

Michael Schlander:

Health Economics & Pricing:

Integrating a New Functional Area into the Pharmaceutical Corporation

Abstract	2
Cost Containment and Pricing Flexibility	2
Stakeholder Dynamics:	
The Emergence of New Decision-Makers	9
The Role of Health Economics	13
Integrating Health Economics	18
Recommended Further Reading	21

based on a presentation given at the University of Witten/Herdecke,
Witten, August 28/29, 1998

reprint from:

W. Braun, R. Schaltenbrand (eds.)

Die Nutzung der Ressource "Synergie"

Zukunftssicherung für Forschung, Marketing und Vertrieb

Witten: Universität Witten/Herdecke Verlagsgesellschaft, 1998.

pp. 150-170.

With contributions by H.J. Ahrens, K.D. Henke, K. Meyer-Lutterloh, K.J. Preuß, D. Graf v. Stillfried, T.R. Weihrauch, C. Yzer, and R. Zeiner

**Health Economics & Pricing:
Integrating a New Functional Area into the Pharmaceutical Corporation**

Michael Schlander

Abstract

Ever-increasing cost containment efforts combined with the escalating time and cost of new drug development result in growing pressures on the research-based pharmaceutical industry. Cost-cutting exercises can provide short-term relief but no solution.

Traditionally, the industry has perceived health economics as a threat, potentially even adding a “fourth hurdle” to the drug approval process. Indeed precisely this has happened in Australia, Canada and some further markets.

The industry is reacting by incorporating health economics as a new discipline, either as a separate function or integrated into existing departments. Health economic data and analyses now greatly assist in the decision-making process regarding an optimal research and development portfolio, price range definition and price justification, and integrated marketing and communications programs. The options for structural integration of an internal competence center for health economics will be discussed.

Cost Containment and Pricing Flexibility

Despite substantial efforts to contain costs, health care spending has grown steadily over the past decades. This increase has exceeded that of national income in most industrialized economies. As the only completely private sector within the highly regulated and largely socialized health care systems, the pharmaceutical industry and its products have become a prime target for measures aimed at reducing health care

expenditures. The resulting pressure on the industry is enhanced by the public perception of its above-average profitability (cf. Fig. 1).

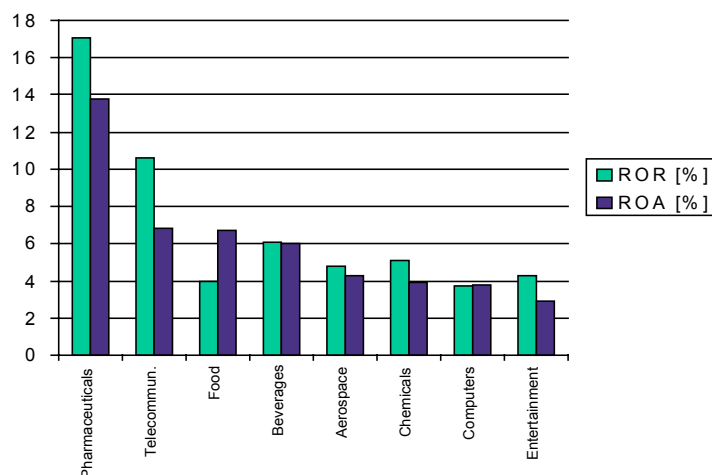


Figure 1: Profitability of the pharmaceutical industry

Median return on revenues (ROR) and return on assets (ROA) for the United States pharmaceutical industry, compared to other industry segments with above-average profitability. Data source: The Fortune Global Five Hundred. Fortune Magazine, 1997.

Pharmaceutical cost containment efforts have involved both *demand side regulation* as well as supply side restrictions (cf. Tab. 1). On the one hand, demand has been influenced by increased patient co-payments, by prescribing budgets for doctors, by formularies listing drugs suitable for reimbursement and other types of “positive lists”, and by straight “negative lists” excluding groups of products from reimbursement - either altogether, or for defined indications. In some countries, specific measures have been introduced to control “off-label” use of drugs. A prominent example for controls of off-label prescribing are the “Références Médicales Opposables” (RMOs) in France.

