Efficacy and Cost-containment in Hospital Pharmacotherapy: State of the Art and Future Directions

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DESPITE THE CENTRAL ROLE OF PHYSICIANS in determining the safety, efficacy, and efficiency of drug utilization, relatively few studies have investigated approaches designed to improve the ways physicians make drug-use decisions. Quality assurance approaches, including those of the Joint Commission on Hospital Accreditation, often emphasize audit and identification of problems, but are less oriented toward the establishment of effective mechanisms to change the problems thus identified (Anderson and Shields 1982). Traditional continuing education programs, relying on voluntary participation of physicians, have generally failed to reach those physicians most in need of training (Lewis and Hassanein 1970). The pharmaceutical industry has taken a central role in continuing drug education for the practicing physician, but there is concern that the commercial origins of such efforts may have a biasing effect on the information thus provided (Avorn, Chen, and Hartley 1982). Medication use in hospitals accounts for a large proportion of the $25 billion spent annually on drugs in the United States (Freeland and Schendler 1983), and represents an important percentage of hospital expenditures.

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If the clinical and economic consequences of improper drug utilization are taken into account as well, these costs would be considerably higher. Therefore, an important opportunity exists for cost-savings as well as improved health outcomes if programs to improve inhospital drug decision-making could be identified and adequately evaluated. The need for well-designed research into optimizing physician-prescribing decisions is made even more timely by the rapid emergence and exuberant marketing of major new drugs of great efficacy, cost, and risk of toxicity (calcium channel blockers, beta blockers, cephalosporins, and benzodiazepenes). These issues become particularly urgent at a time of federal, state, and private initiatives to contain hospital costs. This paper attempts to assess the current state of the art in this increasingly important area.

Numerous studies have documented the extent of inappropriate drug use in hospitals and its morbid and economic consequences (see Kunin, Tupasi, and Craig 1973; Steel et al. 1981; Fineberg and Pearlman 1982). From the perspective of health, the occurrence of preventable adverse drug reactions (ADRs) is the most important consequence of inappropriate prescribing. In one study of 714 medical inpatients in a teaching hospital 17 percent experienced adverse drug reactions, 70 percent of which developed during hospitalization (Seidl et al. 1966). A more recent study of 815 hospitalized patients (Steel et al. 1981) indicated a prevalence rate of 36 percent for iatrogenic illnesses, almost half of which were caused by drugs. Six to 9 percent of these drug complications were classified as "major" or "severe." In both studies, increased lengths of stay were associated with the occurrence of ADRs. Patients with drug reactions were more likely to be elderly and to be receiving a large number of concurrent medications (an average of 14 in Seidl et al. 1966). An estimated 0.1 percent of 26,462 inpatients in the Boston Collaborative Studies were estimated to have died as a result of adverse drug reactions (Porter and Jick 1977). Many of these adverse reactions are unavoidable consequences of the use of powerful therapeutic agents in desperately ill people. Yet a large proportion of inhospital adverse drug effects are the result of inappropriate drug therapy decisions. Melmon (1971) has suggested that as many as one-seventh of all hospital days are devoted to the care of drug toxicity and has estimated that about 70 percent of adverse effects are predictable and preventable through logical application of existing information. Some of the errors leading to preventable

ADRs include: use of a potentially toxic drug when one with less risk of toxicity would work as well; use of the wrong drug for a given indication; concurrent administration of an excessive number of drugs, increasing the possibility of interaction effects; excessive doses, especially for elderly patients; continued use of a drug after evidence becomes available concerning major toxic or even lethal side effects. Much less documented, but of considerable consequence, is the avoidable morbidity and mortality caused by failure of physicians to prescribe an effective drug for a treatable disease.

Inappropriate drug use also results in major economic costs which may largely be avoidable. The use of expensive drugs when a less costly preparation would be equally effective, prolonged use of medications beyond pharmacologic necessity, or the prescribing of unnecessary drugs all waste limited health care resources. Several studies in both community and teaching hospitals (Castle et al. 1977; Kunin, Tupasi, and Craig 1973; Roberts and Visconti 1972; Scheckler and Bennett 1970) have indicated that from 52 percent to 66 percent of patients on antimicrobial therapy received inappropriate doses or did not require such therapy at all. Since antibiotics account for approximately one-fifth of total drug costs (U.S. Department of Commerce 1978, 151–53), the potential for savings in this therapeutic category alone is substantial. A further consequence of excessive antibiotic use has been the increase in the reservoir of multiple drug-resistant bacteria in hospitals, forcing reliance on still more toxic or expensive antibiotic regimens (Levy 1982).

Because of the critical importance of the drug decision-making process, a number of papers have reviewed the factors which influence this decision (Stolley and Lasagna 1969; Miller 1973–1974). While marketing data on this subject also exist within the pharmaceutical industry, this information is generally not available publicly. Some controversy exists concerning the relative impact of the various sources of influence on prescribing behavior. Avorn, Chen, and Hartley (1982) have shown that even when primary care physicians claim that they are not heavily influenced by drug advertisements or salespeople, their beliefs concerning the efficacy of two drug groups studied (propoxyphene and cerebral "vasodilators") are congruent with messages received through commercial channels rather than those received through scientific channels. They, like previous authors, conclude that drug advertising plays a very large role in shaping physician-prescribing behavior.

