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"For Professional Recognition of the Health Actuary"

The Formulary Decision Process: What Are They Doing in There and Can Actuaries Help?

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Many prescription drugs are cost-effective treatment options.[i] With so many prescription drugs available, which ones should be covered and encouraged by health plans and which should not? It is the Food and Drug Administration's (FDA) job to ensure that only safe and effective pharmaceuticals are available in the United States. Given that this agency does its job well, why give the issue any further thought?

In the past, this line of thinking may have been acceptable. Health plans could allow their members access to whatever drugs were prescribed by their physicians. The difficulty has come with the explosion in cost in this area of health care. While total health care expenditure trends have ranged from 9 percent to 16 percent over the past five years, pharmaceutical benefit trends have increased at rates of 17 percent to 18 percent.[ii] These pharmaceutical cost trends have been attributed to increases in drug utilization (39 percent), increases in drug prices (37 percent), and shifts to higher priced drugs (24 percent).[iii]

The more recent innovations in biotechnology have helped to fuel this trend and seem poised to continue to do so. The term "biotechnology drug" refers to a pharmaceutical treatment with three characteristics. First, the drug is derived from particularly sophisticated technology. Second, these drugs require more complicated administration. They are injectable drugs, some requiring physician administration. Third, because of the expensive development costs and the additional administration costs, these drugs are very expensive, typically more than $1000 per month per patient. For example, Xolair is a biotechnology drug for the treatment of asthma that costs about $1000 per month. Another

example is Fabrazyme for Fabry's Disease. While this condition is rare, the cost of the drug is about $250,000 per patient per year.

There are over 100 biotechnology drugs currently available, and the drug pipeline promises many more after 2006. These drugs currently account for roughly 10 percent of the pharmacy budget.

Pharmacy Benefit Management and the Use of Data

To manage this expense, health plans in recent years have had to consider carefully which

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pharmaceuticals to cover. Formularies have been implemented, relying upon differences in cost sharing to steer members and their physicians toward less costly or more cost effective choices. A critical role in this process is deciding which pharmaceuticals are to be covered and at what level of cost sharing. Pharmacy and Therapeutics (P&T) Committees typically make these formulary decisions, and to do this effectively, they need good information. To make the best drug coverage decisions, a P&T Committee should study efficacy, safety, effectiveness, and pharmacoeconomic data.

Since the FDA requires extensive efficacy and safety data in order for a drug to gain its approval for sale in the United States, pharmaceutical companies have this type of information readily available.

Efficacy research is designed to prove a drug's scientific value in an ideal setting. However, this setting will not be seen outside of a specifically designed and controlled experimental environment. Use of a drug in a typical health care environment, where compliance may be less than perfect and patients may have concurrent medical conditions, is more apropos. A drug's usefulness for treatment in the latter environment is called effectiveness. Effectiveness gives a better idea as to how pharmaceutical use will impact patients in the real world. However, effectiveness studies are less common because they are not necessary to gain FDA approval for a drug and they are expensive to conduct.

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More rare are studies of the pharmacoeconomic properties of pharmaceutical use. Such studies attempt to show the costs associated with using a drug. Costs are typically assessed in one of several ways, which will be discussed later in more detail.

Standard Pharmacoeconomic Analysis Methods

As a field, pharmacoeconomics is fairly young and has a very academic feel. Much of the research done on the cost impacts of pharmaceuticals uses techniques adapted from the field of economics, including cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis. These methods are described below.

Cost-minimization analysis (CMA) is the simplest of the methods listed. Cost-minimization analysis identifies the least expensive option among several with equivalent effectiveness.[iv] For example, a cost-minimization analysis would conclude that the less expensive of two equally effective ace inhibitors is the preferred choice. CMAs are rarely done because few clinical trials result in the conclusion that a drug is equal to its comparator. Most aim to show its superiority.[v] This method neglects other important variables such as the cost or unpleasantness of possible side effects.

