenance organizations, other primary care centers, hospital outpatient clinics, emergency rooms, and entire populations of physicians in states or in countries with national health services.

### *Dissemination of Printed Educational Materials*

The most ubiquitous form of prescribing education is the distribution of printed educational materials, including newsletters, drug bulletins, illustrated "un-advertisements," drug therapy protocols, etc. Most of these interventions are based on the optimistic view that information deficits are an important reason for inappropriate prescribing, and that exposing physicians to correct information will cause them to improve their prescribing patterns spontaneously. While there is good reason to believe that this "rational informational" model is an insufficient basis for correcting many prescribing problems (Soumerai and Avorn 1984), it is still relied on exclusively in many prescribing education programs. We have divided such intervention studies into four broad categories: (a) mailed print materials; (b) protocols and guidelines; (c) self-education materials; and (d) mailed materials as components of national warning campaigns.

*Mailed Print Materials.* Only two studies employed physician-level prescription data and large populations of experimental and control group physicians to test the effectiveness of printed materials to improve prescribing decisions. Avorn and Soumerai (1983) reported the results of a randomized controlled trial in which 435 physicians participating in the Medicaid programs of four states were assigned to two experimental or control groups. One of the experimental groups ( $n = 132$ ) received a series of "un-advertisements" prepared by the Harvard Medical School Drug Information Program, consisting of four-color brochures with large headlines, professionally illustrated graphs, and other illustrations supported by current data from clinical research. The program encouraged restrained use of three target drug groups: propoxyphene, a marginally effective but abusable analgesic; peripheral/

cerebral vasodilators, ineffective agents for claudication and senile dementia; and an overused cephalosporin antibiotic. Analysis of prescribing levels nine months before and nine months after the program indicated that there was no significant difference between control and "print only" physicians in the rate of relinquishment of these drugs. A subsequent benefit-cost study (Soumerai and Avorn 1986) of this approach, however, did note a slight, although nonsignificant, trend toward less use of target drugs among print-only physicians (-4 percent) which, if real, might have achieved greater savings than the cost of their production and distribution.

A preliminary but uncontrolled study by Schaffner, Ray, and Federpiel (1979) had suggested that an informative advisory letter mailed to physicians might be effective in reducing physicians' inappropriate prescribing of chloramphenicol in outpatient settings and tetracycline for young children. In a subsequent series of better-controlled studies (Schaffner et al. 1983; Ray, Fink, et al. 1985), this same group used data from Tennessee's Medicaid Management Information System to examine the effect on prescribing practices of attractively designed mailed brochures, emanating from the state medical society. Physicians in the study had been identified as heavy prescribers of three antibiotics generally not indicated in ambulatory practice (chloramphenicol, clindamycin, and tetracycline for pediatric use), or of oral cephalosporins, which although safe and effective, are far more costly than alternative products. Although not randomized by physician, the study employed physician-level prescribing data and utilized large regional comparison groups. After adjusting for strong secular trends toward reduced prescribing of these drugs, results indicated no detectable differences in prescribing rates between physicians receiving the printed material and controls. This result appeared to be consistent with the finding that only 33 percent of doctors appeared to keep the brochure even though the mailed material was designed to be as attractive as possible.

Two other studies employing educational print materials suffered from lack of control groups or preintervention observations and should thus be interpreted cautiously. Watson, Stenhouse, and Jellett (1975) utilized concurrent regional and nationwide comparison groups to monitor changes in the prescribing practices of 430 general practitioners in the state of Western Australia who were sent information in a handy index-card format. Recommended therapies were based on

common problems identified by an audit and expert review of prescription practices. Improvement in prescribing for six drug groups was found, which differed significantly from the prescribing patterns observed in other states and the entire country after a one to two year follow-up period. These differences should be interpreted cautiously, however, owing to the lack of preintervention data needed to demonstrate preprogram comparability between the study regions. The second study (Kunin and Dierks 1969) utilized a pre-post design to examine the impact of a joint physician-pharmacist-medical society resolution sent to physicians in a United States community, recommending increased generic prescribing for specified drugs. This approach effectively capitalized on the potential influence of local medical authorities. Prescription audits indicated that, although 36 percent of the index drugs had been prescribed generically before the mailing, this had risen to 60 percent three months after the mailing. Measures of prescribing were based on audits of a small sample of drugs and pharmacies over a short period of time, and the potential impact of unrelated factors (such as increasing national publicity on generic prescribing or random fluctuation) could not be determined.

*Protocols and Guidelines.* Dissemination of protocols and guidelines through clinical channels, but without any other reinforcement, is another type of print-based intervention which has been employed in an attempt to change prescribing behaviors. This approach specifies explicit, appropriate courses of action to be undertaken in response to specified diagnoses or symptoms. Neither of the following two studies incorporated large enough samples or control groups to meet our research design criteria.

A university-based HMO was the study site for the implementation of a drug therapy protocol for the treatment of middle-ear infection (Bush, Rabin, and Spector 1979). The protocol included recommendations about prescription and over-the-counter drugs as well as drug costs. The protocol was designed at site 1 and then implemented at both sites 1 and 2, both centers within the same health plan; a third center within the same plan served as a control site. Results suggested that physicians at site 1 conformed more strongly to the protocol than physicians at site 2. Among those physicians at site 1 it was those who were involved in the design of the protocol who were most influenced by it. A questionnaire distributed to physicians suggested that personal involvement in the design of the protocol and clinical experience were



the most important factors in influencing a physician's decision to implement a protocol of treatment. The authors concluded that if involvement by the individual physician in protocol design was an important factor in its subsequent implementation, then the effectiveness of this method might be severely limited.

A prepaid group practice was the setting for a pre-post study without controls of the effects of mailed literature reviews and prescribing guidelines suggesting reduced use of combination preparations and antihistamines for the treatment of upper respiratory infections (URIs) (West et al. 1977). No effect was observed on the quantities of several combination products prescribed six months following the physician mailing, except for one product deleted from the formulary. Use of antihistamines did decrease, however, by about 44 percent following the mailing of both physician education materials *and* patient education pamphlets to all enrollees, though no statistical tests were used to determine the significance of this change. The authors noted, however, two discouraging observations. First, major decreases in drug use occurred only when an irrational combination was completely removed from the formulary. Second, use of other combination products with comparably dubious therapeutic credentials rose to replace the deleted preparation.

*Self-instruction Materials.* It has often been argued that "participatory learning" is an important component of efforts to improve physician practice patterns (Eisenberg 1986). Self-instruction programs attempt to increase individual physician involvement and clinical relevance over that achieved with standard didactic materials alone.

In a randomized controlled trial in Canada, Evans et al. reported the effects of mailing packets of self-study materials (patterned on the Australian study above [Watson et al. 1985]) to primary care physicians to improve hypertension treatment. Study physicians received 14 weekly installments of practice-oriented information including description of the consequences of inadequate control of hypertension. No changes were found in long-term physician knowledge, treatment practice, or patient outcomes (Evans et al. 1986).

In a randomized controlled trial using educational, administrative, and combined interventions, Dickinson et al. (1981) described a self-instruction program among physicians caring for hypertensive patients. Physicians were divided arbitrarily into one control and three experimental groups. There appeared to be good initial comparability across

the four groups in terms of baseline knowledge, level of training, and patient mix. The experimental groups received a self-administered educational program on hypertension management which included three exercises given over a 4-month period. Despite significantly higher scores on knowledge of hypertension management, experimental physicians did not appear to translate newly acquired information into improved management of their patients. No significant difference in blood pressure was found between the control group and any combination of experimental groups. In another uncontrolled study with very small sample sizes and without statistical analyses, Sheldon (1979) reported that self-audit forms distributed to physicians might lead to decreases in prescribing of inefficient or costly drugs.

Analysis of the best-controlled studies of mailed, printed educational materials cited above failed to support the claim that they are effective *when used alone* in changing physician prescribing behavior. If the small but insignificant trends that were observed in the two controlled trials (Avorn and Soumerai 1983; Schaffner et al. 1983) are indeed real, however, the low costs of printed materials indicate that they may be worth implementing. Further, one inconclusive study (Fendler, Gumbhir, and Sall 1984) suggests that printed materials may have a differential effect on various classes of drugs. Perhaps most important, print-based materials may play a useful role in laying the groundwork for other, more effective approaches described below.

*Dissemination of Mailed Materials as Components of National Warning Campaigns.* When drugs are identified as causing severe adverse effects, distribution of mailed educational materials to physicians is often part of a national warning campaign. However, because these campaigns involve a multimedia approach which usually includes the medical and popular press, newspapers, television and the radio, it is difficult to assess the unique influence of the mailed materials in directing physician prescribing away from problem drugs.