Other factors also contribute importantly to excessive or inappropriate drug use by hospital-based physicians. These include: simple errors of omission; physician ignorance of cost issues in prescribing; failure to review medication orders frequently and critically; inability to keep abreast of fast-moving developments in pharmacology; insulation of physician and patient from cost considerations because of third-party coverage; and lack of communication between physician and pharmacist.

The objectives of this paper, then, are to describe the several approaches to improving inhospital drug utilization and to assess the evidence for their effectiveness in actually changing prescribing practices. Statements concerning the relative merits of regulation versus education often imply that "education" is a unidimensional intervention which is either effective or ineffective (Jones et al. 1977). In reality, a wide range of "educational" strategies exists, with correspondingly varying efficacies. The purpose of this review is to point the way toward more useful interventions and to identify those areas in need of further research, by considering which approaches to improving physicians' drug-use decisions have been more or less effective, and why.

Methods

Selection and Categorization of Studies

All published studies of noncommercial programs to improve the appropriateness of physician-prescribing for hospitalized patients were initially screened for review. The medical, pharmacy, public health, and social science literature from 1970 to 1983 was systematically searched with the aid of Medline, Toxline, and other computer-assisted retrieval services. Only those studies which attempted to document changes in prescribing behavior were included for review. Numerous studies were excluded because they described educational programs but presented no data, or simply reported physician attitudes or satisfaction with programs. Studies in which drugs were simply removed from formularies or their use constrained by regulations were also excluded; however, papers describing limited control programs (i.e., consultations required before using specific drugs) were reviewed. Only 31 studies met these criteria.

The intervention programs reviewed made use of a variety of strategies, and are grouped together here on this basis. The 6 categories into

which studies are grouped are: (1) dissemination of printed drug information alone; (2) drug-utilization audit followed by a single notice of aggregated results; (3) group education through lectures or rounds; (4) drug-utilization audit followed by interactive group discussions; (5) one-to-one education initiated by a drug-utilization expert; and (6) required consultation or justification prior to use of specific drugs. In general, the first two categories are less intensive, can be less costly, and do not rely on person-to-person interaction, as contrasted with the people-based educational interventions represented in the latter four categories. Category 6 relies on the use of power and authority as well for its effect.

Classification of Research Designs

The classifications of Campbell and Stanley (1963) are used to describe the evaluation or research designs employed in the various studies. In table 1, "0" refers to observation periods and "X" to intervention programs; these symbols are ordered from left to right by time of occurrence. The symbol "⊗" indicates the simultaneous occurrence of an observation and program treatment. Observations of control groups or additional experimental groups are listed on separate lines. The symbol "R" indicates that randomization procedures were used to assign physicians to experimental and control groups. The adequacy of the research design to control for nonprogram effects is rated in the seventh column with a (±) indicating the use of only partially satisfactory controls, and (+) identifying well-controlled studies. In general, simple one-group designs with single observations before and after a program (OXO) were considered inadequate to control for nonprogram influences on drug prescribing; these studies are, therefore, not presented in table 1. They are, however, briefly considered in the text for a better understanding of current variations in program design. Time series experiments (OOXOO) using at least two observations at different time periods before and after the intervention were considered to have partially satisfactory controls since preexisting trends in prescribing behavior could be quantified and compared with postprogram results. Studies utilizing randomly selected control groups or well-matched concurrent controls were considered well controlled. It should be noted that some hospital settings precluded the use of randomly selected control groups within the same institution; the

TABLE 1
Description of Adequately Controlled Studies

Study	Target drugs	Target group	Program description	Research design*	Use of adequate control**	Follow-up period	Reported results
I. *Dissemination of printed drug information alone*							
May, Stewart, and Cluff (1974)	Pentazocine	All medical staff, residents and senior medical students on a 65-bed general medical service of a teaching hospital	*Drug letter:* Faculty-prepared pharmacy and therapeutic committee drug letter (1 issue) cautioned against routine use of pentazocine	000X000	±	2⅔ yrs. following letter	No effect Same results for 5 other drug categories for which no data reported
[illegible]is et al. 982)	Propoxyphene, aspirin, acetaminophen, codeine	All physicians in an Australian teaching hospital	*Audit/drug bulletin:* Drug bulletin (1 issue) publicized inappropriate oral analgesic use; recommended nonprescription drugs instead of propoxyphene for mild pain, codeine for moderate pain	000X000	±	7 weeks	Decrease in propoxyphene use from ~60% of inpatients to ~30% in third week (post) *Effect not sustained* in fifth week (post) Similar short-term increase in aspirin, acetaminophen
[illegible]der, Caffey, d Lorei 979)	Anti-Parkinson and antipsychotic drugs, polypharmacy	Physicians treating approximately 300 schizophrenic patients in 42 Veterans Administration Hospitals	*Various educational materials* Group 1 were controls, Group 2 received articles, Group 3 received videotapes, Group 4 received articles and videotapes; all attempted to reduce excessive use of target drugs. Simple feedback of audit was background condition in all groups	RO_1 O_1 RO_2XO_2 RO_3XO_3 RO_4XO_4	+	?	No significant differences between groups, although group 2 had most desirable mean scores on 7 drug-use indices

II. *Drug-utilization audit followed by a single notice of aggregated results*

(None of the studies were adequately controlled.)