Cost-effectiveness analysis (CEA) is done to determine the cost per unit of effectiveness, resulting in a cost-effectiveness ratio. This ratio can be stated as the cost per unit of outcome, or units of outcome per dollar spent. Outcomes are measured in terms of clinical events such as heart attacks, hospital days avoided or life-years saved. A lower cost-effectiveness ratio (cost per unit of outcome) is associated with a preferred treatment choice. The preferred choice is not necessarily the least expensive one, however, since the health gain of the options can vary as well. CEA can be a robust analysis, taking all associated costs and savings into account. However, there is considerable variation across CEA studies with respect to types of patients examined, measures of effectiveness and costs used, and the way in which cost-effectiveness ratios are calculated and reported, which can make their interpretation and comparison difficult.[vii]

The most meaningful CEA analysis is the calculation of the incremental cost effectiveness ratio (ICER) between two alternative treatments. This requires data from head-to-head trials or at least from different trials that were fairly similar in study population and methodology. Since most clinical trials are sponsored by the manufacturer of one of the drug products within the study, they rarely provide all the direct comparison data needed to answer the questions a health plan is asking. A rare exception is the recently published PROVE IT study, which compared two cholesterol-lowering drugs, Pravachol and Lipitor. Although the maker of Pravachol funded the study, it showed that Lipitor was better.[viii] This outcome probably makes it is less likely that other drug companies will want to fund head-to-head trials in the future.

Cost-utility analysis (CUA) is done to assess the cost per outcome unit that is adjusted for patient value placed on those outcomes.[ix] Rather than simply assessing life-years saved, for example, the CUA would assess the cost per Quality-Adjusted Life-Years (QALYs) saved. For example, a patient whose work requires a lot of standing and walking might assign more utility to an orthotic device (a gait-correcting shoe insert) than a patient who does little standing or walking. Critics of CUA maintain

that it is difficult to use and compare because there are numerous different ways to assign health status, no agreement upon what constitutes the gold standard, and whose preferences are measured—patients, providers or public—affects the results.[x]

Cost-benefit analysis (CBA) measures the cost per outcome where outcomes are translated into dollars. In the example above, the patient whose work requires a lot of standing and walking might be willing to pay more for an orthotic device than the patient who does little standing or walking. The cost to buy the device can be assessed against its value stated in dollars. This method has the drawback of having to obtain assessments of the monetary worth of health outcomes. In evaluating pharmaceuticals, CBA is often used to compare the cost of a more expensive drug with the expected savings from reduced need for other medical costs such as physician visits, hospitalization or emergency room care, thereby sidestepping this drawback.

Whereas studies using the methods above may be available to P&T Committee members, their results are not well suited to the needs of a health plan. Such results may help to determine which of the drugs compared in one study seems to be the better choice from a cost perspective, but they do little to help health plan decision-makers quantify how and where drugs will have an impact on the overall budget.

Pharmacoeconomic analyses often rely upon information from multiple sources, with potentially complicated study designs, making them difficult to perform and analyze. A study of submissions reviewed by the Australian Pharmaceutical Advisory Committee found that 67 percent of 326 pharmacoeconomic analyses had serious flaws.[xii] The resources available to make that assessment were considerable, possibly beyond the capacity of many individual health plans. While this may contribute to a health plan's reluctance to use such information, to avoid doing so misses a real opportunity to add value to the formulary decision process.

The Development of the AMCP Format for Formulary Submissions

In an effort to counter some of the problems with available research on pharmaceutical costs, the Academy of Managed Care Pharmacy (AMCP) developed and disseminated the first Format for Formulary Submissions in 2000. Version 2 of the Format, released in 2002, incorporates user feedback.[xiii,xiv] The Format is a guideline that specifies what information health plans want to see from drug manufacturers in order to help them make informed, evidence-based, drug coverage decisions. This information includes data on efficacy, safety, effectiveness and economic impact of a new drug. The Format puts responsibility on pharmaceutical manufacturers to provide all information available in a standardized format.

Since the release of the latest guidelines, AMCP reports that adoption is spreading at a rapid pace. To date, no large studies exist on the impact of the Format on patient outcomes.

Proponents of formulary guidelines maintain that the Format makes great strides in leveling the playing field between manufacturers and health plans. The Format creates a standard for constructing, presenting and critiquing models. Early experience suggested that manufacturers were unwilling to comply with dossier requests. However, recent information has suggested that most are now submitting dossiers, but they are frequently incomplete.

