B S Bloom
Issues in mandatory economic assessment of pharmaceuticals
Health Affairs 11, no.4 (1992):197-201
doi: 10.1377/hlthaff.11.4.197

The online version of this article, along with updated information and services, is available at:
http://content.healthaffairs.org/content/11/4/197.citation

For Reprints, Links & Permissions : http://content.healthaffairs.org/1340_reprints.php

Email Alertings :
http://content.healthaffairs.org/subscriptions/etoc.dtl

Not for commercial use or unauthorized distribution
Australia is expanding assessment of pharmaceuticals by requiring economic evaluation before drugs are marketed. While such assessment is voluntary at first for pharmaceutical firms, it becomes mandatory by January 1993. Michael Drummond has provided an excellent analysis of this new policy initiative, describing in detail the means, methods, and implications of economic assessment. Much of this analysis is equally applicable to other countries.

Economic analysis is becoming a standard tool in drug policy development. In the United States, for example, health policymakers use results of economic assessments in developing drug formularies (lists of drugs that will be reimbursed by various payers). Pharmaceutical firms use them as marketing tools and to compare clinical and economic effects of competing products or therapies. In many European countries, economic evaluations are used to assist regulatory authorities and insurers in setting and justifying prices.

Here I discuss some of the unique characteristics of the pharmaceutical industry and its peculiar competitive nature, both of which set it apart from other health sectors. I also raise two questions that are related to required economic evaluation of medications and that have not been adequately debated. The first is, Why focus on pharmaceuticals now, especially requirements for economic evaluation prior to marketing? The second relates to the cost-effectiveness of requiring cost-effectiveness analysis: What are the costs and benefits of further regulation of the pharmaceutical industry, by way of requiring economic evaluation of medicines?

Bernard Bloom is a research professor in the University of Pennsylvania's Departments of Dental Care Systems, Psychiatry, and Health Care Systems. He is a senior fellow at Penn's Leonard Davis Institute of Health Economics.

Unique Characteristics Of The Pharmaceutical Industry

A number of qualities of the pharmaceutical industry set it apart from other health care industries. First, it is a for-profit industry, but it markets mainly to not-for-profit organizations (particularly hospitals). It is also highly visible. Most of us fill at least one prescription during the year and pay at least part of its price directly, so we have some knowledge of its cost. Conversely, we rarely know the cost of hospitalization—the largest portion of medical care expenditures—nor do we often see any sort of bill. Even if we do, the portion paid out of pocket is inevitably small compared to the total. This makes pharmaceuticals an easier target than hospital costs for academics and policymakers looking for ways to cut costs.

Second, the end user (the patient) has little say in product decision. The pharmacy that retails the product is also generally for-profit, but it too has little decision-making responsibility other than an occasional opportunity to substitute generic for brand-name medications. In essence, pharmaceutical marketing is to an intermediary (a physician) whose decisions influence other intermediaries (hospitals and retail pharmacies) that sell to the end users (patients), whose care is usually paid for by still another intermediary (an insurer). The perverse incentives of such a system are well recognized, such as lack of consumer knowledge or concern with cost and inability to evaluate trade-offs among alternative therapies.

Third, the pharmaceutical industry is a research-based, high-technology, global industry that faces different regulatory, cultural, and political environments in every country in which it tries to market its products. This leads to differing responses to regulations and incentives, different prices for a product in each national market (transnational cross-subsidization), and market distortions such as parallel imports. Within a unified Europe this is supposed to
end, but only time will tell if a unified market with comparable prices will emerge or if indirect barriers will replace direct ones. This industry faces a mixture of intense competition among products that have similar action, the "me-too drugs," and true monopoly because of patent protection that can lead to opportunities for monopoly profits.

Fourth, pharmaceuticals are the only health sector that is required to prove safety and efficacy prior to wide clinical use. This occurs in essentially every high-income country, where there exist large, complex, and sophisticated organizations to ensure safety and efficacy. For example, the U.S. Food and Drug Administration (FDA) employs over 1,000 professionals who approve between seven and twenty-six new drugs each year; a total of 441 medications for humans between 1963 and 1990. It is not known how much this regulatory process costs pharmaceutical firms (cost of meeting regulatory requirements plus income forgone or delayed), the FDA (cost of regulation for safety and efficacy), and society (cost of potential benefit delayed or forgone or danger averted).

While most countries may not have such a complex organization as the FDA, they certainly have one that approximates it in function and scope. This requirement for safety and efficacy prior to marketing, and often prior to being allowed a specific price in countries that also regulate pharmaceutical prices, puts medications at a disadvantage relative to other forms of therapy. In general, diagnostic and therapeutic medical and surgical interventions are not required to prove safety, efficacy, or effectiveness before being widely used (and paid for) in clinical practice. Their use rests on physicians' preference and belief of effectiveness, often based on criteria other than those flowing from controlled study. It might be time to rethink this cavalier attitude toward medical and surgical interventions and to require that they too be subjected to similar rigorous controlled clinical investigations before being used widely among patients. (This does not preclude the possibility of postmarketing testing of safety, efficacy, and cost-effectiveness by, for example, use of case control and cohort control studies.)