In the mid-1960s, it became clear that major blood dyscrasias were resulting from commonly used drugs, including dipyrone (agranulocytosis) and chloramphenicol (aplastic anemia). In Sweden, in addition to articles appearing in the medical literature, the Swedish Adverse Drug Committee mailed warning letters concerning these drugs to all physicians, and simultaneously published the warnings in the *Journal of the Swedish Medical Association*. Using time-series data spanning a six-year period, Böttiger and Westerholm (1973) documented a precipitous 60

percent decrease in national expenditures for dipyrrone and an 80 percent decrease in dipyrrone-induced agranulocytosis following the dissemination of this information. Of course, the relative impact of the warning letters cannot be separated from the effect of the letters and articles appearing at the same time in the medical literature and material in the lay media.

Two British studies (Wade and Hood 1972; Inman and Adelstein 1969) also utilized time-series data to document substantial reductions (25 to 50 percent) in national prescribing rates of chloramphenicol and pressurized aerosols (associated with increased mortality in asthmatics). The decrease in aerosol sales was accompanied by a sharp (50 percent) decrease in death rates among asthmatics in England and Wales. Journal articles, manufacturers' warnings, and patient input very likely added to the effect of warnings mailed to physicians by the British government drug safety committee. In a highly publicized time-series study in Northern Ireland aimed at curbing barbiturate use, all physicians received mailed materials on appropriate barbiturate use; but the downward, secular trend observed in barbiturate use was probably associated with influences other than the national program (King et al. 1980).

In the mid-1970s propoxyphene (e.g., Darvon), a popular but marginally effective analgesic, was found to have a high risk of both habituation and intentional and accidental overdose. Soumerai et al. (1987a) conducted a time-series analysis of nationwide propoxyphene prescribing patterns and overdose deaths before and after an informational campaign conducted by the U.S. Food and Drug Administration and the drug's manufacturer. In addition to labeling changes and press releases, the FDA mailed warnings to physicians specifically recommending a no-refill policy for this drug. In contrast to the European studies and despite the physician-specific nature of the no-refill recommendations, the propoxyphene campaign failed to reduce either refill prescriptions or the risk of propoxyphene-related deaths. The authors concluded that propoxyphene use problems were resistant to such weak interventions, and that sustained face-to-face education or stronger regulation would be required to address the problem.

The above studies suggest that in some situations involving significant risks to patients, physicians may reduce their prescribing of hazardous agents in response to information from a variety of sources. Nonetheless, even after mailed warnings, journal articles, and lay pub-

licity, prescribing of potentially lethal agents may remain at alarmingly high rates. Mailed warning campaigns may likewise be ineffective in achieving the difficult objective of reducing high-risk use of drugs with abuse potential once patient and physician demand for the drug is well established (Soumerai, Avorn, Gortmaker et al. 1987a).

### *Reporting of Patient-specific Listings of Prescribed Medications*

Four studies examined the effect of simply reporting lists of individual patients' prescribed medications to physicians. Two of these were randomized controlled trials (Johnson et al. 1976; Hershey et al. 1986); the others utilized pre-post comparison group designs (Dickinson et al. 1981; Koepsell et al. 1983). In the first well-controlled study, Johnson et al. (1976) examined the hypothesis that up-to-date listings of all prescribed medications inserted prominently in the medical records of patients would reduce excessive or duplicative prescribing in a prepaid group practice. No differences were observed, however, in numbers of prescriptions or expenditures between study and control groups.

In the second randomized controlled study, conducted at a university outpatient clinic, Hershey et al. (1986) focused on reducing the costs of drugs which accounted for one-third of all patient charges in the clinic. Ninety-six resident physicians were randomly assigned to either study or control groups. At monthly intervals physicians received computer-generated profiles of their patients' drug use and total dollar charges. Although the authors reported a small but significant difference between experimental and control groups in the last month of the 9-month follow-up period, the overall data fail to document the efficacy of this approach.

In a less well-controlled study than the previous two, Koepsell et al. (1983) described a computer reporting system in an outpatient service of a prepaid clinic. Eighty percent of all clinic patients were "approximately" randomly assigned to an experimental group and 20 percent to a non-profile control group. After a 4-month period of passive data collection, drug prescription profiles were reported to physicians of the experimental patients for 20 months. Analyses compared 3,089 controls with a 25 percent random sample of 3,097 patients in the profile group. The research team found no effects on prescribing volume, co-

ordination of drug refills, or visit schedules. The incidence of preventable drug/drug interactions also remained unaffected.

The Dickinson et al. study (1981) cited above presented records to physicians to help identify patients with either uncontrolled blood pressure or overdue appointments. A 5-month baseline period was established in two physician groups; one received computer-generated profiles alone and the other received the profiles in addition to the self-education materials. Groups were compared at baseline and during the seven-month intervention period. No effects were observed, however, indicating the failure of profile reporting with or without educational programs to achieve improved clinical outcomes.

The above four studies, which all met our research design criteria, strongly suggest that merely reporting detailed drug use profiles of individual patients—without follow-up or explicit suggestions for changes in behavior—is unlikely to affect the prescribing habits of busy physicians.

### *Group Education: Rounds, Conferences, Lectures, Seminars, and Tutorials*

Most group education measures rely primarily upon traditional didactic learning to effect a change in physician behavior. Rounds, conferences, seminars, and tutorials have been part of ongoing physician education for generations. Yet, despite their prevalence, only three studies met research design criteria.

Inui, Yourtee, and Williamson (1976) conducted a randomized controlled trial describing the effects of an educational intervention on physicians caring for hypertensive patients in a university medical clinic. Experimental physicians participated in small-group teaching sessions which consisted of a dialogue with a senior faculty member dealing with hypertension and its therapy. These physicians made correct estimates of blood pressure control in 89 percent of cases compared to 48 percent among controls ( $p < 0.005$ ). In addition, tutored physicians were more skeptical of patient compliance than controls and spent more time reviewing medications and educating patients than controls, resulting in improved patient understanding of treatment. However, the relative effects of pharmacologic and non-drug treatments (e.g., changes in diet and exercise) cannot be separated from improvements in clinical benefit which are due to prescribing changes.

In a smaller well-controlled study, Klein, Charache, and Johannes

(1981) studied the impact of individual tutorials concerning drug therapy for urinary tract infections, given to house staff of a large teaching hospital. A survey of house staff perceptions of this condition and its treatment revealed several important misconceptions, and formed the basis for the remedial sessions. The tutorials, which lasted for 15 minutes, dealt with safety, efficacy, and cost of several therapies. Based on comparisons with a control group of non-medical residents, the brief program resulted in significant (50 to 460 percent) improvements in prescribing of individual drugs.

In a small-sample controlled trial ( $n = 35$ ), Pozen and Gloger (1976) examined the impact on house officers of an educational intervention in medical outpatient clinics at an urban hospital. Thirty-five physicians were randomly divided into six groups: two educational groups, two administrative support groups, and two controls. In the educational groups two respected faculty members were assigned to educate the house officers on outpatient problems, including indications and techniques of drug use. A physician-specific drug prescribing index (DPI) was calculated for "each drug prescribed during the preceding month for each patient, including a calculation of the dosage days provided by each prescription." This index was intended to measure under- or over-prescribing patterns, but was not validated. No effect of the intervention was observed; however, because of the unreliability of the measure and the small sample size, there is reason to question this study's power to detect any true program effects.

In another in-service educational intervention, a clinical pharmacist was employed to examine the effect of reviewing the indications and cost of oral cephalosporins (Ives et al. 1987). The study utilized a single group pre-post design, making valid inferences difficult. Results of the intervention, however, suggested some reduction in prescribing of cephalosporins. In another uncontrolled pretest-posttest study, Kaufman et al. (1972) described a comprehensive approach, including both education and administrative controls, to control tranquilizer prescribing in a clinic serving an American Indian population. The program included an intensive educational program for all clinic staff (including nurses and social workers), mandatory re-evaluations of medications, limits on refills, and patient education brochures. Reductions in tranquilizer prescribing two months following initiation of the program is highly suggestive of the impact of these measures. The relative impact of education versus regulation (e.g., refill limits) cannot be deter-

mined, however, nor can the duration of the observed changes. Rosser et al. (1981) used therapeutic guidelines, an audio-visual presentation, and individualized reviews by senior physicians in an uncontrolled pre-post study of a combined educational and administrative intervention in an academically based family practice center. They reported reduced use and doses of benzodiazepines, especially long-acting products, among elderly patients cared for by twenty-three residents and seven other physicians.

The above six studies suggest that group educational interventions, such as in-service lectures and tutorials, may change physician attitudes and knowledge; however, whether these effects result in improved prescribing practice remains unclear. It is sobering to consider how little empirical evidence underlies this most common approach to physician education.