The P&T Committee

To better understand the process used by P&T Committees in formulary development, one of the authors did some informal observations of P&T Committees and their decision processes. Another of the authors is a formulary manager and leading member of a P&T Committee. This section will discuss P&T Committee features, relying to a large extent upon these observations.

A lot of research is gathered in preperation for a P&T Committee meeting where drug coverage decisions are made. As discussed above, information is gleaned from pharmaceutical manufacturer dossiers, published research, FDA analyses published on their Web site, and possibly modeling and analysis done by the health plan itself. The pharmacy staff normally conducts a search for relevant primary literature using MEDLINE and possibly other databases. Secondary sources such as Cochrane reviews may also be consulted. Summaries of the information from these sources, and sometimes research articles themselves, are distributed to P&T Committee members prior to a meeting.

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The P&T Committees we have seen are comprised of primarily physicians and pharmacists. Other members included a psychologist, an osteopath, registered nurses and employer representatives. Two of the committees explicitly noted that only members not employed directly by the health plan were allowed to vote on formulary decisions. The PBM committee profiled allowed one vote per client, a representative of which sat on the P&T Committee. These committees ranged in size from 11 to 25 people.

In each meeting, a pharmacist or team of pharmacists gave a presentation of information about the new drugs under consideration. These presentations were brief, the details having been supplied to the members prior to the meeting, included formulary recommendations, and were followed by discussion from the group in general. The discussions were very interactive, with many questions and dissenting points of view. In every meeting observed, at least one recommendation made by the presenting pharmacist(s) was not accepted.

If needed, experts outside of the standard P&T Committee were asked to give relevant opinions and observations. The pharmacists who prepare formulary reviews usually consulted with one or more such experts prior to writing their recommendations.

Most of the discussion during the meeting revolved around drug safety and effectiveness. Information for this included both research findings and observations from clinical practice. Costs were not discussed much, although the price of the drugs and patient copays were mentioned several times. Cost offsets and total budget impacts were never discussed during meetings. One group explicitly avoided the subject of costs, focusing instead on selecting the most effective and safe drugs from a class of drugs and narrowing that list down to the best few. Once that list was determined, final formulary placement was determined by the deals that could be negotiated with the manufacturers.

While the subjects discussed were pertinent to the particular drugs under consideration, several interesting and fairly animated discussions occurred around the following topics.

- During the educational component of one meeting, a presentation was given on special features of biotech drugs, their anticipated utilization and costs as a class, and strategic initiatives to appropriately plan for their influence on treatment and the pharmacy budget.

- One group brought up a perceived connection between the FDA and the pharmaceutical industry and the expected impact on the FDA's ability to provide impartial expert opinions on products reviewed.

- Another discussion involved the desirability of covering drugs that provided no unique benefit to patients other than convenience. An example of such a drug is Seasonale, a new 3-month course of oral contraceptive that allows the user to restrict menses to four times per year.

- Concern over the convenience and cost to patients when using the pharmacy benefit surfaced in several meetings. For example, some new drugs combine two drugs that are already available separately, but having them combined under one copay would save members money at the pharmacy.

- In another meeting, members expressed concern that patients might be confused when required to obtain prior authorization for an injectable drug and then have to write a large check at the pharmacy when this was not required for other drugs. The up-front payment requirement could discourage some members from filling prescriptions.

- Most meetings included some discussion of manufacturer strategic maneuverings. These included acknowledgements that drugs like

Clarinex which is slightly different from Claritin, or Nexium which is slightly different from Prilosec, or new formulations such as Wellbutrin XL (once per day) are developed to capture market share from another product from the same manufacturer that is about to lose patent protection.

- One meeting included a discussion on using clinical trial and other data to approve a drug for the formulary when much of the anticipated usage of that drug, such as the epilepsy drug Trileptal, would be off-label psychiatric use for which data was not available.

- Only one committee (a large PBM) specifically talked about rejecting pharmaceutical manufacturer models in favor of doing its own economic analysis. Other groups discussed costs of the drugs or copays, or mentioned when economic research was not part of the dossier (evidently not uncommon).

With increasing public attention to pharmacy benefit management processes, health plans should implement formulary decision making processes with the goals of improving clinical outcomes and reducing overall cost of care rather than simply maximizing rebates and minimizing drug expenditures. These strategies may also help to align incentives for health plans, physicians, pharmacists and patients. [xix]

Formulary Decision Making—What Do We Know About the Process?