III. *Group education through lectures or rounds*

(1973)	Heparin (route of administration)	Internists, general and family practitioners, and pediatricians at a California community hospital	*Educational outreach:* Medical school faculty provided 2 lectures (1 week apart), including recommendations to administer heparin intravenously	000X000	±	1½ yrs.	Decrease in average (quarterly) subcutaneous units from 723 × 10^4 to 161 × 10^4 Increase in intravenous units from 221 × 10^4 to 792 × 10^4

close proximity of physicians in these settings increases the likelihood that doctors assigned to different groups would share information and thus invalidate the findings.

Results

Dissemination of Printed Drug Information Alone

All three studies in this category utilized reasonably satisfactory research designs and are listed in table 1. In general, these studies investigated the effects of written drug bulletins or other publications prepared by experts on the prescribing of a variety of drugs commonly used in hospital settings. Using several years of time-series data, May, Stewart, and Cluff (1974) assessed the impact of a pharmacy and therapeutics committee drug letter (prepared by faculty) cautioning against routine use of pentazocine (Talwin), a costly pain medication with limited efficacy and considerable abuse potential. The bulletin had no detectable effect on average patient drug exposures to this agent. Similarly, five other drug letters failed to influence the use of minor tranquilizers, anti-inflammatory drugs in the management of rheumatic disease, diuretics, gentamicin, and antibiotics in patients with impaired renal function. On the other hand, subsequent formulary changes resulted in marked changes not only in deleted or added drugs, but in substitute therapies as well. For example, utilization of acetaminophen (e.g., Tylenol) increased dramatically when propoxyphene (Darvon) was removed from the formulary.

A slightly different result was reported by Berbatis et al. (1982) in a time-series analysis of the impact of a drug bulletin suggesting that physicians substitute aspirin or acetaminophen (e.g., Tylenol) for propoxyphene (Darvon) in treating mild pain because of propoxyphene's high cost, limited efficacy, and potential toxicity. Propoxyphene use declined dramatically by almost half ($p \leq .05$) in the two weeks following the mailing, but began to return to pretreatment levels in the third and fourth weeks. Similarly, short-term aspirin and acetaminophen prescribing almost doubled, but this effect also quickly deteriorated. The different results of this study from the previous investigation may be explained by the shorter observation periods (and, thus, greater sensitivity to detect short-term fluctuations) or by the inclusion of hospital-drug audit data in the bulletin.

Finally, the results of a randomized controlled trial conducted in 42 Veterans Administration (VA) hospitals considered the appropriateness of medications used in the treatment of schizophrenia (Schroeder, Caffey, and Lorei 1979). The authors were unable to document any improvements in therapy attributed to providing either reprints or videotapes, or a combination of the two.

The above studies strongly suggest that printed drug informational materials, when used alone, are not effective in changing a wide variety of drug-utilization behaviors. At best, drug bulletins, articles, and videotapes may cause very short-term effects on drug use which need to be followed up by stronger intervention strategies.

Drug-utilization Audit Followed by a Single Notice of Aggregated Results

Key features of this approach include some form of retrospective review of prescribing performance followed by simple, one-time notifications to physicians that their practice either failed to meet predetermined criteria or was at variance with group norms of behavior. Audit reports may be based on individual or group performance, or both. The three studies reviewed below did not include any educational or regulatory strategies other than feedback of a single audit result. Unfortunately, none of the investigations provided control-group data for nonfeedback physicians and are, therefore, not described in table 1.

Aggregated feedback of a survey reporting the percentage of "rational" versus "irrational" antibiotic prescribing was the central feature of an investigation in a teaching hospital (Achong et al. 1977). Decreases in inappropriate prescribing were reported on the surgical and gynecological wards, while an increase in "irrational" antibiotic use was observed on the medical ward. These conflicting results are uninterpretable because of the study's suboptimal research design. Similarly, the effects of a community hospital infections committee sending reports on antibiotic use to individual departments are also unclear, owing to the absence of both preprogram performance data and comparison groups (Latorraca and Martins 1979). A secondary analysis of the previously cited VA study on instructional materials (Schroeder, Caffey, and Lorei 1979) observed changes in antipsychotic drug use before and after each of the 42 hospitals received individual audit reports. Across all groups there were statistically significant improvements

in only 3 of the 7 drug use indices; however, 2 of these were so small as to be of uncertain validity and little practical consequence.

The above studies, taken together, are suggestive of the ineffectiveness of retrospective drug-use reviews followed by one-time feedback of the results; however, no well-controlled trial of this strategy has yet been reported in the inpatient setting.

