

Establishing value in managed care: Cost-effectiveness or budgetary impact?

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In the managed care setting, pharmacy benefit managers face considerable challenges when making decisions regarding drug coverage. Although scientifically valid data may be available from randomized, double-blind, placebo-controlled trials, this type of information does not shed light on potential differences between medications in the same class. Furthermore, properly designed, comparative trials are rarely conducted. Randomized naturalistic or pragmatic pharmacoeconomic studies can provide valuable information but are likewise infrequently performed. Economic modeling is an alternative but is not widely accepted because of the potential for bias. Retrospective analyses of information from patient surveys or existing databases are emerging as more popular methods of supporting informed formulary decisions. In the absence of a large-scale, prospective, naturalistic, pharmacoeconomic study, an alternative indication of product superiority can be derived from a continuum of different types of studies (from basic science to clinical trials to retrospective pharmacoeconomic analysis) conducted in a variety of patient care settings. The consistency with which a product demonstrates superiority across all types of studies is critical and is a crucial determinant of whether a health care provider would be likely to use the information for the purpose of decision making. (*J Allergy Clin Immunol* 2002;109:S511-4.)

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In most managed care organizations, the management of pharmacy benefits is performed by departments that are separate and independent from those responsible for managing the cost of medical services.¹ Pharmacy benefit management departments typically have their own cost management (containment) goals, independent of strategies used to manage use and costs of medical services. Consequently, managed care organizations are accused of creating so-called budget silos, which inhibit the management of the pharmacy budget within the context of all use of medical services—use that can be modified by the potential advantages of new pharmaceutical therapies.^{2,3} Few managed care organizations will dispute this.

Employers contract with pharmacy benefit managers, and managed care organizations dedicate separate staff to this function and/or contract with a pharmacy benefit manager to help contain increases in pharmacy spending, as well as to assist in making clinical decisions regarding coverage of safe and effective prescription drugs. In their

decision processes, pharmacy benefit managers and managed care organizations consider the clinical benefits of new prescription drugs but must also weigh the budgetary impact of paying for new, expensive therapies and the impact on the employers' and members' health care premiums. Few pharmacy benefit managers or managed care organizations have the data or staff expertise to perform pharmacoeconomic analyses that would evaluate the marginal clinical gain of a new product in relation to the marginal increase in costs.⁴

However, managed care organizations do seek scientifically valid information on which to base drug coverage decisions, balancing evidence of potential increases in therapeutic benefit from new therapies against the budgetary impact resulting from their use. The main sources of clinical information on new drugs at the time of their release to the market are randomized, double-blind, placebo-controlled trials that have been sanctioned by the US Food and Drug Administration—the so-called gold standard of evidence-based medicine. When available, randomized trials that compare treatments can be more useful if comparisons are made between the new agent and the most relevant or most frequently used products within the therapeutic class. Studies published in peer-reviewed medical or scientific journals are of greatest use to pharmacy benefit managers who are attempting to establish the value of various pharmaceutical products. The results of published, randomized, controlled trials can generally be expected to be valid and reliable and provide the highest level of evidence for use in decision making.

When sufficiently powered to demonstrate meaningful differences, randomized comparative trials are of greatest use to managed care organizations. Such investigations allow for direct comparisons between alternative therapies and have the most direct application to coverage decisions. However, these types of trials are rarely conducted and are often designed only to demonstrate an advantage of one drug over an older, pharmacologically less-specific compound. Without the availability of good comparative trials, managed care organizations must rely on the results of placebo-controlled studies and the clinical judgment of specialists as to whether one product in a class may have advantages with regard to effectiveness or side effects. This approach can determine statistical superiority of a compound compared with placebo and generates clinical perceptions as to a drug's potential place in therapy but provides little real evidence regarding the comparative properties of treatments.

Some managed care organizations have adopted a systematic approach to test relationships regarding treatment outcome advantages of a new product and the additional

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costs associated with use of that therapy.^{5,6} Although these models most often do not contain information from randomized comparison studies, they provide a more systematic approach to addressing issues of therapeutic and economic comparability of products. Among the measures of morbidity, mortality, patient-reported outcomes, and health care use included in such models, the drug acquisition price is frequently the factor that has the greatest influence on cost-effectiveness or cost per outcome. This may lead some to dismiss the need for economic models, overemphasizing acquisition cost.

PREDICTING THE POTENTIAL VALUE OF NEW PHARMACEUTICALS IN THE CLINICAL CARE SETTING

Compared with the highly controlled clinical trial setting, the implementation of treatments in the clinical care environment is prone to multiple inefficiencies because of potential misdiagnosis; selection of a less-than-optimal treatment; application of treatments to a broader sector of patients with disease than those in clinical trials; drug interactions; poor patient adherence to medication regimens; and many other genetic, environmental, and behavioral factors. New medications may never be as efficient in producing therapeutic effects in actual clinical use as they are during clinical trials. By using clinical trial data to obtain an estimate of a medication's effect size and degree of patient response variability, pharmacy benefit managers could be better equipped to identify the treatments most likely to overcome some of the inefficiencies inherent in the clinical treatment process. Pharmacy benefit managers could then estimate the potential gain to health and the estimated "value" of a treatment based on the relative acquisition costs.