### *Feedback of Prescribing Patterns*

Feedback interventions present physicians' past prescribing patterns and may also include a comparison of these patterns to peer behavior and/or accepted standards (Eisenberg 1986). The feedback studies below examine the hypothesis that notifying individuals or groups about deviations from peer behavior or accepted clinical criteria will lead to improved physician performance. Gehlbach et al. (1984) described a randomized controlled trial of computerized feedback of individual physicians' monthly prescribing patterns with suggestions for alternative treatments. The goal of the study was to increase generic prescribing, and assumed that many physicians were unaware of generic alternatives. Forty-four family practice residents were randomly assigned to an experimental or control group. Twenty-eight commonly prescribed drugs were chosen for monthly feedback. In addition, 16 "silent" control drugs were identified to serve as a comparison with the 28-drug list. Although data on branded and generic forms of the "silent" drugs were collected, feedback on these drugs was not provided to physicians in either group. In order to increase physician interest, additional information on the monthly profile report included suggested therapeutic alternatives and "hint of the month" advice on topics ranging from ratings of sunscreen preparations to dosing penicillin. After a baseline period of four months, nine months of follow-up indicated a significant increase in generic prescribing of about 80 percent over controls ( $p =$

0.01). This difference persisted one year after the end of the program. For the "silent" list of non-feedback drugs there were no observed differences between control and experimental physicians. This study supports the hypothesis that by giving *explicit* alternatives to a physician's usual therapy, ongoing feedback can change prescribing patterns, at least for generic drugs.

Pozen and Gloger (1976), in a study already cited, examined the impact of an administrative intervention on house officers' prescribing patterns and utilization of laboratory procedures in a hospital outpatient department. Physicians were randomly assigned to one of three conditions: a control, intensive education, or an administrative support. In the administrative support group, a unit coordinator served as a facilitator to the physicians and as an advocate for the patients. An unvalidated "drug performance index," intended to indicate individual physicians' patterns of under- or over-prescribing, was reported to physicians over 10 months. No other overt effort was made to change prescribing (or laboratory utilization) patterns. The information feedback among physicians in the administrative support clinics was associated with a decrease in the drug-prescribing index of about 64 percent relative to controls, although there was no change in laboratory utilization. Although the results of this study are suggestive, the small sample sizes and unreliable outcome measure make the results more tenuous.

In an attempt to reduce antibiotic prescribing for viral URIs, Grimm et al. (1975), in a pre/post study without controls, observed the impact of a protocol-based feedback intervention on the management of acute pharyngitis in a university health service. Physicians were provided with standardized forms to complete for all patients complaining of sore throat, and were provided with protocols indicating appropriate therapeutic responses. Weekly audits of physicians' records were followed by individual feedback to physicians, presented as mailed comments by the medical director. Antibiotics had been prescribed to 56 percent of patients with sore throat before introduction of the protocol; after the intervention this dropped to 18 percent.

In an uncontrolled study Hamley et al. (1981) reported that feedback of physician-specific summary statistics and individualized suggestions for more rational prescribing appeared to reduce inappropriate prescribing of hypnotics, antibiotics, and minor analgesics. Similarly, a pre-post study without comparison groups suggested that notifying physicians about patients with problematic or exceptional use of am-



phetamines or other habit-forming drugs was associated with reduced frequencies of problematic cases (Hlynka, Danforth, and Kerr 1981). Another uncontrolled study of peer-comparison feedback evaluated the effect of cost audits mailed to faculty internists, allowing them to compare the costs of their overall prescribing with those of their peers. It was hypothesized that recognition of the financial impact of clinical decisions would lead to more economical prescribing. Costs of prescribed medications, however, actually increased by 6 percent three months following the report (Schroeder et al. 1973).

In a posttest-only study of computer-generated drug use review and feedback in the Florida Medicaid program, Groves (1985) reported that physicians changed their drug therapy about 50 percent of the time after notification by mail of overuse or underuse of medications, contra-indicated drug combinations, therapy contraindicated by diagnosis, or adverse drug reactions. Owing to regression towards the mean and other biases, however, it is impossible to know how long the aberrant prescriptions would have continued, even without the program's feedback. Since all modifications in prescribing were counted, some changes credited to the program may well have occurred even before receipt of the feedback information. Although this program is one of the most popular drug-use review programs in state Medicaid programs, no well-designed study has confirmed the effectiveness of its approach, despite large sums spent on it by already constrained Medicaid programs. At present, it is impossible to know what effect the review and feedback program had on prescribing decisions, because of the absence of any control groups.

Several of these studies suggest that ongoing feedback, particularly from credible sources, can be effective in increasing generic prescribing rates and compliance with protocols. No well-controlled studies of this approach have been reported, however, in less organized office-practice settings.

### *Reminders at the Time of Prescribing*

Many of the interventions reviewed thus far have attempted to improve prescribing decisions by using education to enhance physicians' inadequate knowledge about the target drugs. Many errors in prescribing are not the result of ignorance, however, but are instead due to oversight. Barnett et al. (1978) have successfully demonstrated that in these situa-

tions concurrent computerized reminders are remarkably effective at reducing failure rates, if they are based on adherence to already-agreed-upon prescribing standards. In this study, physicians and nurses in an HMO agreed on standards for antibiotic treatment following positive culture for streptococcal pharyngitis. The computerized medical record system was then programmed to issue patient-specific reminders to physicians if no treatment was recorded within four days after a positive culture. If antibiotic treatment was still unrecorded two days later, a follow-up notice to the physician was again automatically printed. Four years of time-series data showed a marked reduction in the percentage of untreated patients, from over 10 percent to approximately 3 percent during the program. When reminders were discontinued, however, failure rates immediately returned to pre-program levels, suggesting that these deficiencies were not knowledge-related but simply due to the difficulty in recalling every event requiring follow-up. Because the computerized medical information system was already in operation, the incremental cost of this program was small in relation to the benefits of improving prescribing.

In a second well-controlled study by this research group, Barnett et al. (1983) utilized a computer-based medical record system to improve follow-up for newly identified hypertensive patients in an HMO. Patients were targeted if in the six months following initial measurement of an elevated diastolic blood pressure there were fewer than two visits during which blood pressure was determined. Targeted patients were randomly assigned to experimental or control groups. In the experimental group, computer-generated reminders were sent to the patients' primary care physicians informing them of deviations from accepted treatment standards. In addition, an "encounter form" was given to the physician indicating the recommended date of the next follow-up visit. If the visit did not occur, the computer generated another reminder. Monitoring terminated with appropriate follow-up. One-hundred-fifteen patients whose care did not meet these standards were randomized. Follow-up was satisfactory in the next 6 to 12 months in 84 percent of experimental patients and only 25 percent of controls. In a longer follow-up period of up to 2 years, follow-up was satisfactory in 98 percent of experimental patients and 46 percent of controls.

In another investigation by this team (Feldman, Wilner, and Winickoff 1982), the computerized medical record system was again utilized—this time to improve adherence to lithium treatment stan-

dards. In this case the experimental intervention consisted of a group lecture, provision of checklists on proper lithium prescribing, and designation of a psychiatrist as a "lithium consultant." This was immediately followed by a system of individualized, concurrent reminders whenever computerized audits found noncompliance with standards for necessary pre-treatment work-ups, monitoring of initial therapy, periodic follow-up, and management of side effects. Based on analyses of care given to 30 experimental (prospective) patients compared to 24 retrospective cases, the combined program led to significant improvements in performance scores for pre-treatment work-ups, with smaller changes noted in other areas. Again, performance quickly returned to control levels when the reminders and education program were discontinued.

McDonald (1976) examined the effect of computerized messages utilizing 390 protocols (primarily for drug-managed conditions) on the actions of nine interns and residents. The results, based on a controlled, crossover design, indicated a two-fold increase in appropriate physician-prescribing responses to clinical events when prompted by computerized suggestions. Interestingly, the group which first received computer-generated reminders and later served as controls showed *no* advantage during their control period when compared with the control-first group. That is, no "training effect" was found once the reminder messages were stopped. This supports the author's contention (and the three previous studies) that in many cases of inappropriate drug use, a secretarial-type reminder function is needed, rather than a teaching function.

Building on the work described above, Tierney, Hui, and McDonald (1986) utilized a randomized controlled crossover design to examine the effects of monthly reports of physician compliance with 13 preventive care protocols in comparison with concurrent reminders at the time of patient visits. House staff ( $n = 135$ ) were randomized to control or experimental groups receiving monthly feedback alone, concurrent reminders alone, or both feedback and reminders. Although the authors report that house staff receiving feedback complied with all protocols more than controls ( $p < 0.01$ ) and that reminders enhanced compliance for some of these protocols, no effects were reported for six of the eight drug-use protocols. Further study is needed to determine why many drug-use behaviors were unaffected by either intervention.