Group Education through Lectures or Rounds

The major distinguishing feature of this intervention type is its reliance on interpersonal communication (in groups) as a means of upgrading prescribing practice. Lectures, rounds, and seminars on a wide variety of drug and other health care topics have been common elements of continuing education in hospitals for decades. The only adequately controlled study of group lectures, alone, on prescribing appropriateness (see table 1) was reported by Rubenstein (1973) as part of an experimental evaluation of the Stanford University Medical School "back-to-school" program. This innovative program involved continuing education by visiting faculty physicians that included weekly lectures over several years at a community hospital in California. The educators attempted to target practical patient-care topics that were perceived as important by practicing physicians. Two of the lectures recommended administration of heparin intravenously rather than subcutaneously. Time-series data clearly document a hospital-wide reduction in average subcutaneous units administered (for three months) from 723×10^4 (pre) to 161×10^4 (post); simultaneously, average intravenous administration rose markedly from 221×10^4 (pre) to 792×10^4 (post) ($p < .001$ for both effects). These effects may be attributed to the personal involvement of highly regarded faculty as well as the active educational outreach approach. It is unlikely that these changes could have been caused only by the emerging clinical literature on heparin use since the marked change in prescribing patterns occurred immediately following the intervention.

Drug-utilization Audit Followed by Interactive Group Discussions

This large group of studies examined the results of interactive discussions, lectures, and meetings which utilized medication-audit results as part of the educational process. Commonly, seminars were

led by inhouse experts and senior medical staff on drug-therapy problem areas identified in the audits; these were often supplemented by checklists or other printed educational materials. Unfortunately, none of these studies met the research-design criteria necessary for inclusion in table 1; therefore, their conclusions must be interpreted cautiously.

The powerful but potentially toxic antibiotic gentamicin was targeted in two studies (Johnson et al. 1982; Gilbert, Eubanks, and Jackson 1978). Excessive doses or unnecessary use of this drug can lead to serious damage to hearing or renal function, much of which can be prevented by careful dosing or use of another antibiotic. The first program (Johnson et al. 1982) was directed at medical interns in a teaching hospital and utilized weekly meetings to discuss the optimal way of choosing and administering this drug based on the results of a preintervention audit. In addition, established criteria were posted at nursing stations and published in a hospital bulletin. The percentage of pharmacologically "acceptable" courses of gentamicin increased from 52 percent to 78 percent following the two-month program. However, the lack of a control group and the use of a different group of interns in the preintervention period make it difficult to identify the program as the only contributor to these observed improvements. An earlier study, also focusing on gentamicin, targeted all medical staff in a community hospital (Gilbert, Eubanks, and Jackson 1978). In this case, physicians received audit results, the implications of which were discussed in staff seminars as well as mailed to all physicians. Checklists were also provided as a guide to optimal therapy. The authors reported significant increases two months after the program in the following areas: percentage of appropriate indications for therapy; use of pre-treatment cultures; determination of serum gentamicin concentrations; and prescribing of less toxic antibiotics.

Only one study (Ogilvie and Ruedy 1972) attempted to measure the effects of audit and group education on patient health outcomes as well as on clinical decision-making. The program focused on the safe use of digitalis at a Canadian teaching hospital, and was followed by a reduction in the incidence of death and toxicity due to the drug in the two years following the start of the program. Although the study was uncontrolled, the authors were able to rule out several possible confounding effects likely to account for the 22 percent decrease in death rates associated with this drug.

A participative approach to continuing education in pharmacology was evaluated in one Canadian study (Laxdal et al. 1978). The program

was based on a monitoring-education-feedback model (Williamson, Alexander, and Miller 1968) which utilized chart reviews to establish priority problem areas by consensus among 15 volunteer target physicians. In this unusual program, the physicians chose their own subject areas for audits. For each problem area a recommended standard of care was established (e.g., vitamin K should be administered to every newborn). After lectures and group discussions were conducted for the identified problems, periodic chart reviews provided physicians with continuing aggregated feedback of their progress. Drug-utilization data were also collected for a control group of physicians at another hospital where no program was conducted. The authors reported a 31 percent difference between study and control groups in the reduction of prescribing errors. However, this effect may not be generalizable owing to self-selection on the part of the very small sample of experimental physicians, as well as other important differences between the study and control hospitals. In addition, this participative problem-selection process may fail to identify important prescribing errors unknown to a particular group of practitioners.

An audit-based educational program at a Veterans Administration hospital (Jones et al. 1977) utilized group presentations at medical rounds, small group meetings, and memoranda to illustrate irrational antibiotic practices with audit data. The program had no overall impact on prescribing, and the authors concluded that more coercive antibiotic control measures might be required to reduce inappropriate prescribing. However, the small amount of prescribing per drug category probably reduced the statistical power of the study to detect any effects. While analogous approaches were taken in several other studies (Spector and Heller 1978; DiMascio 1974) the absence of any adequate evaluation makes it impossible to derive useful information from them.

In summary, although numerous studies of audits combined with group educational strategies have been conducted, their effects have been mixed and difficult to interpret due to research design limitations. Despite the numerous occasions over many years in which such approaches have been tried, not one well-controlled study has been published.