On the other hand, *supply side regulation* has emerged as direct price controls, reference pricing, price freezes and even enforced price cuts; its more sophisticated forms include promotional budget curbs such as in France, and profit ceilings, as have been integral part of the British Pharmaceutical Price Regulation Scheme (PPRS).

Table 1: Overview of cost containment measures for prescription drugs.

Category of measure	Type of measure	Countries applicable (examples)
Supply side regulation	Price cuts	across Europe
	Price freezes	across Europe
	Reference pricing	Germany, Netherlands
	Promotional budget limits	France
	Profit limits	United Kingdom
	Direct price controls	France, Italy, Spain, Canada, Australia
Demand side regulation	Positive or negative lists	across Europe, Canada, Australia
	Patient co-payments	France, Germany, Italy
	Prescribing budgets for doctors	France, Germany, United Kingdom

Currently the *United States of America* have the least regulated health care system, closest to the model of a free market economy. Consequently, overall spending for health care is highest in the United States, both in absolute and in relative terms (cf. Fig. 2). In this context, it is an interesting observation that countries with a global top-down approach to determining overall health care spending, such as the United Kingdom, have the lowest health care expenditure relative to their gross domestic product. France and Germany, with a mixed bottom-up and top-down determination of health care spending, rank in between these two extremes.

Correspondingly the United States have become the single most attractive market for pharmaceutical corporations. It is not surprising that this has turned into a competitive advantage for pharmaceutical companies operating in the United States. Indeed, not only growth rates for U.S. based companies - and those with a strong presence in the U.S. market - have been much higher on average. The favorable

market environment in the United States is also one key factor contributing to the extraordinary profitability of the industry in this country (cf. Fig. 1) which is not matched, at least on average, by European and Japanese pharmaceutical companies. Further, the attractiveness of the U.S. American market has been one of the reasons why many non-U.S. companies have begun shifting resources into this region. The German company Hoechst has provided a striking example for this trend, moving the global headquarters of its pharmaceutical subsidiary HMR to the United States. While the jury is still out on the success of that strategic move, this fact nevertheless may serve as a clear indicator of the industrial policy implications of cost containment and price regulation efforts targeting the pharmaceutical industry.

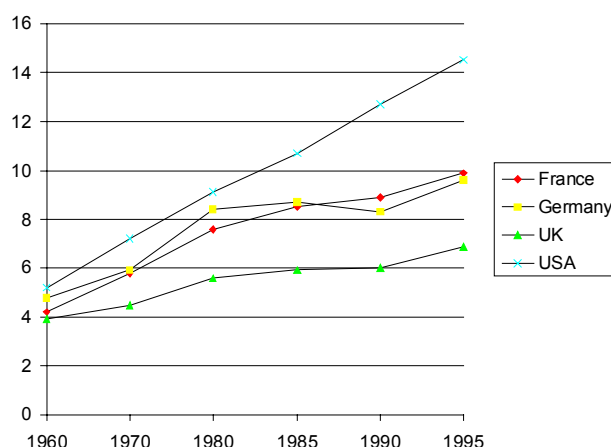


Figure 2: Relative health care expenditure is highest in the United States.

Total spending on health care as percentage of gross domestic product (GDP) in France, Germany, the United Kingdom and the United States of America. Source: OECD Health Data, 1996.

As a consequence of cost-containment policies, the pharmaceutical industry has lost, over the past decade, its *pricing flexibility* to a large extent. Reimbursement of new products requires price approval by authorities not only in Australia and Canada, probably currently the countries with the most advanced health economic standards, insisting on evidence for the economic impact of the products in question on overall health care spending under guidelines specifically developed for that purpose. Also

France and Italy provide examples of positive lists, access to which is granted only after successful completion of a negotiation process with a “Transparency Commission” (France) or an official committee (“CUF”, Italy) associated with the respective Health Ministries.

