Pharmaceuticals and Health Care Costs

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Presented at the International Health Care Forum

"Health Care Policy and the Pharmaceutical Industry"

Gotemba, Japan

October 1992

September 1992

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Introduction

Given the escalation in public and private medical expenditures that has occurred on a worldwide basis, the growing concern of policymakers with health care costs is certainly appropriate and desirable. Nevertheless, a few points are worth emphasizing at the outset concerning the linkage between pharmaceuticals and overall health costs. These points are relevant to the development of sound public policy in this area.

The first point is that pharmaceuticals are not only safe and effective, but also are generally a cost-effective approach to health care. Historically where pharmaceuticals have replaced other forms of medical intervention, there have not only been significant medical gains, but also real cost savings to society. There are many examples of this phenomena--the use of antibiotics to treat infectious diseases like tuberculosis which formerly required hospitalization in long term health care facilities, vaccines that have prevented very costly and agonizing diseases like polio, cardiovascular drugs that can substitute for costly bypass surgery, and psychotropic drugs that have reduced the average stay in mental hospitals significantly.

A second point is that the costs to society of the diseases and illnesses for which we now have no treatment, or can treat only in a very inadequate way, are very large. Three leading causes of death at the present time are heart

disease, cancer, and stroke. A study by Hartunian, Smart and Thompson estimated the direct and indirect costs from these diseases in the US at over 80 billion Dollars (1). This is their estimate expressed in 1986 Dollar terms. Furthermore, they found the so called indirect economic costs, the lost wages and production due to premature death and illness, were *three times* the direct costs of medical treatment for these diseases. Since they have omitted many costs of illness that are not easily quantified, their estimates are very conservative in nature. Nevertheless, their study demonstrates the large patient benefits, and savings in national resources, that are potentially realizable from better therapies and preventive measures.

How can we be assured that current and future new drug introductions will indeed provide net benefits to society? Increasingly drug firms are performing prospective economic analysis in their new drug clinical trials to document incremental health care benefits and costs. These techniques are variously denoted as cost benefit, cost effectiveness and cost utility analyses. In the future, economic analyses are likely to be as important as traditional safety and efficacy studies in determining market acceptance and commercial success. If properly utilized, the generation of more sophisticated analytical tools for measuring the benefits and costs to medical intervention is a very optimistic development for both the research based pharmaceutical industry and society as a whole.

There is also a danger, however, that these economic studies will be misused by policymakers. In particular, rather than being an instrument to encourage efficient utilization of overall health care, they can alternatively be used as another hurdle to achieve short-term drug-specific cost containment goals. There is some evidence that this is already occurring in the proposed

drug registration guidelines being developed by officials in several countries (2).

In my talk today I want to highlight some of the important R&D opportunities and challenges to the pharmaceutical industry presented by current health care sector developments. I also wish to discuss some of the basic aspects of R&D competition in pharmaceuticals. The purpose is to show that the incentives for new drug innovation can be influenced in a positive or negative fashion by the actions of the policymakers in the major developed countries.

R&D Opportunities

In terms of scientific opportunities, the environment for drug innovation is currently very exciting. Over the past several years, there has emerged a much better understanding of the underlying causes of many diseases. The combined research efforts of academia, government, and industry have produced major advances in biomedical science, many of which offer promising clinical applications. Increased knowledge of physiological processes at the molecular level enable researchers to develop more selective and potent pharmaceutical targets. New research tools, such as electron microscope and X-ray crystallography, and new research techniques associated with biotechnology have helped enhance the search for significant new compounds. In this regard, it has been estimated that one in three drugs in the clinical trials are now based on biotechnology, as compared to less than one in ten a decade ago (3). Because of these advancements, pharmaceutical industry R&D now can be categorized more as a "discovery by design" approach, as opposed to the random screening of compounds that was once prevalent.