Most of the studies reviewed thus far have attempted to curtail inappropriate prescribing of common agents or reduce oversight errors. En-

couraging physicians to adopt unfamiliar drugs is an equally important undertaking, however. Wirtschafter, Carpenter, and Mesel (1979) implemented a computer-based "consultant extender system" to help a self-selected group of physicians use chemotherapy in patients with breast cancer. Seventy-three community physicians (mostly surgeons) and 195 patients participated in this prospective program with a posttest-only research design. Data on patient status, laboratory results, and clinical course were collected by the physician and applied to a computer algorithm prepared by oncologists and available by telephone from all areas of the state. The algorithm then instructed the physician on appropriate drug use for that visit. Analysis of the program indicated that appropriate chemotherapy was delivered in 97 percent of visits. Disease-free intervals of the patients in the experimental program were reported as "indistinguishable" from those of comparable patients treated in academic centers. Because of self-selection of the study physicians as well as the possibility of nonequivalent comparison groups, however, generalization of the results of this study is difficult to make.

### *Face-to-face Educational Outreach*

Based on health-education studies, it has been suggested that one-on-one educational methods are one of the most effective approaches to change health behavior (Leventhal and Cleary 1980). Several hospital-based studies of prescribing behaviors have also supported the efficacy of such an approach (Soumerai and Avorn 1984). The efficiency of this approach has been suggested for years by the marketing behavior of the pharmaceutical industry whose sales representatives visit physicians frequently to promote their company's portfolio of products. This section of the review examines eight reports on the effectiveness of face-to-face educational interventions in improving prescribing in the ambulatory setting.

In the four-state randomized controlled trial already cited above (Avorn and Soumerai 1983), the authors described a medical-school-based educational outreach program in which seven doctoral-level clinical pharmacists visited physicians who were moderate to heavy prescribers of one or more problematic drug categories. The clinical pharmacists were trained in such behavior-change principles as emphasizing the credibility of the sponsoring medical school, brevity, use of graphic

aids, repetition and positive reinforcement, two-way communication, and presenting both sides of controversies. The intervention did not include feedback of physician prescribing performance, as it was designed to test a purely educational intervention. The study population consisted of 435 physicians who were moderate to high prescribers of an oral cephalosporin (Keflex), cerebral and peripheral vasodilators, and propoxyphene (e.g., Darvon), and were targeted through a review of 12 months of Medicaid prescription claims data. Subjects were randomly assigned to: (1) a group that received two face-to-face educational visits by a trained pharmacist, in addition to headlined and illustrated "un-advertisements"; (2) a group receiving only the mailed print materials; or (c) a control group. Although the print-only intervention did not result in statistically significant effects (see above), the group receiving one-to-one educational visits in addition to the print materials reduced prescribing of the targeted drugs by 14 percent ( $p = 0.0001$ ) in comparison to controls. The vast majority of visited physicians were receptive to the educational outreach intervention: 92 percent agreed to meet with the "academic detailers." The reduced prescribing of the targeted drugs persisted for at least nine months after the beginning of the intervention.

In a formal economic and policy analysis of the above intervention utilizing prescription-specific reimbursement data, Soumerai and Avorn (1986) report that implementation of this intervention for 10,000 physicians would lead to Medicaid drug savings of over \$2 million (1981) while costing only about \$1 million. Since high prescribers reduced their target drug use at the same rate as low prescribers, it was estimated that targeting of higher-volume prescribers would be associated with a benefit/cost ratio of 3.0 or more. The authors also carefully examined physician substitution to other appropriate and inappropriate drugs, and detected only an increase in aspirin use ( $p = 0.08$ ), a recommended alternative to propoxyphene. Net benefits would have been even higher if the analysis had included non-Medicaid savings and improvements in quality of care. It was also estimated that while the print materials might have been marginally cost effective, given greater power to detect modest effects, the print plus face-to-face approach yielded greater net savings. Another analysis by the same researchers (Soumerai and Avorn 1987) indicated that when physicians were grouped according to background characteristics—including age, board certification, specialty, rural versus urban practice, intensity of previous

target drug use, and size of Medicaid practice—results were independent of these characteristics. A follow-up reinforcement visit to the targeted physician was a strong independent predictor of prescribing change ( $p < 0.05$ ) and was associated with an approximate doubling of effectiveness, suggesting the importance of repetition and positive reinforcement in achieving important changes in behavior.

In another study utilizing a large group of study physicians and regional controls, Schaffner et al. (1983) reported that inappropriate prescribing of targeted drugs declined when practitioners were visited by “physician counselors.” The study employed three different interventions in an attempt to reduce inappropriate prescribing of oral cephalosporins and three other antibiotics contraindicated in general office practice or in particular patient groups (e.g., children): (1) an attractive and commercially prepared mailed brochure; (2) a visit to targeted physicians by a pharmacist drug-educator who was a recent honors pharmacy graduate and whose role was modeled after that of the pharmaceutical sales representative; and (3) a visit to targeted physicians by physician-counselors. Both the pharmacist and the physician-counselor received instruction in the appropriate uses of the antibiotics as well as training in interviewing techniques by the study’s authors. The visit with the physician consisted of a discussion of less than 15 minutes’ duration that presented information contained in a brochure which was left with the doctor at the conclusion of the visit. Individual physicians’ prescribing patterns were not discussed unless the physician asked how targeting had occurred. Interview results suggest that both the pharmacist and the physician counselor visits were well received. Based on one year of follow-up data, results indicated that the mailed brochure had no significant effect (see above). After controlling for strong secular declines in the use of study drugs, data indicated that the pharmacist visits did not significantly reduce the proportion of physicians prescribing the contraindicated antibiotics nor reduce the average number of patients per doctor receiving the antibiotics. The average number of prescriptions written per doctor, however, was reduced by 34 percent among these physicians. Visits by the physician-counselors were associated with an 18 percent reduction in the number of doctors prescribing the contraindicated drugs ( $p = 0.04$ ); a 44 percent reduction in the number of patients per physician receiving these drugs ( $p = 0.001$ ); and a 54 percent reduction in the mean number of prescriptions per physician ( $p = 0.001$ ).

Since the Harvard four-state study discussed above (Avorn and Soumerai 1983) found that seven doctoral-level pharmacists were successful in changing prescribing habits, the finding concerning the single pharmacist's lack of success in this study should be interpreted cautiously. Possible explanations for the difference include the fact that the pharmacist in the Tennessee study was a recent graduate, while the physicians were experienced senior practitioners; a gender difference between the pharmacist educator (female) and the physician counselor might also have affected results. In addition, there was only one educational session per targeted doctor, versus two in the Harvard study.

The persistence of improvement in antibiotic use in the Tennessee study was examined by Ray, Schaffner, and Federspiel (1985) in the second year following the educational intervention. Results indicated that doctors who had been visited by physician-counselors persisted in their improved prescribing behaviors for all study drugs, although the effect in the second year was less than in the first year. The mean decrease in inappropriate prescribing of the drugs was 55 percent in year one, compared to 29 percent in year two. At the end of the second year, the decreases in inappropriate prescribing of oral cephalosporins was associated with reductions in Medicaid expenditures of \$43,474, or \$950 per physician.

In another analysis of the above experiment, Ray et al. (1986) evaluated the effect of the physician-counselor visit on the rate of diazepam (e.g., Valium) prescribing. Forty-three experimental and 142 control physicians who were the most frequent prescribers of diazepam in their geographic regions were targeted for the visit from the same senior physician, who had received training from a psychiatrist on the indications for diazepam. The visit included information on the adverse effects of the drug, appropriate and inappropriate indications, as well as a specific protocol for withdrawing patients from the drug if use were judged inappropriate. As in the Schaffner et al. study cited above (1983), the information covered in the visit was summarized in a commercially prepared brochure that was given to the physician at the end of the visit. In the year following the visit there were no differences in the rate of decline in overall diazepam prescribing among visited versus control physicians. In subgroup analyses, however, long-term user rates among visited physicians did decline by 18 percent relative to controls. When the subgroup of doctors who used the withdrawal protocol was examined separately, the effect of the visit was even more pronounced:

33 percent of these physicians reduced long-term diazepam use among their patients. Because use of the withdrawal schedule was not randomly allocated, however, selection bias probably explains much of this subgroup effect.

A less well-controlled study (McConnell et al. 1982) was undertaken to change the prescribing patterns of physicians in the New Mexico Medicaid program who were targeted as the most frequent prescribers of tetracycline for viral upper respiratory tract infections. Thirty-three physicians were randomly assigned to experimental or control groups. A 6-month average pre-intervention prescribing rate for tetracyclines among the experimental physicians was almost twice as great than among controls. Five physician counselors (two pediatricians, two internists, and one family practitioner) visited the targeted physicians to explain that tetracycline was not indicated for streptococcal infections or viral URIs. During the visit of approximately 30 minutes, the physician-counselors maintained an educational, nonthreatening tone and presented individual feedback as well as educational materials on indications for tetracyclines. During a 6-month follow-up period the mean number of prescriptions decreased within both groups, suggesting contamination of controls. The effect appeared to be greater among experimental physicians, but conclusions are clouded by virtue of the fact that the baseline prescribing rates for the two groups were so different, and no between-group statistical analysis was reported.