One-to-one Education Initiated by a Drug Utilization Expert

A variety of studies in the psychological literature have shown that personal contact is one of the most effective means of persuading a

subject to change behavior—a fact well utilized by pharmaceutical companies in attempting to influence physician prescribing (Silverman and Lee 1974). A number of studies attempted to substantiate the efficacy of clinical pharmacist-consultants, a group which has often had problems with authority and credibility in the view of many physicians. Over the past decade the traditional function of pharmacists has been expanded to include drug therapy consultations to individual patients, physicians, and other health care professionals. Accreditation requirements for hospital drug-use reviews and the 1974 federal regulations requiring monthly reviews of medications in skilled nursing facilities (Federal Register 1974) have helped to spur the development of new training programs in clinical pharmacy through the doctoral level. While physician resistance to expanded health care roles of pharmacists has been frequently cited, many studies (see below) suggest the potential acceptability of pharmacists as drug consultants in some settings. Among the many published articles describing these expanded services, the fourteen studies below have attempted to observe the impact of clinical pharmacy services on the drug-utilization decisions of physicians and nurses in hospitals. Although there was some variation among these programs, pharmacist services generally included developing and reviewing patient drug profiles, monitoring therapeutic responses and drug reactions, and communicating personally with physicians and nurses regarding drug dosages, selection, toxicity and adverse reactions.

Only two of the clinical pharmacy studies met minimally acceptable research-design criteria; these are included in table 1. In the first study (Brooks et al. 1977) the assignment of a clinical pharmacist to a general medical unit for six months was accompanied by a reduction in the average per patient number of prescribed drugs from 3.4 to 1.9 at the time of discharge. Three months after discontinuation of the program, the number immediately returned to preprogram levels. The pharmacist interventions consisted simply of talking with nurses during daily rounds and physicians on a once-a-week basis. The rapid decay in drug-utilization effects was explained by the rapid rotations of house staff in this teaching hospital. The second, partially controlled study in a U.S. teaching hospital (Herfindal, Bernstein, and Kishi 1983) observed the effects of a clinical pharmacist making rounds with an orthopedic team in an attempt to reduce excessive drug use. The small but significant reductions (table 1) over a nonequivalent control hospital were sustained only as long as the program continued

to operate; as in the previous study, these effects quickly deteriorated following withdrawal of the pharmacist.

Uncontrolled studies not listed in table 1 tend to support these findings, but should be interpreted cautiously. In one study (Sohn, Wolter, and McSweeney 1980), a retrospective audit revealed inefficient dosing and use of two cephalosporin antibiotics (cephapirin and cefazolin). Written educational guidelines were provided to physicians and then supplemented by personal visits and phone calls to those whose orders varied from the recommendations. The intervention was associated with reduced dosages and an overall cost-saving shift in prescribing (from cephapirin to cefazolin). However, the findings were based only on a one-month postobservation period, and no data were provided on the statistical significance of these results. Another uncontrolled analysis (Witte, Nelson, and Hutchinson 1980) of the effects of pharmacist consultations in combination with an antimicrobial drug-therapy protocol produced mixed results in the surgical and medical units of an acute-care teaching hospital.

An institution for the mentally retarded was the setting for another investigation (Ellenor and Frisk 1977) in which a clinical pharmacist monitored and made patient-specific recommendations on psychoactive drug therapy; the recommendations were approved by a "behavioral review committee" consisting of a physician, nurses, pharmacists, therapists, and other care providers. A two-year follow-up of 208 patients compared pre- and postintervention prescribing rates (January 1974 vs. January 1976). The use of all psychoactive drug groups decreased substantially based on these limited data. However, no significant relationship was found between assessments of patients' maladaptive behavior and medication usage.

The effects of clinical pharmacy services on the incidence of adverse drug reactions (ADRs) on the medical wards of a teaching hospital were also investigated by McKenney and Wasserman (1979). Adverse-reaction prevention guidelines for a wide variety of commonly used medications were utilized by pharmacists in evaluating drug regimens. Recommendations for correcting potential patient-specific problems were provided on an ongoing basis to house staff. The moderate, but statistically insignificant, reduction in the proportion of patients experiencing adverse drug reactions (from 21 percent to 14 percent) after implementation of the consulting service is difficult to interpret without knowing the true background variation of the measures.

Eight studies attempted to evaluate clinical pharmacy services by simply reviewing patient charts to determine the percentage compliance by physicians with recommendations (Bell et al. 1973; Hull and Eckel 1973; Briggs and Smith 1974; Greenlaw 1977; Schweigert, Oppenheimer, and Smith 1982; Lipman, Devenport, and Page 1982; Bouchard et al. 1972; Hulse et al. 1976). The overall acceptance rate of clinical pharmacists' suggestions ranged from 58 to 96 percent. However, interpretation of these results is impossible because of the absence of adequate study design. In general, no observations were made of physician behavior before or without the information services being studied. Moreover, the types of communications varied immensely; these ranged from simple reminders regarding recording policies to notifications of adverse reactions. It is probable that compliance rates differed depending on problem severity and many other factors. Two of the above studies (Bouchard et al. 1972; Hulse et al. 1976) used computerized systems for screening potential drug interactions as an aid to the pharmacist in evaluation and communications with physicians.