More recently, the government of the United Kingdom has launched an initiative to establish a National Institute of Clinical Excellence (“NICE”), which is supposed to scan the horizon for new medicines and technologies about to reach the market. Once identified and evaluated as being likely to be economically relevant, these are planned

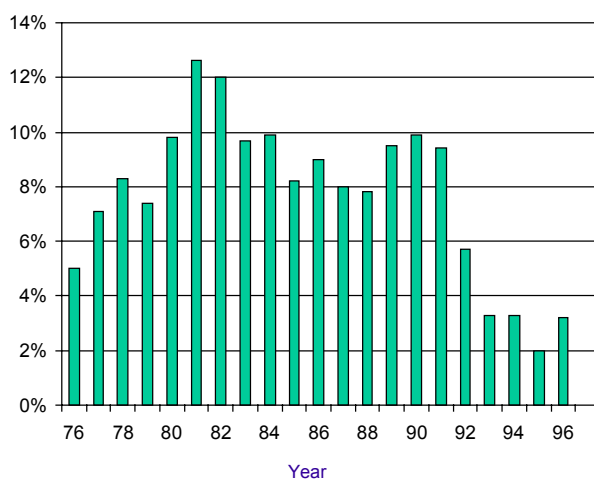


Figure 3: Pharmaceutical price increases in the United States during 1976-1996.

Inflation indicator (CPI) for prescription drugs in United States; data source: U.S. Department of Labor, Bureau of Labor Statistics, 1997.

to be put on a list of thirty to fifty appraisals of the most significant new and existing interventions to take place every year. Based on NICE’s evaluation, recommendations and guidelines will be drawn up on how to use (or, more likely, limit) the products in question. It is evident that this marks a fundamental change, as this move is likely to establish the requirement for data on the cost benefit of new interventions prior to their adoption. Slowed down adoption in the absence of compelling health economic evidence will probably occur as the result of “National

Service Frameworks” (NSFs) that will be set up with a view to benchmark the performance of care groups against pre-defined standards.

Even in the currently least regulated market, the United States, price increases for marketed products, once almost the rule, have decreased dramatically since 1993 (see Fig. 3). In the absence of direct price controls in the United States, the demand side of the U.S. pharmaceutical market has undergone substantial change processes, with three out of four employed U.S. Americans now (by 1996) covered by Health Maintenance Organizations (HMOs), Preferred Provider Organizations (PPOs) and point-of-service plans.

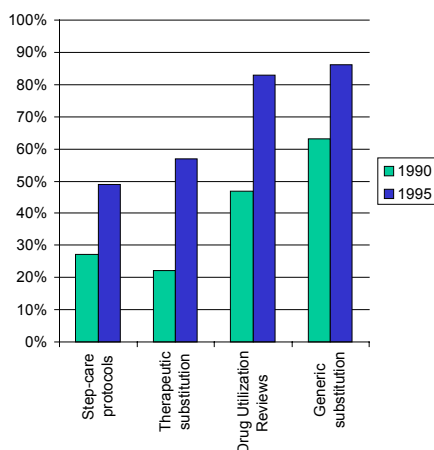


Figure 4: Cost-containment measures used by HMOs in the United States during 1990-1995.

Source: Marion Merrell Dow Managed Care Digest, 1994, and CibaGeneva Pharmacy Benefit Report, 1996.

Most of these organizations operate drug formularies to restrict the use of medicines. Two thirds of these formularies are thought to be “closed” now, i.e., they cover listed drugs *only*. In addition to formularies, HMOs use a number of additional techniques to limit their drugs bill (cf. Fig. 4). Step-care treatment protocols prescribe a defined sequence of treatments to be initiated for a given condition, usually starting with low-cost alternatives and moving up to more expensive treatments only after their failure. Drug utilization reviews (DURs) have been used traditionally as a measure of quality

control, but their focus has been shifting gradually from quality to cost considerations. Therapeutic substitution involves the replacement of a prescribed product by a lower cost alternative, ordinarily belonging to the same class of therapeutics. Finally, in generic substitution an off-patent branded drug is replaced by a cheaper generic copy. As a result, the market penetration of generics has increased continuously in the United States, as has been the case in other pharmaceutical markets, particularly those with less stringent direct price regulation (cf. Fig. 5).