Another important development concerns the changing therapeutic orientation of pharmaceutical R&D. The two leading disease areas in terms of death and disability in the developed countries are cardiovascular problems and cancer. During the past decade, the leading category of global pharmaceutical R&D investment has been cardiovascular agents. This class of drugs also accounted for over half the major new drugs introduced into U.S. and world market over the past several years. In the case of biotechnology drugs, a recent survey indicated that there were 132 drugs currently under clinical development in the United States, and 50 percent were devoted to the treatment of cancer (4).

The introductions of major new products in the cardiovascular area has already had a significant impact on clinical practice. Significantly fewer prescriptions are being written for older therapies such as diuretics. Newer product categories, such as the ACE inhibitors and the cholesterol reducers, now account for a significant and rapidly growing share of the cardiovascular drug market. It is also important to note that the rate of deaths per capita in the United States and other nations from cardiovascular causes has decreased significantly over the past decade (5). This reflects, at least in part, the availability of new and better medicines (5,7).

As we look to the future, there will be a continuing evolution in the orientation of pharmaceutical R&D. Earlier drug therapies were focused on infectious diseases and acute conditions. Thanks in considerable part to the medicines discovered in the first pharmacological revolution, average life expectancy have increased steadily over time. As a consequence, health care has become much more concerned with problems of disability and the quality of life. An increasing share of the medicines currently under development are oriented to

chronic and disabling illnesses such as asthma, depression, hypertension, multiple sclerosis, and senile dementia.

The future clearly present a major challenge to both policymakers and health care providers. An aging population will present many more demands on already financially stressed health care systems. Quality of life concerns will dominate health care resource allocation. New and more sophisticated methods for measuring the quality of life benefits of new therapies will be increasingly important. Furthermore, if the past is a guide, many chronic disease areas are also likely to have an incremental pattern of medical advance rather than be characterized by dramatic breakthroughs. In this environment it will be very important to have mechanisms in the health care sector which accurately assesses and fairly compensates drug innovation. This will be important for both efficient resource allocation as well as the enhancement of the quality of life.

Economics of Pharmaceutical R&D

In order to understand how policymakers can influence the environment for new drug innovation, it is useful to briefly discuss some of the key economic aspects of R & D competition in pharmaceuticals. My perspective here is the U.S. situation. However, many of the trends, such as higher R & D costs, appear to work in all the major world centers of drug innovation including Japan.

R&D Costs

There is strong evidence that the R&D process for new drugs is becoming longer and costlier. The Center for the Study of Drug Development at Tufts

University recently has completed a microeconomic study of R&D costs. The principal author of this study is Joe DiMasi with Ron Hansen, Lou Lasagna, and myself serving as co-authors (8). This analysis is designed to estimate the average R&D cost for NCEs discovered and developed by U.S.-owned firms (i.e., their self-originated NCEs). Data were obtained on a random sample of 93 drugs first tested in humans between 1970 and 1982. In this analysis the costs of drug candidates that fail in pre-clinical and clinical trials are incorporated into the average costs of the new drug introduction. R&D expenditures also are capitalized to the date of marketing introduction to reflect the time costs associated with an investment in pharmaceutical R&D.

Our best estimate is that it takes an average of $231 million (in 1987 dollars) and 12 years to discover and develop a new drug. Of this total, $114 million is the out-of-pocket R&D costs and $117 million is the time cost associated with the 12-year average investment period. Our findings imply that average R&D costs per new drug introduction have been increasing significantly. An analysis by Hansen (9), performed approximately a decade earlier using the same general methodology found an average R&D cost of $100.7 million expressed in 1987 dollars. Hence, in real terms total capitalized costs are about 2.3 times larger in our study than in the earlier period analyzed by Hansen.