In another pre-post, nonequivalent comparison group study, Stross and Bole (1980) report that face-to-face education of primary care providers by physician opinion leaders decreased use of corticosteroids for arthritic patients (with concomitant increase in aspirin use) as well as increased physical therapy utilization. Both therapeutic approaches aimed at improving quality of care, and were stressed in the education of the physicians in six community-hospital settings during informal "teachable moments." The program made use of ongoing, informal associations between educationally influential physicians and colleagues who regularly sought their advice. During informal consultations on specific clinical problems in managing arthritic patients, the physician-educators recommended increased use of salicylates and physical therapy.

The results of the trials just cited support other studies in the hospital setting showing that brief educational visits by an appropriately trained counselor is associated with practically and clinically significant improvements in prescribing. Despite moderately high personnel costs,



some of these programs have been shown to save more dollars than they cost, and to improve quality of care.

### *Clinical Pharmacy Services*

Over the past two decades there has been increasing interest in expanding the traditional role of pharmacists to bring drug information to individual patients, physicians, and other health care providers. The growth of clinical pharmacy training programs and Doctor of Pharmacy degree programs are a direct result of this expanding interest in patient care. Among the many published articles describing these expanded services, three studies have attempted to observe the impact of clinical pharmacy services on the drug-utilization decisions of physicians and nurses in the ambulatory sector. Although there was some variation between these programs, services generally included developing and reviewing patient drug profiles and associated costs, monitoring for therapeutic responses and drug reactions, and communicating with physicians and nurses regarding drug dosage, selection, toxicity, and adverse reactions.

Only two of the studies reviewed met our research design criteria. Stergachis et al. (1987) described a comprehensive clinical pharmacy program in an outpatient clinic of an HMO which examined the effectiveness of such pharmacist consultation to physicians, nurses, and patients in increasing use of low-cost alternatives to nonsteroidal anti-inflammatory drugs (NSAIDs). Seventeen physicians were randomly assigned to experimental or control groups. At the end of the 6-month program no change was observed in prescribing of NSAIDs, although use of salicylates had increased significantly in the experimental group relative to controls. Although performed, statistical results were not reported; in addition, the large standard errors observed and the relatively small number of physicians studied suggest that the power of the study was not sufficient to detect moderate but potentially true effects.

In a second comprehensive clinical pharmacy intervention study (Fortner, Tarrant, and Felton 1985), average drug costs were reported to decrease at the experimental site one year following the start of the program, while at a control site costs continued to increase over the same period. The study reported that for every dollar invested in the program over seven dollars were saved, thus making the benefit/cost ratio of the program highly desirable. Because the program involved a wide

range of multi-service components, however, it is difficult to associate any changes with unique components of the program. In addition, no statistical tests were employed to detect significant changes due to the intervention. In a posttest-only study (Hanlon et al. 1986), a program designed by clinical pharmacists was implemented in a family residency program to teach principles of rational drug therapy. Three years after the implementation of the program overall prescribing was lower than national averages, and "infrequent" prescribing of inappropriate agents suggested that the program might have been effective. A higher-than-average rate of controlled substances prescribing raised serious concerns, however, about the effectiveness of the program.

## Conclusions

The overall findings of this review of empirical studies in primary care settings confirm and extend many of the conclusions drawn from our previous evaluation of hospital-based studies (Soumerai and Avorn 1984). In general, the data in the studies reviewed help to increase our understanding of which strategies are effective or ineffective in changing prescription decision making. First, consistent with this previous literature, there is now excellent evidence from several well-controlled trials that the use of mailed educational materials *alone*—such as drug bulletins, self-education curricula, protocols and guidelines, academically based, graphically illustrated "un-advertisements," or commercially prepared educational brochures—may change knowledge or attitudes, but has little or no detectable effects on actual prescribing behavior. Nevertheless, if the small but nonsignificant effects observed in one large randomized controlled trial (Soumerai and Avorn 1986) are real, the relatively low cost of this approach may make their publication somewhat worthwhile from a benefit/cost perspective, particularly in the absence of sufficient resources to mount more intensive interventions. In addition, well-designed educational materials appear to be an important component of other strategies (e.g., face-to-face education or feedback systems), providing initial exposure to behavior change messages, and subsequent reinforcement of improved practice patterns. When heavy media reporting supplements nationwide warning campaigns concerning extremely toxic drugs, their combined effects may be important in reducing overall demand for these agents. One

time-series study (Soumerai et al. 1987a) failed, however, to document the effectiveness of FDA and commercial warnings alone in reducing use of potentially toxic drugs in high-risk populations.

The results of several adequately designed studies (Johnson et al. 1976; Hershey et al. 1986; Koepsell et al. 1983) are unanimous in confirming that simply distributing computerized listings of patient-specific prescribed medications, without explicit suggestions for changes in practice, likewise has no beneficial effect on overall prescribing patterns or costs. It was hoped that physician awareness of the total prescription regimens of patients would help rationalize prescribing (e.g., reduce duplicate prescriptions), but the twin problems of "information overload" coupled with a large proportion of clinically irrelevant data probably makes this approach untenable in most busy primary care settings.

Despite the universality of educational interventions involving group lectures and discussion, few well-controlled studies exist documenting their effectiveness. Two noteworthy exceptions (Inui, Yourtee, and Williamson 1976; Klein, Charache, and Johannes 1981) concluded that small group discussions conducted by senior physicians in academic primary care practices improved the use of antibiotics and hypertension treatment and control. No studies have been conducted, however, on the effectiveness of this continuing medical education approach in nonacademic settings.

Based on four adequately controlled studies in HMOs and hospital primary care settings (Barnett et al. 1978, 1983; McDonald 1976; Tierney, Hui, McDonald 1986), there is evidence to conclude that ongoing computerized reminder systems could be effective in preventing physicians from omitting essential preventive measures for several diseases such as streptococcal pharyngitis and hypertension. The most recent study reported (Tierney, Hui, McDonald 1986) failed, however, to demonstrate the effectiveness of either reminders or feedback on physicians' compliance with other drug-use protocols. Most of these interventions are more administrative than educational since they correct for errors of omission rather than incorrect beliefs, and can be viewed as "secretarial reminders" to take actions that practitioners agree are important. This view is confirmed by the observation that improved behavior deteriorates quickly after cessation of the intervention. It is not known, however, whether such systems could reduce unnecessary or inappropriate drug use which is based on incorrect facts, peer pressure, patient demand, or other factors.

Based on one randomized controlled trial (Gehlbach et al. 1984) and

several inadequately controlled studies we conclude that ongoing feedback reports of physician-specific prescribing performance may be effective in improving certain types of prescribing practices, such as use of generic drugs, in academic group-practice settings. No well-controlled study has been conducted on the effectiveness of this approach directed at private office practitioners, who may be more resistant to influence from influential colleagues or authority figures than hospital-based on group-practice physicians. In addition, private physicians may be suspicious of such attempts at intervening in their practice and rating their performance.

The largest controlled trials conducted in five states confirm the conclusions of our review of inpatient studies that brief one-to-one educational outreach visits by either specially trained clinical pharmacists (Avorn and Soumerai 1983; Soumerai and Avorn 1986) or physician counselors (Schaffner et al. 1983) are effective in substantially reducing inappropriate prescribing of a wide range of medicines, including use of contraindicated or expensive antibiotics, ineffective drugs for geriatric patients with peripheral vascular disease or senility, potentially addictive analgesics, and psychoactive drugs. The only formal economic analysis based on a randomized controlled trial (Soumerai and Avorn 1986) concluded that targeted education of moderate to high prescribers of the above drugs in Medicaid would lead to government drug savings at least two to three times higher than the operating costs of such a program, without even considering positive spillover effects and improved quality of care. Such effects were independent of physician-background characteristics (Soumerai and Avorn 1987; Ray et al. 1985), were increased by follow-up reinforcement visits (Soumerai and Avorn 1987), and persisted for up to two years (Ray et al. 1985). The above studies represent the only well-controlled trials of interventions in typical single-office practices dominated by primary care practitioners.