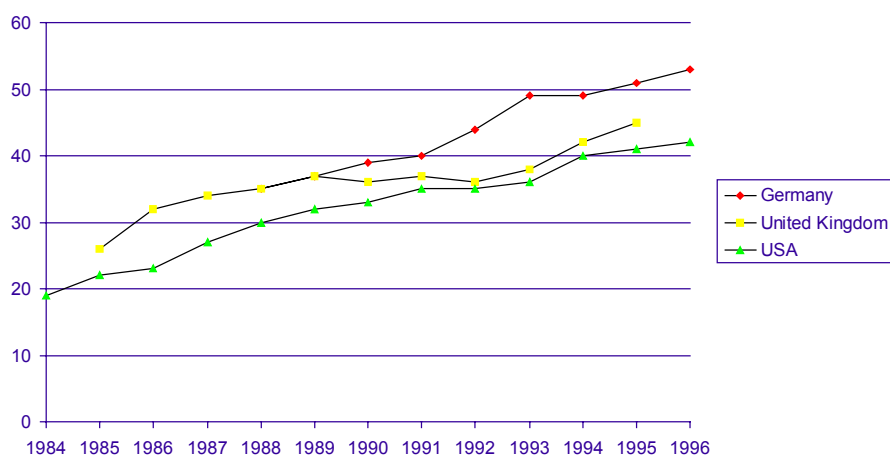


Figure 5: Market penetration by generics in the United States, Germany and United Kingdom.

Percentage market shares; USA: units; Germany and United Kingdom: prescriptions; data sources: PhRMA, 1997; BPI, 1997; DoH, 1996.

These changes have massive implications for the *life cycle* of pharmaceuticals. It has become the norm for products to experience a rapid erosion of revenues, owing to declining prices *and* market shares as the result of generic competition, immediately upon patent expiry. At the same time, new drug development has become more expensive and time consuming than ever. Market introduction can be further delayed by extended periods of price negotiations to gain market access through reimbursement. Relatively high prices, frequently necessary for innovative products, may additionally slow down market penetration in an environment characterized by the prominence of cost-containment efforts. Therefore, the time period of profitability

- and thus research and development payback - for a pharmaceutical product is shortened from both ends (cf. Fig. 6).

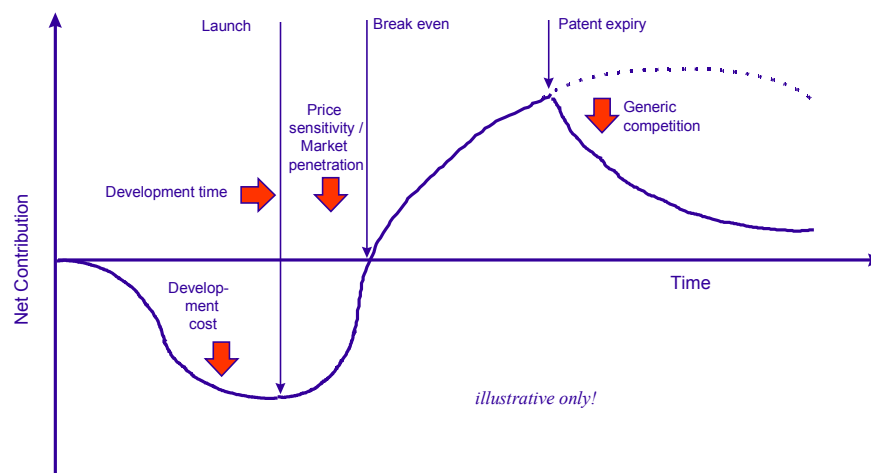


Figure 6: External pressures result in shortened product life cycles.