What factors account for this increase in real R&D costs per new drug introduction? First, pharmaceutical R&D now entails significantly greater expenditures in the discovery phase. A second factor is the shift in research focus toward therapeutics to treat chronic clinical conditions such as cardiovascular disease and cancer. Chronic disease drugs require more long term testing and greater overall resource investments prior to commercial introduction. A third factor accounting for higher R&D costs is the rapid

escalation in the out-of-pocket costs of clinical trials and the greater capital equipment requirements associated with current R&D activities in the pharmaceutical industry. There are striking changes in this regard emerging from our analysis compared to the situation of a decade ago. Understanding the forces underlying this rapid increase in out-of-pocket costs is an important topic for future research.

Returns and Risks

Whereas R&D investment costs have been increasing, product life cycles have been getting shorter. This is the result of faster follow-on from competing new drugs and increased generic competition when patents expire (10). John Vernon and I have studied the life cycles of drugs introduced since the 1970s (11). It appears the sales volume of the average drug tends to peak somewhere around 10 to 12 years after market introduction. This research is ongoing, but there is definite information to suggest faster follow-on from competing drugs than in the past.

It is also important to note that the revenues from new product introductions are also highly skewed, and this adds to the risks of pharmaceutical R&D. This is illustrated in Figure 1. This figure shows the distribution of present values of cash flows by deciles for the sample of 1970s new product introductions. The top-ranked decile has an estimated after-tax present value that is several times the average after-tax R&D investment. At the same time, only the top three deciles have present values in excess of average R&D costs. This means that only one in three new drugs covers the average costs for research and development. The products in the lower deciles may be important

therapeutically and may also contribute economically in terms of incremental cash flows. However, these results mean that from a financial perspective, a firm must have a drug in the top decile of sales every so often if it is to cover the large fixed costs of pharmaceutical R&D (i.e., the common discovery costs and the costs of the compounds that fail in the development phase).

Our research indicates, therefore, that the economics of pharmaceutical R&D are changing in a rapid and fundamental way. New drug introductions of the future will require, on average, substantially higher real R&D costs than previous introductions. Increasingly firms are dependent on a few major blockbuster products to finance their R&D for the new drugs of the future. The race to obtain these products is accelerating and many current drug firms may not be in the competition in another decade (12).

Our analyses also indicates that R&D costs and returns on investment are highly sensitive to development and regulatory approval time. Regulatory approval times for a new drug introduction average more than two years in the United States. In some of our simulation analyses, we found that a one-year decrease in regulatory approval times decreases break-even lifetime by three to four years (12). This is due primarily to the fact that regulatory delays occur at the beginning of the product life cycle. If regulatory clearance times can be shortened, it would not only increase effective patent life, but firms would also realize their return on investment and subsequent profit at an earlier time. This would enable more drugs to cover their R&D costs and would therefore be a stimulus to further innovation. It is therefore worth examining current regulatory approval and clinical development procedures in all countries with an eye to accelerating what has become a very lengthy process. Making this process more efficient could have a high economic and social payoff.

Conclusions

The economic trends indicate overall that pharmaceutical R&D activity is becoming longer, costlier and riskier in nature. It is fortunate that, to date, this has not caused a serious negative global impact on R&D investments of the pharmaceutical industry. The strong prospects for scientific advance and the ability to make strategic responses to the changing economics of R&D in some countries have kept global pharmaceutical R&D investments growing at a strong pace. Whether this will continue in the future is uncertain. All countries are facing pressures to contain health care costs. Pharmaceuticals are a frequent target for this cost containment despite their cost-effective nature and their relatively small share in overall health care costs.

In the current fragile economic environment, the temptations of policymakers responsible for health care sector cost are to try to obtain their prescription drugs at marginal or incremental cost by utilizing price controls and other strategies. Many countries have employed this strategy in an intensive way. However, as more countries try to free ride in this manner and import the burden for innovation costs to other countries, the more the incentives to undertake new innovation activity will be diminished. If all countries try to obtain drugs at marginal production costs, the incentives for new drug innovation will be drastically curtailed. In this case, privately financed R&D investments would be expected to decline even in an environment of strong scientific opportunities.