## Discussion and Implications

The methodological quality of these studies is an important topic. Although the proportion of adequately controlled studies (64 percent) is higher than in our review of inpatient studies (Soumerai and Avorn 1984), a large number of evaluations failed to meet even minimally adequate research-design criteria which could protect against alternative

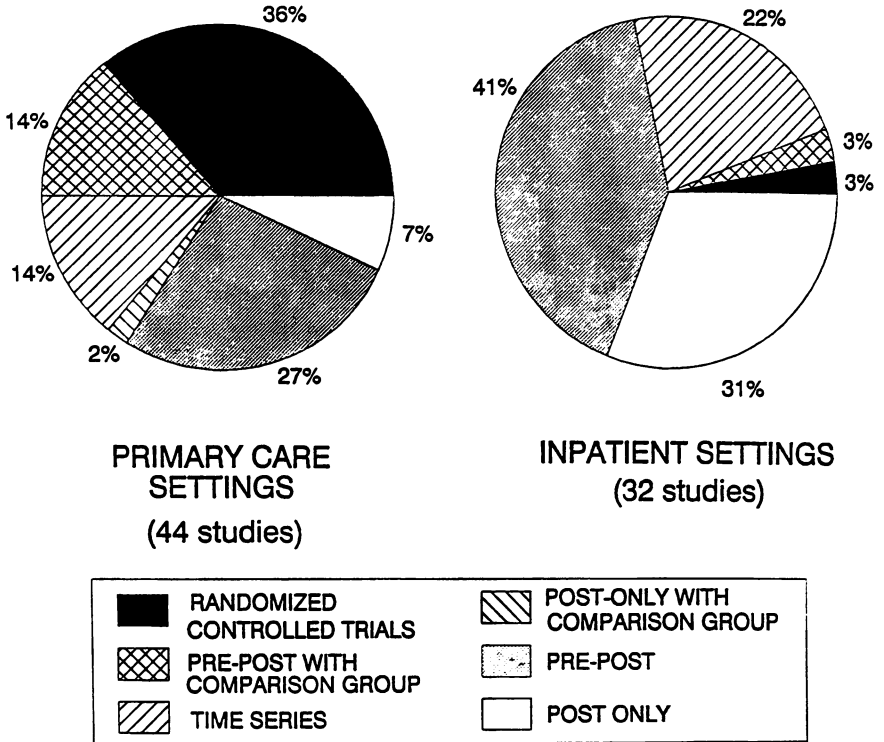


FIG. 1. Distribution of research designs in studies to improve prescribing behavior.

explanations for the "effects" observed (see figure 1). Such factors could include unrelated changes in marketing or the knowledge base for particular products, state or federal regulatory policies, seasonal effects, and (in institutional settings) changes in staffing (e.g., senior or influential physicians). Drug use is not always a stable phenomenon, and the results of one-group pretest-posttest designs or posttest-only designs are extremely sensitive to the effects of many historical factors. It is interesting to note that 85 percent of the inadequately controlled studies reported positive findings, compared to 55 percent of well-controlled studies. For example, figure 2 indicates that printed materials were reported to be ineffective in all adequately controlled studies, whereas every uncontrolled study reported positive "effects" of their programs on prescribing. Interestingly, several of the control groups in the randomized studies (which received no education) exhibited positive trends in prescribing habits as well, probably due to other effects

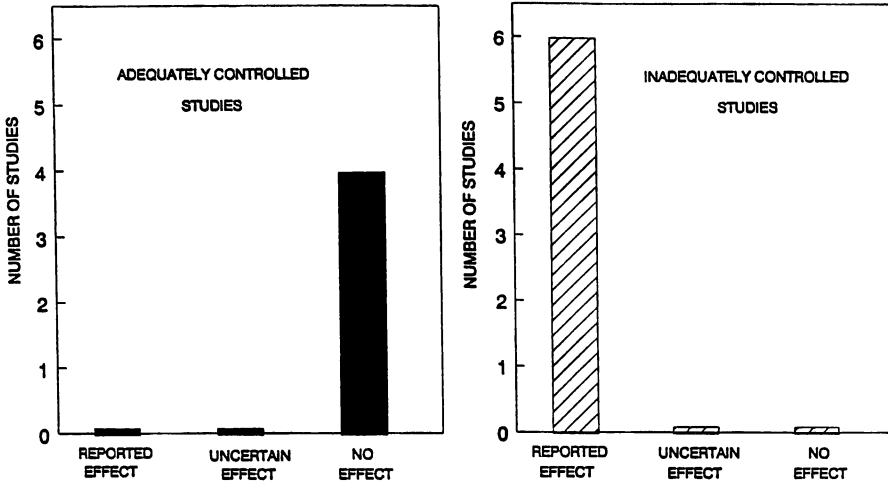


FIG. 2. Reported effectiveness of dissemination of printed educational materials alone in well-designed versus inadequately controlled studies.

of history. By examining differences in trends between experimental and control groups these biases were eliminated, resulting in more accurate and less dramatic estimates of program effectiveness. Within most categories of intervention described above, the results of controlled studies were more consistent than uncontrolled studies.

In a time of limited health care resources which are increasingly being stretched to meet the basic needs of poor and chronically ill patients, it is unwise to base quality assurance and cost-containment program development on the results of badly controlled studies of possibly effective strategies to improve prescribing. For example, a large number of state Medicaid programs are currently spending millions of dollars each year on a computerized Medicaid data feedback system intended to reduce inappropriate drug use and subsequent adverse reactions (Groves 1985), for which there are no minimally adequate studies published in the literature. "Computerized feedback" has all the "high-tech" connotations of new developments in medicine itself, and has been adopted rapidly due to effective marketing and its ease of implementation. But will future well-controlled trials confirm the efficacy of this approach, or will this case resemble the many new medical technologies, like gastric freezing, which after years of use (and cost) are found to be ineffective? Better controlled trials or the use of high-quality quasi-experimental designs (e.g., two-group interrupted time-

series analyses) are needed before policy makers embrace one approach to the exclusion of others.

Currently, a computer revolution is changing the nature of information flow in medical settings. One side effect of this innovation is the use of medical care process data to feedback a variety of information to health care providers. Considerable effort has been spent in developing such computerized "drug utilization review" systems for private and public drug benefit programs. Many administrators of prescribing quality-assurance programs assume, however, that any kind of data will affect physician prescribing patterns. An extreme example of this approach is the delivery of unanalyzed data on patient prescription patterns to busy physicians who do not have the time to evaluate the significance of these patterns. This is not to say that computer-based data feedback is not useful. Studies on computer-generated reminders and on problem-specific feedback to physicians provide evidence of their effectiveness in certain settings. Yet, more attention must be paid to the appropriate use of this tool, as well as the underlying motivations of drug-therapy decision making.

The evidence makes clear that the setting and organization of practice are important influences on the relative efficacy of alternative intervention strategies. For example, group versus individual practice has already been shown to be associated with higher-quality prescribing practice (Becker et al. 1972), and academic centers are more likely to adopt innovative drug technologies. In this review, several effective interventions, such as administrative reminders and feedback systems, seem to be well suited to such group practices where patient-level databases are often available and influential colleagues and authority figures are well established. Conversely, it is not surprising that the most effective approach in less well-organized office practice settings appears to be the more flexible one-on-one educational interventions which resemble, at least structurally, the marketing approaches of pharmaceutical companies.

The well-controlled studies also provide some clues regarding the characteristics of effective behavior-change interventions which could be the topics of future research. For example, several successful studies based the content of their educational programs on "market research" data derived from interviews of physicians themselves in an attempt to pinpoint the important knowledge gaps, motivations, and pressures to prescribe inappropriately. Another group used survey data to identify local "opinion leaders," and they involved such educationally influen-

tial physicians in transmitting up-to-date therapeutic recommendations to their colleagues (Stross and Bole 1980).

Several successful strategies explicitly involve the physician in two-way communication—a theoretically important prerequisite to changing behavior (Eisenberg 1986). Targeted interventions to physicians identified as at risk of inappropriate prescribing was also an important feature of several studies which demonstrated high benefit-to-cost ratios—a necessary economic criterion in today's health care marketplace. Several elements tend to recur in successful interactive programs. These include well-designed graphic aids used in face-to-face encounters, clinically relevant and understandable recommendations for positive alternative actions by physicians, and repetition of messages with reinforcement of improved practice patterns over time. Probably the most important characteristic of such successful strategies was that the intervention was either individualized to the specific needs of physicians or was communicated in one-to-one encounters, or in very small groups of one to two physicians. As discussed previously (Soumerai and Avorn 1984), because they provide the opportunity to discuss prescribing issues interactively with physicians, these approaches can be more flexible in targeting correctable errors, knowledge gaps, or other physician-specific rationales for existing practice. The relative importance of each of the above factors is an important topic for future research. Future studies might also examine innovative strategies not previously evaluated, such as use of television or other media to communicate therapeutic guidelines, or new methods of computerized reminders to physicians in office settings.

Critical evaluation of methods to improve physician prescribing is particularly timely at present, in view of the growth of large-scale automated claims databases, coupled with point-of-sale terminals in many pharmacies. Much attention is being paid to the concept of "drug utilization review" both concurrently and retrospectively, to improve prescribing. However, in many such settings the burden of responsibility for concurrent feedback would fall primarily on the community pharmacist, alerted by computerized messages from the drug claims processors. The pharmacist is then expected to intervene with the physician and initiate correction of problematic prescribing. Unfortunately, virtually no data exist from well-controlled studies demonstrating the efficacy of this approach.