Stakeholder Dynamics:

The Emergence of Non-Traditional Decision-Makers

As a consequence of these trends, the relative influence of drug developers and manufacturers on the pricing of their products will further decline in the foreseeable future. Drug pricing will be increasingly influenced by non-traditional decision-makers, notably state and private health care payers (see Fig. 7). They will focus on cost-containment, typically considering health economic evidence from their particular perspective only. For the current German health care system, for instance, it can therefore be anticipated that the compulsory health insurers (“Gesetzliche Krankenversicherung”, GKV) will most likely continue to be most interested in cost-minimization data, since the possibility of their members to easily switch from one insurance company to another is likely to largely prevent them from adopting a longer term view as required for disease or even case management approaches.

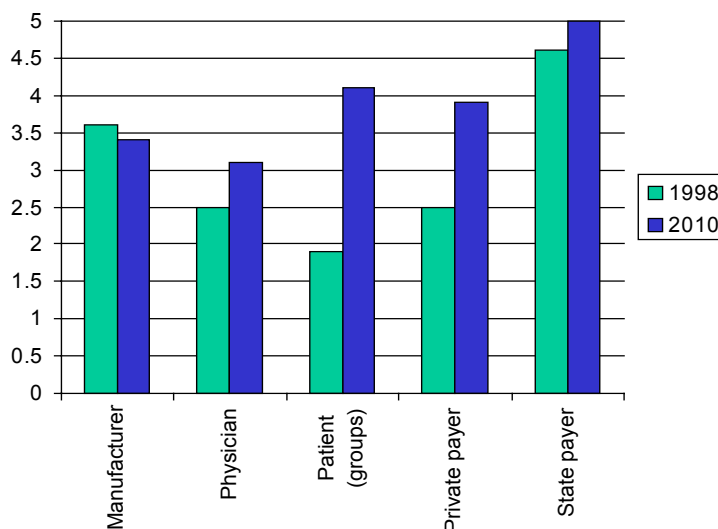


Figure 7: Relative influence of the various stakeholders on pricing of pharmaceuticals, 1998 - 2010.

The importance of third party payers as well as, especially, that of patients and patient advocacy groups for pharmaceutical pricing will increase at the expense of manufacturers' control of the prices of their products. From a global survey undertaken by Reuters Business Insights, 1998. Scale: 0 = no influence, 5 = high influence.

In contrast, private insurance companies (“Private Krankenversicherung”, PKV) may be set to become the pioneers of case management in Germany, given the financial penalties imposed on their members if and when changing the insurance company.

In both cases, health economic and pharmacoeconomic data will be useful to justify and defend pricing decisions, providing they take into account the specific perspective of the third-party payer organizations in question. It is clear that different payers will adopt different perspectives, both within a given health care system as well as, apparently, on the international level. This is especially evident when considering the various regulations guiding reimbursement decision-making. For this and other reasons, there will remain the need to tailor health economic analyses to adequately address these differences. Overall, a recent global survey from Reuters Business Insights confirmed that the availability of appropriate cost benefit data will become the single most influential factor for future pharmaceutical pricing decisions (Fig. 8).