Health plans, PBMs and hospitals follow the same general process when evaluating a new drug for formulary submission.[xx,xxi,xxii] Guiding principles for clinical decision-making have been defined as follows[xxiii]:

- Assess the findings of peer-reviewed medical outcomes research and pharmacoeconomic research,

- Employ published practice guidelines, developed by an acceptable evidence-based process,

- Compare the efficacy, effectiveness, value and therapeutic interchangeability,

- Compare drugs on patient compliance, and

- Do a thorough evaluation of benefits, risks and Adverse Drug Reactions(ADR).

In practice, P&T Committees examine safety and clinical effectiveness first, then the incremental value of a drug compared to existing alternatives. If a drug has superior clinical properties and has no equal counterparts, then it is added to the formulary. If a drug is inferior to an alternative on the formulary, then it is not added. If the drug shows effectiveness equal to a drug currently on the formulary, then costs are considered in the adoption process. If there are unanswered questions about the product's safety, the decision is usually deferred until more data are available.

Most sources of information, including manufacturer dossiers, published literature and FDA documents, focus on clinical and safety issues. Economic information is sometimes available. Current evidence suggests that pharmacoeconomic information is not widely used by decision makers, however.[xxiv,xxv] Some reasons are listed below:

- Health plan decision makers are skeptical of information provided by drug makers.

- Decision makers report being uncomfortable with the extensive use of assumptions in pharmacoeconomic analyses. They prefer observed data.

- Health plan decision makers have a general concern about the aggregation of health benefits into a single index such as Quality–Adjusted Life-Years (QALYs) saved. They prefer to examine independent components.

- Impacts on the budget are often missing. When included, the cost of a new drug is often confined to its effect on the pharmacy budget alone. This misses the impact in other treatment areas.

- The information is not presented in language used by health plans. They want to know the effect on overall cost per member per month of their benefit, rather than the cost to prevent a hospitalization or cost per QALY gained.

- Pharmacoeconomic information typically lacks head-to-head comparisons with the most relevant treatment alternatives.

- Health plan decision makers need to know how a particular drug is going to affect their own population. Concern about transferability of model results is a barrier to their use.

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How Actuaries Can Help

The FDA does not have a mandate to evaluate a drug's cost-effectiveness as a part of the New Drug Application (NDA) process. Although an NDA submission includes a literal truckload of data, the FDA review focuses entirely on safety and efficacy. An expensive drug with only marginal clinical benefit may be approved if the reviewers conclude that the reported efficacy outweighs the potential toxicity, regardless of cost. Therefore, P&T Committees must do their own economic evaluation of new products if they are to weigh value in their decision-making.