Other approaches to influencing prescribing are similarly unrelated to the available evidence on improving medication use. Elsewhere, we



have described the impact of a patient-level Medicaid drug cap in New Hampshire which resulted in drops in use of vital medications like insulin and cardiovascular preparations (Soumerai et al. 1987b). Such measures may jeopardize the health of patients and could be associated with long-term costs that exceed any savings realized from the intervention. Before adopting such restrictive measures, it is essential that policy makers consider the long-range adverse health and financial outcomes of such policies, in relation to the educational efforts described above.

In summary, this important area of health services research has progressed remarkably over the last decade. As evidenced by the above studies, administrators, policy makers, physicians, and other professionals now have an improved knowledge base on which to build programs to improve the effectiveness and efficiency of prescribing practice. Future studies should attempt to implement randomized controlled trials or well-designed quasi-experiments; cost/benefit analyses should be included to compare the relative effectiveness of alternative strategies directed at particular problems; and more emphasis should be placed on intervening in nonacademic office-practice settings where most drug use occurs without the benefits of ongoing monitoring and peer review. Finally, more effort should be directed at determining the clinical and economic importance of inappropriate prescribing in office-practice settings, and the effect of such interventions in reducing drug-induced illness as well as containing costs.

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*Address correspondence to:* Stephen B. Soumerai, Sc.D., Department of Social Medicine, Harvard Medical School, 643 Huntington Avenue, Boston, MA 02115.

TABLE 1 Description of Adequately Controlled Studies

Study	Target drugs	Target group
<b>1. Dissemination of printed educational materials</b>		
<i>A. Mailed print materials</i>		
Avorn & Soumerai (1983)	Propoxyphene (marginally effective analgesic); vasodilators (ineffective agents for senility, claudication); cephalexin (effective but expensive antibiotic)	435 office MDs in Arkansas, Washington, D.C., Vermont and New Hampshire randomized in a block design to control, printed materials only or face-to-face education group
Soumerai & Avorn (1986)		
Schaffner et al. (1983)	Oral cephalosporins, contraindicated antibiotics (chloramphenicol, clindamycin, tetracycline in children), diazepam	For contraindicated antibiotics, 223 Tennessee MDs in office practice, for oral cephalosporins, 300. For diazepam, 185
Ray et al. (1986)		
<i>B. Protocols and guidelines</i> (no studies were adequately controlled)		
<i>C. Self-instruction materials</i>		
Evans et al. (1986)	Hypertension control	76 MDs in 62 practices in two contiguous, urban Canadian communities, randomly assigned to study (41 MDs in 33 practices) or experimental (35 MDs in 29 practices)
Dickinson et al. (1981)	Hypertension control	37 residents & 4 faculty MDs randomized to 3 experimental or 1 control group

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
<p>Print-only MDs received either an informational drug bulletin only or 6 un-advertisements plus the drug bulletin urging restraint in use of target drugs and substitution of more cost-effective agents. The face-to-face MDs received the materials given to print-only MDs as well as 2 visits by a clinical pharmacist trained in principles of communication/persuasion.</p>	<p>RO<sub>1</sub>X<sub>1</sub>O<sub>1</sub>*(+)** RO<sub>2</sub>X<sub>2</sub>O<sub>2</sub> RO<sub>3</sub> O<sub>3</sub></p>	<p>~1 year</p>	<p>No significant effect of print-only intervention</p>
<p>State-wide controlled trial to reduce prescribing through (1) mailed brochures, (2) a pharmacist-educator visit, (3) MD-educator visit. Visited MDs also received brochures.</p>	<p>O<sub>1</sub>X<sub>1</sub>O<sub>1</sub> (±) O<sub>2</sub>X<sub>2</sub>O<sub>2</sub> O<sub>3</sub>X<sub>3</sub>O<sub>3</sub> O<sub>4</sub> O<sub>4</sub></p>	<p>12 month follow-up</p>	<p>Brochure had no effect</p>
<p>14 weeks of brief "practice-oriented" educational materials were mailed to primary care MDs to improve hypertension treatment.</p>	<p>RO<sub>1</sub>XO<sub>1</sub> RO<sub>2</sub> O<sub>2</sub> (+)</p>	<p>~1 year</p>	<p>Over short term, MD knowledge of hypertension treatment increased, but no long-term effect. No improved patient outcomes.</p>
<p>Self-education program (group 1) with (group 2) and without (group 3) concomitant reporting of patients receiving poor follow-up; program consisted of 3 exercises over 4 months to test effect on blood pressure control.</p>	<p>RO<sub>1</sub>X<sub>1</sub>O<sub>1</sub> (±) RO<sub>2</sub>X<sub>2</sub>O<sub>2</sub> RO<sub>3</sub>X<sub>3</sub>O<sub>3</sub> RO<sub>4</sub> O<sub>4</sub></p>	<p>72 months during program</p>	<p>No significant difference between experimental and control groups</p>

*continued*



TABLE 1 continued

Study	Target drugs	Target group
<b>1. Dissemination of printed educational materials (continued)</b>		
<i>D. Dissemination of mailed materials as components of national warning campaigns</i>		
Böttiger & Westerholm (1973)	Dipyrrone (a drug with potential to induce serious blood abnormalities)	All prescribers of targeted drugs in Uppsala, Sweden identified by Swedish Adverse Drug Reaction Committee
Wade & Hood (1972)	Chloramphenicol, a toxic antibiotic rarely, if ever, indicated in outpatient practice	All prescribers of targeted drugs in No. Ireland
Inman & Adelstein (1969)	Pressurized aerosols of sympathomimetic bronchodilators	All MDs in United Kingdom
Soumerai et al. (1987a)	Propoxyphene	MDs in U.S. prescribing propoxyphene from 1974- 1983 as identified in National Prescription Audit

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
3 mailed and published warnings issued by the Swedish Drug Adverse Reaction Committee urging restraint on indiscriminate use.	OOXOO (±)	4-5 years follow-up	80% decrease in dipyrrone-induced agranulocytosis; 66% decrease in sales. Effects of other print and nonprint media on these outcomes are unknown.
Warning issued to all doctors indicating acceptable indications for chloramphenicol.	OOXOO (±)	~3 years	Prescribing decreased by about 50%. Effects of other print and nonprint media on these outcomes are unknown.
Warning to MDs of the possible hazards of pressurized aerosols (e.g., excess mortality among asthmatics).	OOXOO (±)	~18 months	~50% reduction in mortality. Effects of other print and nonprint media are unknown.
Effect of government and intended commercial warnings on propoxyphene related deaths and a no-refill recommendation to MDs.	O <sub>1</sub> O <sub>1</sub> X <sub>1</sub> O <sub>1</sub> O <sub>1</sub> (±) O <sub>2</sub> O <sub>2</sub> X <sub>2</sub> O <sub>2</sub> O <sub>2</sub>	~2 years	No effect on refill rates or drug-related deaths.

*continued*

TABLE 1 continued

Study	Target drugs	Target group
<b>2. Reporting of patient-specific listings of prescribed medications</b>		
Johnson et al. (1976)	All prescribed medications for 1,632 medically indigent patients in an HMO	MDs of 1,632 patients in Oregon region of Kaiser Foundation Medical Care Program
Hershey et al. (1986)	All drugs used in a large ambulatory clinic	96 resident physicians in an Ohio teaching hospital randomized to experimental or control groups
Koepsell et al. (1983)	All drugs in outpatient service	MDs of 6,186 outpatients making ~42,000 visits in a prepaid clinic Public Health Service Hospital in Seattle; patients randomized to experimental or control groups
Dickinson et al. (1981)	See section 1	See section 1
<b>3. Group education: Rounds, conferences, lectures, seminars, and tutorials</b>		
Inui, Yourtee & Williamson (1976)	Hypertension treatment	62 MDs in a university medical clinic at Johns Hopkins University
Klein, Charache & Johannes (1981)	Drugs for urinary tract infections	149 resident MDs and 15 nonresident MDs in an emergency room and primary care center

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
Computer-based, monthly profiles of patients' drug use inserted in front page of medical record.	RO <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (+) RO <sub>2</sub> O <sub>2</sub>	~1 year	No effect on number of prescriptions or costs.
Physician's total monthly drug prescribing: computer-generated reports of physician's prescribing and associated total drug charges.	RO <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (+) RO <sub>2</sub> O <sub>2</sub>	9 months during program	No effects on mean charge/patient, prescriptions/patient or total drug charges.
Computerized drug profiles to MDs over 21 months after a 4-month baseline to examine effect on drug/drug interactions and redundancies.	RO <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (±) RO <sub>2</sub> O <sub>2</sub> O <sub>2</sub>	21 months during program	No effect on prescribing volume, coordination of drug refills, visit schedules, preventable drug/drug interactions or drug interactions.
See section 1	See section 1		No effect.
MDs in groups of 1-2 were involved in a 1-2 hour tutorial session conducted by a physician-educator dealing with hypertension and its therapy and with content relying on data generated by study MDs.	RO <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (+) RO <sub>2</sub> O <sub>2</sub>	1 week and 1 month after tutorial session	Patients of experimental physicians complied with drug regimen 2 times as well as controls (p~0.005). Blood pressure control was nearly twice as great in patients of experimental MDs (69%) compared to controls (36%).
A 15-minute small group tutorial was employed to correct misconceptions about treatment (and costs) of urinary tract infection.	O <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (±) O <sub>2</sub> O <sub>2</sub>	~6 months	50-460% improvements in prescribing of individual drugs which persisted for ~6 months.