There are currently many outstanding opportunities for future medical advances in the global pharmaceutical industry. These can provide significant health benefits to the world and in many instances net savings to the individual

country's health care systems. However, if these benefits are to be achieved, in the difficult environment which lies ahead with respect to the competition for the health care resources, it will require all parties in the innovation process to act in a prudent and responsible manner. It is the major responsibility of the pharmaceutical industry to continue to discover and develop medicines for the world's major diseases and health care problems, and also to provide strong evidence that the new drugs they develop are cost beneficial to society. Correspondingly, it is the responsibility of health care policymakers in all the major developed countries to pursue regulatory, scientific and reimbursement policies that provide attractive economic incentives to the private sector creators of cost-beneficial drug innovations. This includes adequate compensation for the increased costs and risks of R&D. Fulfillment of these responsibilities by all parties will be crucial if the rich promises and opportunities of future medical advances are to be realized.

References

1. Hartunian, N. S., Smart, C. N., Thompson, M. S. "The Incidence and Economic Costs of Cancer, Motor Vehicle Injuries, Coronary Heart Disease and Stroke: A Comparative Analysis," American Journal of Public Health, Vol. 70, December 1980, pp. 1249-1259.
2. Drummond, M. "Australian Guidelines for Cost-Effectiveness Studies of Pharmaceuticals: The Thin Edge of the Boomerang?" PharmacoEconomics, Vol. 1, Supplement 1, 1992, pp. 61-69.
3. Bienz-Tadmor, B., Dicerbo, P. A., Tadmor, G., Lasagna, L. "Biopharmaceuticals and Conventional Drugs: Clinical Success Rates." Biotechnology, Vol. 10, May 1992, pp. 521-525.
4. Pharmaceutical Manufacturer's Association. Biotechnology Drugs in Development, 1991 Survey Report, Washington, D.C., 1991.
5. Battelle Human Affairs Research Centers. "The Value of Pharmaceuticals: A Study of Selected Conditions to Measure the Contribution of Pharmaceuticals to Health Status." BHARC-01390/010, Washington, D.C., March 1990.
6. Holdman, L., Cook, E. F. "The Decline in Ischemic Heart Disease Mortality Rates," Annals of Internal Medicine, Vol. 101, 1984, pp. 825-883.
7. Weinstein, M. C., Stason, W. B. "Cost Effectiveness of Interventions to Prevent or Treat Coronary Heart Disease," Annual Review of Public Health, Vol. 2, 1981, pp. 363-395.
8. DiMasi, J., Hansen, R., Grabowski, H., Lasagna, L. "The Cost of Innovation in the Pharmaceutical Industry," Journal of Health Economics, Vol. 10, June 1991, pp. 107-142.