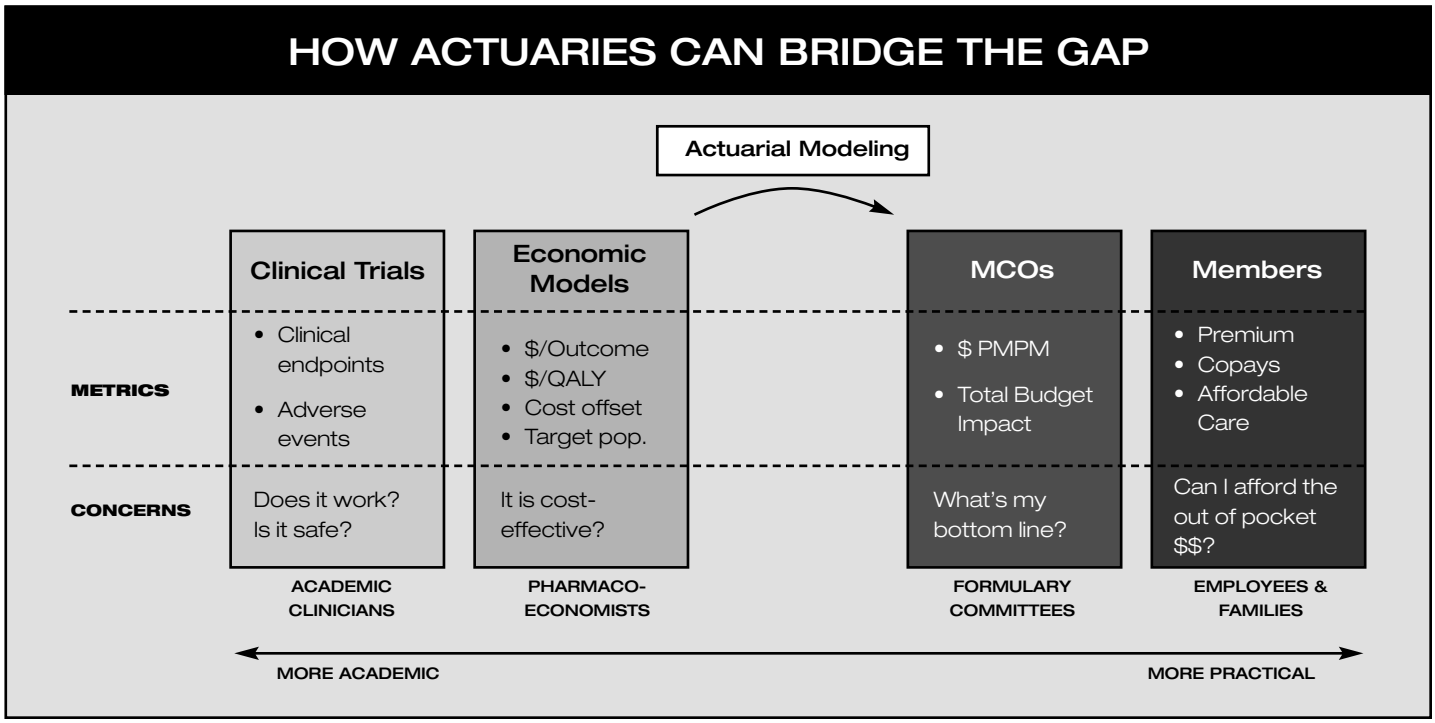
Pharmacoeconomic research currently available to P&T Committees, although much improved following the dissemination of the AMCP Format, is not fully meeting their needs as indicated above. While conducting economic research is not particularly actuarial, modeling is. This seems to be an area where actuarial methods can fill a need.

The primary area in which the pharmacoeconomic modeling falls short is in the inability to specify and quantify any medical cost offsets associated with the use of a drug. While the AMCP Format calls for quantification of budget impacts in the models requested, health plan decision makers have expressed dissatisfaction with this element of the dossiers received. An informal review of dossiers submitted to one health plan over the past three years showed that no more than 15 percent of them contained useful disease-based models. When a reasonably constructed model is submitted, the health plan may still need to adjust the manufacturer's assumptions to get a relevant estimate.

Furthermore, economic models typically compare the manufacturer's own drug to a single comparator or to placebo. A more useful model would incorporate all the relevant treatment options for the medical condition of interest in a single head-to-head comparison.

Models could be made more useful by the use of dynamic population modeling typically used by actuaries. Pharmaceutical company models are often based on populations studied in clinical trials, or on populations that come from canned databases rather than (a) reflecting the population of the health plan, and (b) allowing the user to manipulate the population mix. Population considerations should include features unique to the type of payer, such as commercial, Medicare, Medicaid or TRICARE populations.

An ideal model would incorporate these capabilities, reflect the prescription coverage benefit design, medical condition incidence and prevalence, the rate at which the new drug will enter the system and replace or supplement other treatments, utilization and costs associated with the medical condition and side effects of the treatment options, expected compliance rates, and the level of health care delivery management expected in the system. Estimates of parameters in this model can



be obtained from the medical literature, expert opinion about reasonable clinical pathways, study of prior claims data and other expert judgment.

The people best qualified to create such a model are in the actuarial area. It would not only be a valuable tool for the formulary decision process, but would have much more broad usability within the organization. Economic outcomes expressed in per member per month claim costs could be reviewed and used by actuaries when monitoring experience and preparing for pricing. Specification and quantification of medical cost offsets, or increases, that result from the use of drug treatments could be useful to people in care management and utilization management roles. Ultimately, pharmaceuticals are an integral part of good medical care and their costs should be viewed as part of the total budget. As biotechnology drives up the average cost of new drugs, a strong partnership between actuaries and pharmacists is crucial to the success of a health plan.

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