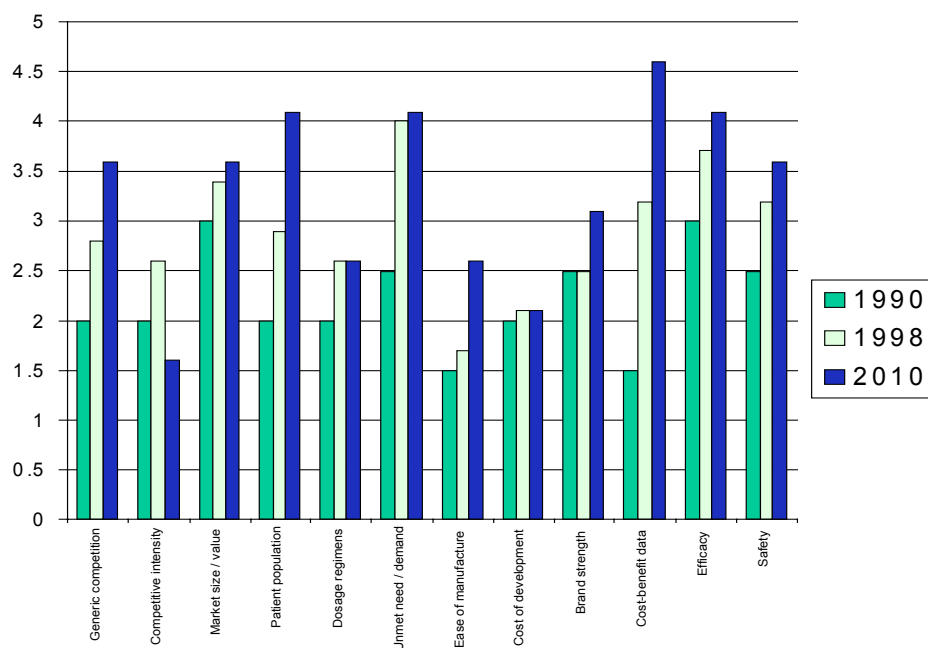


Figure 8: Relative influence of various factors on pricing of pharmaceuticals, 1990 - 2010.

The increasing requirements of health care payers is reflected in the growing importance of all factors directly affecting pricing. The most conspicuous increase is that of health economics (“cost-benefit data”). From a global survey undertaken by Reuters Business Insights, 1998. Scale: 0 = no influence, 5 = high influence. Adapted from: Marketletter, July 8, 1998.

However, it is clear that pharmaceutical manufacturers need to take further aspects into account when making pricing decisions. Health economic data can assist informed decision-making, but invariably will be just one out of a variety of relevant variables. Beyond the traditional criteria such as cost of goods, competitive pricing strategies and price elasticity of demand for any given product category, overall marketing strategy and stakeholder dynamics will play a critical role for pricing decisions (cf. Figs. 7, 8).

In general, all factors important for pricing are likely to gain in relevance, reflecting the increasing difficulties faced by the industry to find (and obtain) optimal price levels for its products. Yet the extent to which the importance of these factors is anticipated to change varies substantially. While more traditional criteria such as unmet medical need tend to increase in importance only slightly, besides health economic data, the most profound change relates to the role of the various

stakeholders: as a group, especially patients will gain influence on drug prices (cf. Fig. 7). In the United States, this trend in some cases has already dwarfed the impact of managed care initiatives. The influence of patients and their advocacy groups - for instance in therapeutic areas such as AIDS and HIV infection or a number of chronic diseases, including certain cancers - has overcome that of third party payers. This has been possible against the background of the conspicuous unwillingness of payers to be seen as rationing medical care. In a broader perspective, the strengthened influence of patients and patient advocacy groups in the United States has been epitomized by the rapid spread of direct-to-consumer (DTC) advertizing.

While the direct influence of patients on pharmaceutical prices has been minimal, the indirect yet powerful consequences of the actions of patient groups should ensure that the industry will work more intensely with patients and thus be more able to negotiate favorable prices. In other situations, manufacturers may even decide to launch new products outside the reimbursement schemes operated by third party payers within the constraints of limited budgets. This has already been the case in European markets for drugs sometimes discriminated as “life style products” - such as Pfizer’s erectile dysfunction medicine Viagra, Roche’s and Knoll’s new obesity treatments Xenical and Meridia/Reductil (Knoll’s drug is still awaiting approval in Europe) and MSD’s recently launched hair growth drug. Such decisions may reflect long-term strategies; in other cases, these moves will be more tactical in nature, with the intent to build patient support and expand economic evidence of the value of products misleadingly labeled as “life style drugs”, in particular the new anti-obesity medicines mentioned above. In the latter case, it stands to reason that any delay of implementation of such (*pre*)marketing initiatives inevitably would have the potential to lead to significant opportunity costs for the respective manufacturers.