Thousands of medications are currently available for physicians to prescribe to health plan members. In addition, the Food and Drug Administration's rate of approving new drugs has accelerated in the past few years. Without the availability of economic modeling or effectiveness comparison studies, managed care organizations resort to a cost-minimization analysis in which—without specific, reliable, comparative information—they assume that all products within a therapeutic class are roughly equivalent with regard to therapeutic effect (allowing for major differences in side effects or differentiation by certain pharmacologic subclasses). They then implement a series of contracting strategies designed to obtain the lowest price for an adequate number of products within a therapeutic class to satisfy the treatment choice demands of physicians, health plan members, and disease advocacy groups, while minimizing the total budgetary impact. Such management strategies have become increasingly strained under the weight of more expensive products and an increased demand for prescription drugs on the part of health plan members. Managed care could benefit from greater use of pharmacoeconomic evaluation methods to help differentiate the value (marginal cost per amount of health gain) of newer, more expensive therapies.^{4,7}

BARRIERS TO USE OF PHARMACOECONOMIC INFORMATION IN MANAGED CARE DECISIONS

With respect to pharmacoeconomics, the equivalent study design to the randomized, comparative clinical trial is the randomized naturalistic or pragmatic trial.⁸ In these types of investigations, patients are randomly assigned to each of two or more treatments being compared and are then instructed to seek care as they would if they were not in a study. The clinical effect of the study drugs, quality of life, health care service use, and costs are measured in the least intrusive manner possible, while still allowing the collection of data to permit valid comparisons between treatments. When conducted appropriately, these types of studies provide data that are the "gold standard" of pharmacoeconomic information. Unfortunately, as with randomized clinical comparison studies, randomized comparison naturalistic trials are rarely conducted. These investigations are expensive to perform, are difficult to control, and require extended follow-up time if the findings are to be relevant. Consequently, even when such studies are performed, the results are not available at the time of product launch. Therefore, managed care pharmacy benefit managers do not have the advantage of access to this type of comparative information when they must make their initial decisions about drug coverage.

Economic modeling is another common method of pharmacoeconomic analysis that is accepted in many European countries, as well as in the United Kingdom, Canada, and Australia. Information on efficacy and safety from clinical trials is combined with information on patient status, health care use, and costs. Such information is obtained through expert opinion, the literature, or existing administrative databases and is mathematically modeled to quantify potential therapeutic benefits and costs, arriving at various cost-effectiveness ratios produced for new drugs in comparison with their competitors. However, pharmacoeconomic models are subject to many assumptions in their development, raising questions regarding credibility or bias, whether they are developed by a product manufacturer or a major payor or purchaser of health care services.^{3,9} Also, these models are most useful when they are developed from the perspective of meeting a societal need rather than an insurer's objective. Consequently, economic models have yet to gain wide acceptance by managed care organizations in the United States.

Retrospective studies in which either patient surveys or analyses of existing databases are used have become a more popular method of supporting informed managed care formulary and drug utilization management decisions. The administrative claims data maintained by health plans through the process of paying providers for services to members are further used to manage many aspects of the health plan's business. Although these data may contain some inaccurate information, when used with appropriate caution, they can be very helpful for analyses of health care service use rates and associated

costs as related to physician and patient use of different treatments. These databases reflect actual physician and patient behaviors as these individuals access and use health care services.

Even though the naturalistic aspects of these databases are their strength, the analysis of treatment effects is confounded by the biases of physicians and patients as reflected in their treatment choices, necessitating the use of powerful statistical methods to adjust for factors that modify treatment effects. These statistical techniques differ from those used to analyze the results of randomized, controlled trials and are relatively new to clinicians, regulators, and pharmacy benefit managers. As a result, many such individuals are reluctant to accept retrospective, comparative analyses of differences in health care service use rates and associated costs as they relate to different drug therapies.

ALTERNATIVES TO SATISFYING THE NEED FOR RELIABLE, VALID DATA ON THE COMPARATIVE VALUE OF DRUGS

As mentioned previously, managed care organizations need reliable, valid evidence of comparative differences in the efficiency of various treatments as applied in the clinical practice setting. In the absence of a large-scale, prospective, naturalistic, pharmacoeconomic study, consistent (reliable) evidence of product superiority can be obtained by creating a continuum of studies of different types—from basic science to clinical trials to retrospective pharmacoeconomic analysis—in a variety of patient care settings. The consistency with which a product demonstrates superiority across all types of studies is critical to this approach and is the key to whether a health care provider would be likely to use the information in decision making. An evidence-based continuum of logic must be visible through the various studies and their results, as follows:

1. The product demonstrates potentially greater pharmacologic or physiologic impact based on comparative information about mechanism of action, without displaying greater toxicity.
2. The product demonstrates superiority to placebo and demonstrates a meaningfully larger effect size compared with other drugs in the therapeutic class.
3. The product demonstrates superiority of clinical effectiveness and in patient self-reported measures in clinical comparison studies versus competitor products of interest.
4. The product can be easily prescribed and used by

physicians and patients and demonstrates greater treatment efficiency and therefore superiority in reducing the types of health care use and costs that are associated with poor treatment response and continued disease symptoms (hospitalizations, emergency department visits, and associated costs).

5. The product is associated with a greater reduction in medical service-associated costs than its associated increase in pharmacy costs.

Ideally, steps 3 through 5 would be demonstrated within randomized, comparison, naturalistic pharmacoeconomic studies of the major therapies used. Because the availability of such studies is unlikely, an appropriate alternative is a stepwise approach with the use of separate prospective clinical trials and retrospective naturalistic studies from administrative claims data in multiple settings.

With multiple studies, chance findings of differences between products are likely. Therefore, the results of linked studies must present clear, consistent, convincing evidence of the superiority of one treatment across all studies and all settings. Only then would a pharmacy benefits manager be comfortable using such a continuum of results to make coverage decisions that favor one product over another. It would be very useful to health care decision makers of all types if more pharmaceutical companies and researchers would engage in research programs designed to produce a continuum of comparative information from basic science to pharmacoeconomics on new and existing products.

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