This could be coupled with effective postuse surveillance to determine broad effects, including side effects of all interventions.

### Uncertainty In The Industry

The pharmaceutical industry faces unique market forces. First, there is no market test for the desirability of a new product. Large sums are invested over a long time period with little foreknowledge that the regulatory process will allow its use and the price the firm may charge. The real cost of bringing a new product to market may not be as high as Joseph DiMasi and colleagues estimate (capitalized cost of $231 million), but by any standard it is an expensive process without knowledge of size of return.

Second, while patents may confer monopoly for some products, other products face competition from pharmaceuticals with similar action or effect and from medical and surgical interventions. At the same time, purchasers are combining in ways that allow them to act as monopsonists, with their own power over price and terms of sale. Pharmaceutical firms must make long-term commitments to research and development while facing these and other short-term vagaries. The recent spate of mergers, comarketing agreements, and other combinations among traditional general pharmaceutical firms shows that these firms feel the need to increase size to compete in global markets. This is offset by the new biotechnology firms with their focus on market niches and boutique medications. The medium-size general pharmaceutical firm may be doomed to extinction by this bifurcation of the industry. Even with this high level of uncertainty, the pharmaceutical industry as a whole has had consistent, impressive growth of revenue, profits, and rates of return.

Third, it is rare that the value of any pharmaceutical is established relative to all realistic alternatives. Most regulations require safety and efficacy to be established against placebo; comparative valuations are rarely done and certainly almost never required, especially between pharmaceutical...
and nonpharmaceutical care options. Australia appears to have proposed a well-thought-out mandatory program of economic assessment of medications, but the alternatives for comparison are other pharmaceuticals. Only in the case of a new breakthrough drug for which there are no other comparators might the alternative be "current clinical practice." This requirement for economic assessment will then depend on an emerging field without agreed-upon guidelines for method, data analysis, interpretation of results, and relationships between funder and investigator. 

Why New Regulation?

Most countries have failed to control growth of overall health expenditures or of the rate of health inflation. Few have had any long-term success, for example, in tying overall expenditures to growth of gross national product (GNP). Great Britain and Canada are among the most widely cited exceptions; more recently Germany, too, has had success in holding down expenditure growth. Most have also failed to control hospital costs and rates of hospital cost inflation, the largest consumer of health resources in nearly every country. For example, U.S. hospital costs account for 43 percent of all health expenditures.

Physicians' resource allocation decisions at the macro level also have not been well controlled. Because physicians make the fundamental decisions about allocating available resources while continually demanding new resources, control of physician behavior is often an unstated but real goal that is as yet mainly unrealized. This conflict is understandable, as physicians are constantly seeking to do what is best for their patients and often believe that the latest technology, techniques, and interventions are needed. Unfortunately, in most instances the new is generally more expensive than the current, the new is as often additive as substitutive for current technology, and the marginal benefit relative to the marginal increment in cost is almost never calculated.

Thus, the perceived failure to control any of the large expenditure sectors of health care (hospital cost and physician resource allocation) has led finally to attempts to control costs of the relatively small but not insignificant pharmaceutical sector. Germany is among the first to do so, with its multilevel pharmaceutical reimbursement system. I suppose the dictum applies here that anything achieved is better than nothing. But the unasked question is, What realistic level of savings can be achieved, and what are the monetary and other costs of achieving such savings?

Effects Of Mandated Evaluation

The goal of the Australian program requiring economic evaluation of pharmaceuticals before marketing is to help policymakers decide whether to allow registration of new medications and the price at which they will be reimbursed, especially from the public purse. As Drummond has clearly shown, the process is highly rational and the requirements are seemingly appropriate, all the while expecting use of well-accepted methods of economic evaluation. But mandatory economic evaluation raises as yet unaddressed issues.

Unanticipated problems. First, what have we learned from other areas of pharmaceutical regulation that can shed light on what may happen following implementation of mandatory economic evaluation? The emphasis on determining clinical safety and efficacy that has been in effect for at least three decades, most will agree, has served the public well, although it has not been without its problems, such as the length of the regulatory review process. There were few alternatives to the original focus on placebo-controlled trials as the basis to test for absolute safety and efficacy. Unfortunately, no such consensus exists as we enter the era of economic evaluation. As an aside, placebo-controlled trials have long since lost their major value. The best study of any intervention, of course, would be against the next-best alternatives for like conditions, diagnoses, or diseases.

Competition. Second, the requirement
for safety and efficacy determination prior to marketing has been anticompetitive. The high cost of controlled clinical trials helped to drive small firms from the market. Only recently have new biotechnology firms returned to the pharmaceutical industry, often by carving out unique product or market niches. Will added regulation be achieved at further cost to competition, again driving small firms from the market because they lack resources to meet new requirements for economic in addition to clinical evaluation? If this occurs, what effects on price and product competition can be expected from increased concentration of economic power in ever fewer but larger firms?