*continued*

TABLE 1 continued

Study	Target drugs	Target group
<b>4. Feedback of prescribing patterns</b>		
Gehlbach et al. (1984)	Generic drugs	44 MDs in a fee-for-service family medicine center in Durham, N.C.
<b>5. Reminders at time of prescribing</b>		
Barnett et al. (1978)	Antibiotics for streptococcal pharyngitis	60 physicians and 45 nurses in a Massachusetts HMO
Barnett et al. (1983)	Hypertension treatment	MDs of 115 patients enrolled in a Massachusetts HMO failing to receive appropriate follow-up of newly diagnosed diastolic hypertension
McDonald (1976)	Drugs in 390 patient-care protocols, ranging from cardiovascular products to antacids	9 physicians in an academic general medical clinic in Indiana
Tierney, Hui & McDonald (1986)	Antacids, aspirin, beta-blockers, antidepressants, long-acting nitrates, metronidazole	135 faculty internists, interns and residents in an academic general medicine clinic, randomized to 3 groups which received feedback and/or reminders for 13 preventive care protocols.

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
<p>A RCT involving physician-specific computerized feedback at monthly intervals of 28 prescribed brand-name drugs vs. alternative generics, with potential cost savings. A "non-feedback" drug control was used in both groups.</p>	<p>RO<sub>1</sub>X<sub>1</sub>O<sub>1</sub> (+) RO<sub>2</sub>O<sub>2</sub>O<sub>2</sub></p>	<p>9 months during program with an additional 12-month follow-up</p>	<p>~46% increase in median weighted generic prescribing rate of feedback drugs, relative to control, at the end of the 9-month program. For "non-feedback" drugs there was no change.</p>
<p>Concurrent computerized reminders to alert health providers of lack of adherence to an agreed upon protocol of antibiotics for streptococcal pharyngitis.</p>	<p>OOXOO (±)</p>	<p>32 months during program and 6 months after end</p>	<p>During the program the percentage of patients untreated declined from 10% to 3%. Upon termination of program, the level increased to ~10%.</p>
<p>A computer-based reminder system to alert physicians of lack of follow-up in the 6-month period following diagnosis.</p>	<p>RO<sub>1</sub>XO<sub>1</sub>O<sub>1</sub> (+) RO<sub>2</sub> O<sub>2</sub>O<sub>2</sub></p>	<p>6-12 months and 6-24 months after diagnosis. 9 clinic sessions after cross-over</p>	<p>In the shorter follow-up period follow-up was attempted or achieved in 84% of experimental cases and 25% in controls (p &lt; 0.01). In the longer follow-up period follow-up was attempted or achieved in 98% of experimental cases and in 46% of control MDs (p &lt; 0.01).</p>
<p>Physicians received computerized messages recommending actions along predefined care protocols at weekly intervals for ~2 months.</p>	<p>See text for description of design (±)</p>	<p>9 clinic sessions after cross-over</p>	<p>~2-fold increase in appropriate clinical actions during program; no significant effect once reminders were stopped.</p>
<p>Program to examine effect of feedback of physicians' noncompliance with preventive care guidelines vs. reminders vs. both feedback and reminders.</p>	<p>See text for description of design (+)</p>	<p>7 months during program</p>	<p>Relative to controls, feedback with reminders did not affect drug use in 6 of 8 protocols. These approaches were effective in increasing compliance with some nondrug protocols.</p>

*continued*

TABLE 1 continued

Study	Target drugs	Target group
<b>6. Face-to-face educational outreach</b>		
Avorn & Soumerai (1983)	See section 1	
Schaffner et al. (1983)	See section 1	
Ray, Schaffner, and Federspiel (1985)		
Soumerai & Avorn (1986)	Quantifiable costs and benefits of academic detailing described in Avorn & Soumerai, 1983 (see above); outcomes included: operational program costs, increases in Medicaid costs of intended and unintended substitute drugs, effects on costs of target drugs, net benefits by different MD targeting criteria (based on prior use of target drugs), stability of cost effects over time	See section 1
Soumerai & Avorn (1987)		

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
See section 1	See section 1		Face-to-face MDs reduced average prescribing of all target drugs by 14% compared to controls (p = 0.0001).
See section 1			Compared to controls, MD educator visits resulted in number of MDs prescribing drugs (p = .04); 54% reduction in mean number prescriptions per MD at 12 months (p = .001), and 29% at end of year 2. Pharmacist counselor had no effect on number of MDs prescribing drugs, but did result in a 34% reduction in the number of prescriptions per MD (p = .02).
See section 1	RO <sub>1</sub> X <sub>1</sub> O <sub>1</sub> (+) RO <sub>2</sub> X <sub>2</sub> O <sub>2</sub> RO <sub>3</sub> O <sub>3</sub> (also for subgroups of prescribers based on prior-use rates)	~1 year	Estimated Medicaid savings of >\$2M in 1981 vs. \$1M of program cost at operational scale. Increase in only recommended substitute drugs (aspirin); no unintended substitute effects. Benefit/cost ~3:1 for high prescribers. Effect independent of physician background characteristics. Two visits versus one visit associated with a two-fold greater effect.

*continued*



TABLE 1 continued

Study	Target drugs	Target group
<b>6. Face-to-face educational outreach (continued)</b>		
Ray et al. (1986)	Diazepam	185 MDs in Tennessee who were most frequent prescribers of diazepam in their geographic areas
McConnell et al. (1982)	Tetracycline	33 MDs targeted as inappropriate prescribers of tetracycline, randomly assigned to experimental or control groups
Stross & Bole (1980)	Aspirin, gold, NSAIDs, corticosteroids	22 MDs in 6 communities which were randomly assigned to control or experimental groups (communities and <i>not</i> MDs randomized)
<b>7. Clinical pharmacy services</b>		
Stergachis et al. (1987)	Aspirin, low-cost non-steroidal anti-inflammatory drugs (NSAIDs), high-cost NSAIDs	17 physicians in an outpatient clinic of an HMO in Puget Sound, Seattle Washington
Fortner, Tarrant & Felton (1985)	All drugs in an outpatient family practice of an HMO	MDs at 2 of 3 sites in HMO with enrollment of 24,000

Program description	Research design (adequacy <sup>1</sup> )	Follow-up period	Reported results
Face-to-face education in a brief visit by 3 trained physician counselors including a patient withdrawal schedule.	O <sub>1</sub> XO <sub>1</sub> (±) O <sub>2</sub> O <sub>2</sub>	12 months	No between-group effect on overall diazepam use. Subgroup analysis among experimental MDs suggestive of an 18% decline in long-term user rates, relative to controls.
One-to-one visits to targeted MDs by physician-counselors with presentation on appropriate tetracycline use.	RO <sub>1</sub> XO <sub>1</sub> (±) RO <sub>2</sub> O <sub>2</sub>	6 months	8/17 experimental MDs continued inappropriate drug use in contrast to 15/16 of controls (p < .01).
Face-to-face education by opinion-leader physicians about improved quality of care for arthritic patients.	O <sub>1</sub> XO <sub>1</sub> (±) O <sub>2</sub> O <sub>2</sub>	1 year	Experimental group reduced use of corticosteroids by about 55% (p < 0.05) compared to controls with a concomitant increase in aspirin use. Otherwise, there were no changes.
Services provided to MDs, nurses and patients, including information on dosing, adverse effects, costs, patient-counseling; lectures; patient drug-use review with goal of increased use of low-cost NSAIDs.	RO <sub>1</sub> XO <sub>1</sub> (±) RO <sub>2</sub> O <sub>2</sub>	6 months during program	No change in prescribing of either high-cost or low-cost NSAIDs, but use of salicylates increased in experimental group by ~40% relative to controls.
Comprehensive clinical pharmacy program including: physician and patient education, drug utilization reviews; monitoring of patient health measures.	O <sub>1</sub> O <sub>1</sub> XO <sub>1</sub> O <sub>1</sub> (±) O <sub>2</sub> O <sub>2</sub> O <sub>2</sub> O <sub>2</sub> O <sub>2</sub>	12 months	Apparent reductions in number of prescriptions and costs at experimental site relative to control site; no statistical analysis.

\* O refers to observation periods and X to intervention programs. OOXOO indicate two or more preprogram and postprogram observations respectively.

\*\* The symbols + and ± indicate well-controlled and partially satisfactory controls, respectively.

<sup>1</sup> In some cases, the adequacy of the research design was downgraded because of concerns about other features of the study, e.g., reliability of outcome measure or small sample size (<20 per study group).