In summary, there is some evidence from at least two partially controlled studies of the efficacy of clinical pharmacist consultations in reducing inappropriate drug utilization. More data from controlled trials are needed, however, particularly in relation to the cost-effectiveness of such approaches.

Required Consultation or Justification Prior to Use of Specific Drugs

Although interventions involving outright restrictions on prescribing behavior were not reviewed, several studies examined the effects of "mild" controls, such as required consultations and justification for the use of specific agents. It was hypothesized that this approach would promote more careful consideration of the need for the controlled drug as well as provide an educational encounter with the consultant. Several of these programs were developed in response to external requirements to control improper use of antibiotics, a group accounting for about 18 percent of the total cost of all prescription drug products in the United States (U.S. Department of Commerce 1978, 151–53).

The best controlled of these studies (Kunin, Tupasi, and Craig 1973; McGowan and Finland 1974, 1976; Craig et al. 1978) demonstrated significant reductions in costs and quantities of restricted antibiotics

following required consultations with an infectious disease specialist (see table 1). Even though the recommendations of the specialists were not binding, the required consultation acted as a powerful disincentive and effectively reduced antibiotic expenditures by as much as 30 percent (Craig et al. 1978). Although control groups were impractical in these three hospitals, time-series analyses based on multiple observations provide ample evidence of the efficacy of the approach. In the case of the program at Boston City Hospital (McGowan and Finland 1974), a subsequent comparison with other control hospitals further corroborated the earlier conclusions (McGowan and Finland 1976).

In an uncontrolled study, Zeman, Pike, and Samet (1974) also reported a decrease in expenditures that followed a requirement that justification for prescribing a particular antibiotic be put in the medical record. When its use seemed inappropriate, members of a drug review committee communicated personally with the physician.

An important finding is that when the programs were withdrawn, prescribing of the restricted drugs immediately began to rise to preintervention levels (McGowan and Finland 1974, 1976; Craig et al. 1978). This problem has also been observed in other compliance-based quality-assurance programs targeting physician practices (Greene and Simmons 1976).

Conclusions

A number of specific conclusions can be drawn from the best-designed studies in each program category (see table 1). First, the provision of printed drug bulletins or articles, used alone, has been relatively ineffective in changing prescribing behavior. This conclusion is in agreement with other research on prescribing (Avorn and Soumerai 1983; Schaffner et al. 1983). It is also congruent with the literature on improving patient drug-utilization, such as recent studies by the Rand Corporation (Kanouse et al. 1981) indicating that although patient drug package inserts are widely read and improve drug knowledge, they do not seem to affect compliance behavior. It should be emphasized, however, that written drug information may cause only temporary improvements (Berbatis et al. 1982) or provide initial exposure (at low cost) to reinforce messages communicated in other more powerful interventions. For example, pharmaceutical company marketing strategies rely almost universally on face-to-face visits by

detail people to reinforce printed advertisements. On the other hand, it is quite likely that printed materials are necessary but not sufficient in improving prescribing, providing a cognitive foundation on which other forms of behavior change can be built.

Single notices providing aggregated results of drug-therapy audits have not been demonstrated to be effective in the inpatient setting, although no well-controlled trial of this strategy has been conducted. This conclusion would seem to be at variance with a number of feedback studies conducted in ambulatory settings (e.g., see Barnett et al. 1978; McDonald 1976) which have produced positive results. However, these latter studies utilized repeated feedback of explicit recommendations relevant to specific patients. Even in these programs, positive effects disappeared immediately following program discontinuation.

Both group education through lectures or rounds and group discussions of audits have produced mixed effects which are ambiguous, given the lack of adequately controlled studies. The one exception in these categories is the demonstrated effectiveness of an educational outreach program conducted by medical school faculty in a community hospital (Rubenstein 1973). The inconclusive nature of these studies is unfortunate given the widespread use of this form of intervention and its demonstrated efficacy in at least one other study of test-ordering behavior (Martin et al. 1980).

One-to-one education initiated by a clinical pharmacist has been shown in two partially controlled studies (Brooks et al. 1977; Herfindal, Bernstein, and Kishi 1983) to reduce the overall number or cost of drugs prescribed to inpatients. These results agree with the findings of a large-scale, controlled trial utilizing doctoral-level clinical pharmacists as educational outreach consultants to improve prescribing in the ambulatory setting (Avorn and Soumerai 1983). Furthermore, the superiority of face-to-face education has been documented in a wide variety of settings and problem areas, including patient compliance with hypertensive drug-use recommendations (Sackett and Haynes 1976), smoking cessation (Leventhal and Cleary 1980), and years of marketing experience among pharmaceutical companies.

Required consultations or justification prior to use of specific drugs clearly and markedly reduces prescribing of specific antibiotics in hospitals; however, the positive effects on prescribing decay rapidly once the controls are discontinued. Thus, this strategy is probably

only generalizable to a few high-risk drugs and to large hospitals with the expertise to provide ongoing consultations.