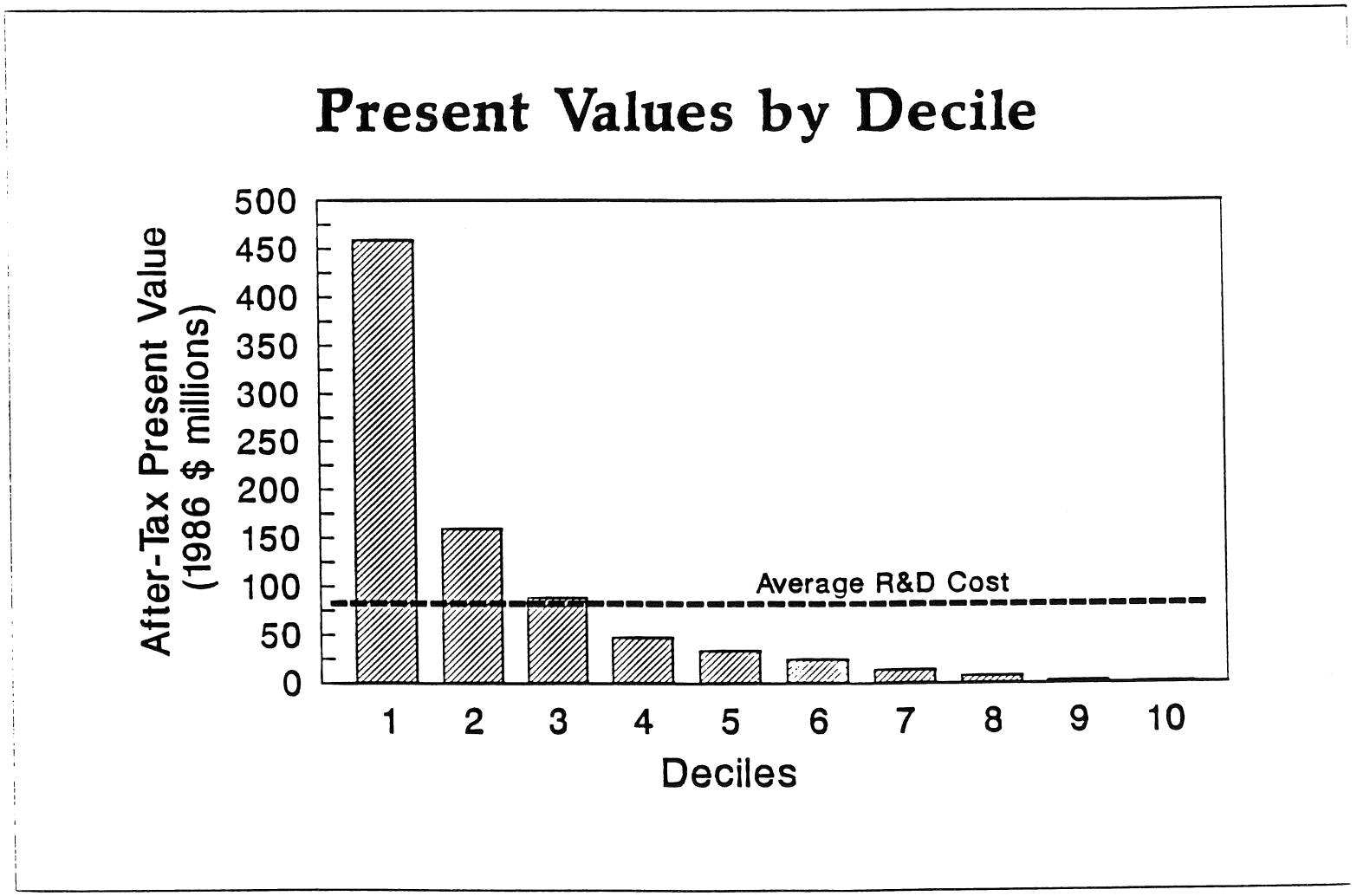
9. Hansen, R. W. "The Pharmaceutical Development Process: Estimates of Current Development Costs and Times and the Effects of Regulatory Changes," In R. I. Chien, Ed. Issues in Pharmaceutical Economics, Lexington, Mass.: Lexington Books, 1979, pp. 151-187.

10. Grabowski, H., Vernon, J. "Brand Loyalty, Entry and Price Competition in Pharmaceuticals after the 1984 Drug Act," forthcoming in the Journal of Law and Economics, October 1992.

11. Grabowski, H., Vernon, J. "A New Look at the Returns and Risks to Pharmaceutical R&D," Management Science, Vol. 36, 1990, pp. 804-821.

12. Grabowski, H. "Pharmaceutical Research and Development: Returns and Risk," Centre for Medicines Research Annual Lecture, Carshalton, Surrey, England, 1991.

Figure 1


Present Values by Decile
After-Tax Present Value
(1986 $ millions)
500
450
400
350
300
250
200
150
100
50
0
Average R&D Cost
1
2
3
4
5
6
7
8
9
10
Deciles