**Unique benefit.** Much has been made of the fact that a disproportionate number of pharmaceuticals reaching the market are nothing more than “me-too” medications that provide essentially no improvement over those already available. What truly are the positive effects (marginal benefits) of the fifth beta blocker or cephalosporin? Some argue that so much effort and expense go into producing these similar pharmaceuticals that effort, attention, and resources are diverted from opportunities to produce truly useful medications. If more effort and attention were focused on knottier disease problems, the argument continues, more innovative pharmaceutical interventions would be available. On the other hand, H₂ blockers, Cyclosporine, and similar breakthrough medications occur rather infrequently.

How will mandatory economic assessment evaluate multiple products of like effect, and how will study results lead to pricing? Will “me-too” products be kept off the market either by direct edict or by setting a price so low that it provides no economic return to the pharmaceutical firm? Lastly, who defines a “me-too” product? For example, initial study of efficacy of antihypertensive medications found that those of different classes achieved comparable reductions of blood pressure. But during actual clinical use, differential effectiveness was observed among drugs of the same and different class related to patients’ age, sex, and race. How can this be determined a priori in efficacy trials on only a few hundred patients? Thus, some benefits will be lost and some costs avoided. But we cannot ever know ahead of time the value of this trade-off.

### The Cost/Benefit Calculus

The first issue to be raised when requiring determinations of economic value in addition to efficacy and safety of pharmaceuticals prior to marketing is, Against what alternatives will the economic evaluations of individual medications be measured? If studies of cost and benefit are to be done in tandem with controlled clinical trials of safety and efficacy, how can the artificial results of efficacy be translated into effectiveness criteria so that “appropriate” policy and other decisions can be made by political authorities? This is a methodological issue that has only been partially resolved recently by use, for example, of simulation and other techniques that translate efficacy data into effectiveness results for both clinical and economic use. If safety and efficacy are proved first and then cost-effectiveness or cost/benefit analysis is done after marketing so that actual use is defined in clinical practice, then the premarketing purpose of the Australian requirement for economic evaluation is bypassed. Additionally, how will time cost be evaluated—that is, the monetary and health cost to potential patients and payers of delaying a product’s arrival on the market? Will any commission regulating pharmaceuticals allow or encourage controlled trials against interventions other than placebo or other drugs, including medical or surgical interventions?

A second issue relates to uses of results of economic evaluation. Will only medicines with a specific cost-effectiveness ratio be allowed to be sold? How will the academic cost-versus-benefit result be used in making political decisions regarding registration and pricing? Will the calculated marginal benefit of a new medication be used to set the price? For example, if a new pharmaceutical saves or extends many lives, will a relatively high price be granted? At the same time, what criteria for pricing will be used on medications having different effects, such as...
those that save lives versus those that reduce symptoms versus those that improve functioning and quality of life versus those that cure disease versus those that retard disease progression? How are the comparative values upon which price is presumably to be based to be made amongst the array of different pharmaceuticals with different targeted effects in different populations and for different conditions and diseases?

Based on calculations by the Organization for Economic Cooperation and Development (OECD), I estimate that annual spending on medical care in high-income countries was approximately $1.3 trillion in 1991.8 Of this total, 13.6 percent, or about $180 billion, was spent on pharmaceuticals. Total worldwide pharmaceutical spending is less than U.S. hospital spending alone was expected to be in 1991. Realistically, how much savings can be achieved, and at what cost, by focusing a large measure of any cost control effort on pharmaceuticals, while throwing up our hands in despair at the inability to control or reorganize other larger health sectors, or to affect total spending for the entire system in any of these countries?

Because we have been, in general, so spectacularly unsuccessful in controlling health costs as a whole, we are now turning our attempts to micromanagement of the pharmaceutical sector. Bear in mind, we have also not been particularly successful with micromanagement of other individual sectors, either, particularly hospitals.

Mandating economic evaluation of pharmaceuticals as an important tool of cost containment will, I predict, be as unsuccessful as micromanagement of other health sectors has been. However, this is no reason not to undertake economic evaluation of pharmaceuticals (and all other diagnostic, therapeutic, and rehabilitative care). To the original reason for mandated clinical evaluation-safety and efficacy for the patient-can now be added the need for more information on economic effects. Together they provide a fuller view of risks, benefits, and costs for all decisionmakers. But a long-term view must be taken, one that emphasizes equally initial and ongoing evaluation of pharmaceuticals to elucidate value. And, as with current clinical evaluation, acceptable scientific guidelines for all aspects of the performance of such studies must be agreed upon and adhered to by investigator, regulator, and funder alike. The same, of course, can be said of all other health and medical care services, especially when the vast majority of them have never been exposed to well-controlled investigation.

Ultimately, some good may come from the perceived need to expand the processes of evaluation. But it is more likely to benefit patients and clinicians than it is to benefit those responsible for financial control. All in all, this is not a bad bit of progress, although it may not have been Australia’s (or any other country’s) primary goal.

NOTES