In contrast to prevalent opinion (Eisenberg and Williams 1981) the overall conclusion from this review is that education *can* upgrade physicians' clinical decision-making in the hospital without recourse to restraining their therapeutic prerogatives. This is particularly important because most prescribing, like other kinds of medical resource allocation decisions, requires that effective therapies be readily available but used selectively—a need that simple regulation or formulary restriction violates. Yet not all educational strategies are effective, nor will their impact be sustained without continuing reinforcement of desired practices. For example, dissemination of one-time printed educational materials and single reports of drug therapy audits are less effective than approaches that also include ongoing and person-to-person interaction in the educational programs.

Face-to-face educational interventions may hold the greatest promise of success for a number of reasons. First, the educational messages can be targeted directly to the particular clinical circumstances of individual physicians and their stated reasons for prescribing. Second, the trust that develops through direct communication on an ongoing basis may lead to more open discussion of factors affecting drug use patterns. Third, the ongoing use of voluntary consultations in hospitals is a tradition generally well accepted by the medical profession—at least when physicians do the consulting. With increasing awareness of the capacities of other health professionals, such as pharmacists, these groups may increasingly become valued (and cost-effective) consultants in their own areas of expertise.

The findings described above also corroborate basic theoretical models for bringing about planned change in human systems (see Chin and Benne 1976). For example, we would expect that simple, "rational-informational strategies" (scientific information alone) may update knowledge, but still fail to change behavior consistently because they lack relevance to existing practices. Thus, for example, the provision of more data in a pharmacy bulletin on the relative efficacy of aspirin versus more expensive (but not necessarily more effective) nonsteroidal anti-inflammatory drugs may be useless to the physician whose main reason for utilizing the prescription product is patient demand. Similarly, a physician who, because of oversight, neglects to prescribe an antibiotic following laboratory confirmation of a streptococcal throat infection

would not benefit from one-time, clinically-based feedback on this subject. From a more practical point of view, printed educational materials probably remain unread by a substantial proportion of busy physicians, who are inundated daily with a flood of promotional literature on drug therapy.

A more promising "normative re-educative" approach, as described by Chin and Benne, is one that also takes into account nonintellectual factors affecting particular behaviors. In the case of prescribing practices, these might include attitudes and beliefs about drugs, diseases, or patients; views of respected opinion leaders; patient demands; fear of malpractice; financial incentives, etc. In this formulation, the greater efficacy of face-to-face education may result in part from its capacity to identify individual motivations for existing practice and provide on-the-spot acceptable alternatives that satisfy these perceived needs.

One of the greatest problems in applying the normative re-educative approach is the difficulty and effort involved in accurately identifying the motivations for particular prescribing behaviors. Pharmaceutical companies expend substantial resources attempting to learn about the nonpharmacological bases of prescribing decisions through focus-group interviews and market surveys, as well as direct communications between company representatives and physicians during "detail" visits. These factors are very influential in guiding the form and content of the industry's marketing programs (Smith 1975). As an example of this approach in a noncommercial setting, Klein, Charache, and Johannes (1981) conducted surveys to determine house officers' beliefs regarding the use of expensive antibiotics and then effectively targeted common misconceptions in person-to-person tutorials conducted by respected peer leaders.

The characteristics of particular drugs themselves will affect the success of both rational and normative re-educative approaches. For example, efficacy and safety are more important determinants of drug product choices than cost (Lilja 1976). Logically, then, physicians may respond quickly to new evidence of important lethal effects of drugs they have been prescribing. On the other hand, if cost-effectiveness is at issue, a more powerful and intensive effort to change attitudes may be required.

A third approach defined by Chin and Benne is characterized primarily by the application of power through sanctions or regulations. These strategies rely on the compliance of those with less power to the

directives of the more powerful (whether based on organizational structure, legal authority, or political strength). Extreme examples of this approach in the hospital prescribing arena include removing a drug product from the formulary, restricting prescribing decisions for selected drugs to specialists, and imposition of automatic stop-order policies. Though clearly effective, these measures are politically cumbersome, especially where questions of poor efficacy rather than toxicity are at issue. In particular, making drugs unavailable for use does not address the more common problem of inappropriate use of otherwise legitimate drugs, such as antibiotics. Such "fiat" means of altering prescribing were, however, not considered in this paper, because they do not depend on (or necessarily result in) improving the physician's decision-making process. On the other hand, we reviewed limited-control programs which require consultations with specialists or justifications for use of particular drugs. In these cases, although power and authority are main ingredients of the interventions, the final decision to prescribe rests with the physician requesting the drug. In general, these strategies did succeed in changing prescribing behaviors during program operations. However, it is not known to what extent physicians may have simply switched to other undesirable drugs as a means of complying with requirements (e.g., see Shenfield, Jones, and Paterson 1980; Greene and Simmons 1976).

Very few, if any, of the effective educational interventions in this review produced long-term effects on prescribing behavior once the experimental programs were discontinued. This finding should not be surprising or disappointing; physicians are subject to the same human frailties of habit and forgetfulness as other professions. In addition, one methodological point bears special mention: the rapid rotation of house officers in and out of teaching hospitals would result in automatic "decay" of effects seen within that hospital, although possible lasting effects may remain with individual trainees for longer periods of time. The implication for practice is that continuing reinforcement of desired practices, at least on a periodic basis, is necessary for a sustained impact. The resulting cost-savings effects of more efficient and safe drug use, in many cases, may well be worth the low marginal costs of continuing an existing program once developmental costs have been realized. This is not new information to drug companies or their pharmaceutical representatives who recognize that follow-up visits with physicians are absolutely essential to ensure that their products continue to be prescribed on an ongoing basis.

Implications for Future Research

It is ironic that many of the studies, founded on the assumption that controlled clinical research should be the basis for rational drug prescribing, did not themselves include well-controlled designs in trials of "therapies" for improving prescribing practices. Of the 31 designs employed in these studies, 22 (or 71 percent) utilized inadequately controlled designs (post-test-only evaluation or pre-test-post-test without controls). This proportion is similar to that found in reviews of other clinical decision-making interventions. Using somewhat stricter criteria, Haynes et al. (1984) found that only 13 percent of 248 studies of continuing medical education utilized randomized, controlled trials to evaluate program effects. Despite the acknowledged difficulty in implementing control-group designs in hospital settings, this method of investigation remains the most useful—and least common—in such research. When out-of-institution controls cannot be found, careful collection and analysis of multiple observations at several time periods before and after initiation of the program can increase the validity of conclusions about program effects. In addition, observation periods must be sufficiently long to control for transient fluctuations such as seasonal changes in disease incidence and resultant prescribing behavior, as well as the ebb and flow of new house officers through teaching hospitals.

Several promising strategies for improving inpatient drug utilization have not been adequately studied. For example, we were not able to locate one well-controlled inhospital trial of ongoing feedback of prescribing performance to physicians based on well-accepted criteria or comparisons with peers. This repetitious feedback has been shown to be somewhat effective in ambulatory settings (such as health maintenance organizations [HMOs]), particularly when physicians are already in agreement with the clinical rationale, but simply make errors of omission which can be flagged by computer-guided review (McDonald 1976; Barnett et al. 1978). Better-controlled trials are also needed to evaluate the effects of group discussions of drug therapy audits.

Other dimensions of the problem have barely been touched in the existing literature. Good data on the economic costs and benefits of drug therapy education are lacking even in the well-controlled studies reviewed here; few studies even attempted to measure the direct resources expended in order to achieve drug savings. Clinical outcomes are likewise rarely studied. Lastly, analyses of the economic and quality-

of-care effects of unexpected drug substitutions need to be considered in such studies.

Financial incentives and disincentives, possibly in combination with education, are also promising strategies which merit further research (Eisenberg and Williams 1981). In the ambulatory setting, retrospective denial of Medicaid payments for inappropriate injections have been shown to reduce their use (Buck and White 1974; Brook and Williams 1976).

The comparative cost-effectiveness of physicians and pharmacists in the role of face-to-face pharmaceutical educators is also of great interest, since the costs of pharmacist time are considerably lower. Although the effectiveness of physician opinion leaders and tutorials have been shown in the ambulatory setting (Stross and Bole 1980; Klein, Charache, and Johannes 1981; Schaffner et al. 1983), this work has not been replicated in inpatient settings.

In an ongoing study at the Beth Israel Hospital in Boston, we are currently utilizing both physicians and pharmacists as drug educators in a program that attempts to bring together the insights from previous work discussed above. The choice of personnel in particular situations is perhaps best based on the nature of the problem as perceived by the prescriber and its "fit" with the area of expertise (and credibility) of the educator. When there is poor information on highly complex clinical subjects (e.g., the comparative toxicity of antibiotics), physician specialists are probably more effective as educators; however, for other topics further removed from clinical acumen (e.g., proper drug dosing intervals), pharmacists may be more cost-effective educators. The costs of ongoing person-to-person education are probably less than imagined—in one study (Klein, Charache, and Johannes 1981), impressive results were made in the prescribing of house officers after one 15-minute tutorial session. Our earlier work on changing ambulatory prescribing tends to confirm this impression (Avorn and Soumerai 1983).

The nature of the specific prescribing problem is of critical importance and should ideally guide the development of future approaches. For example, is the particular problem based on a gap in knowledge, errors of omission, patient demands, or a combination of these factors? Simple mailed reminders, sent on an ongoing basis, might be the optimal approach in reducing errors based on agreed-upon (but neglected) standards of practice. However, person-to-person contact with credible experts may be necessary to improve long-standing prescribing behaviors which are influenced by attitudes or beliefs about the drug or patient problem. These, too, are testable questions.

The generalizability of study findings to other settings is another important consideration in evaluating the interventions. Many of the most successful interventions were conducted in academic medical centers; yet results obtained with interns and residents may not be generalizable to physicians who are more removed from their training and whose behaviors are more established. More studies are needed in nonacademic, community hospital settings.

As hospitals continue to face increasing pressure to contain costs, it will become even more important to learn how therapeutic decision-making in all sectors of care can be optimized. As this field of inquiry matures, it may generate approaches which will improve the quality of patient care and, at the same time, reduce unnecessary costs. In drug therapy and perhaps in other areas as well, it might be possible to achieve these two often conflicting goals—if proper attention is paid to clinical, economic, and behavioral/organizational considerations in program design.

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