The Role of Health Economics

Originally, health and pharmaco-economic approaches were adopted by the pharmaceutical industry to defend prices perceived to be (too) high by paymasters and to demonstrate the value of its products. Accordingly, one of the first products to be evaluated in economic terms was Tagamet (cimetidine), the first drug to exceed the magic 1 billion US-\$ revenues threshold. The commercial success of Tagamet was reason for major concern to health authorities, sick funds and other third party payers. In a first series of “macroeconomic studies” sponsored by the developer and manufacturer, SmithKline, a marked reduction in surgery for peptic ulcer disease could be shown to be closely correlated with the availability of Tagamet (Fig. 9). As expected on the basis of clinical trials data on cimetidine, multivariate analyses supported the causal relationship of this profound effect with the use of cimetidine.

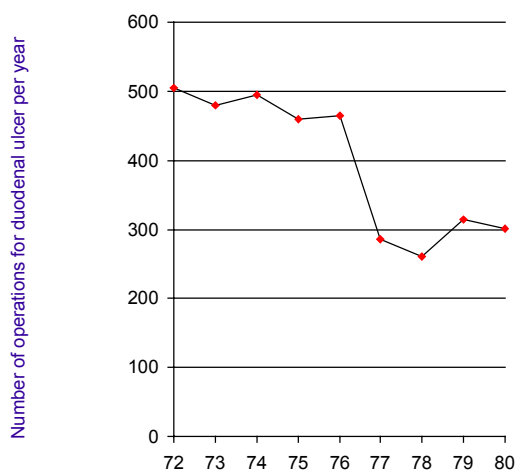


Figure 9: Surgery for duodenal ulcer during 1972 - 1980.

The introduction of cimetidine (Tagamet) in 1976 was followed by a marked reduction in the number of operations for duodenal ulcer. Data from six medical centers in the United Kingdom; source: Paterson, 1983; Drummond et al., 1988; Schlander, 1998.

Further “microeconomic studies” were conducted to assess the impact of Tagamet treatment on the level of individual patients. The computerized patient records of Medicaid in Michigan provided the data basis for the classic analysis by Geweke and Weisbrod (1982) who demonstrated that the higher cost of drug treatment for patients

receiving Tagamet was more than offset by the reduction of costs associated with hospital care (Fig. 10).

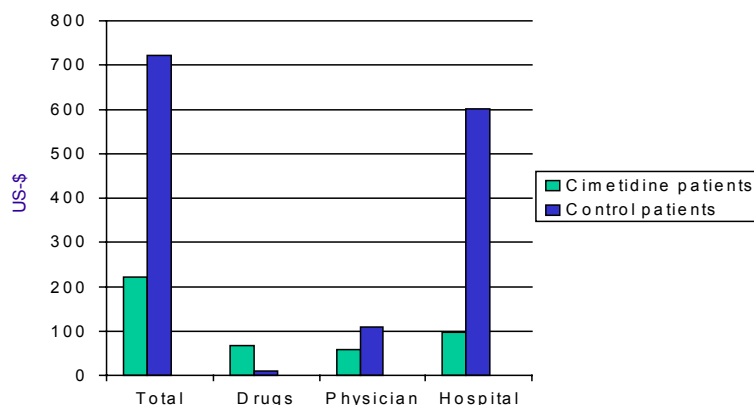


Figure 10: Medicaid expenses for duodenal ulcer patients (Michigan).

Geweke and Weisbrod (1982) used the computerized reimbursement records of Medicaid in Michigan to compare ulcer-related treatment costs for patients receiving cimetidine (Tagamet) with those of ulcer patients not treated with cimetidine.

Like other “blockbuster” products with very high revenues, Tagamet did not escape the effects of generic competition immediately upon patent expiry (Fig. 11).

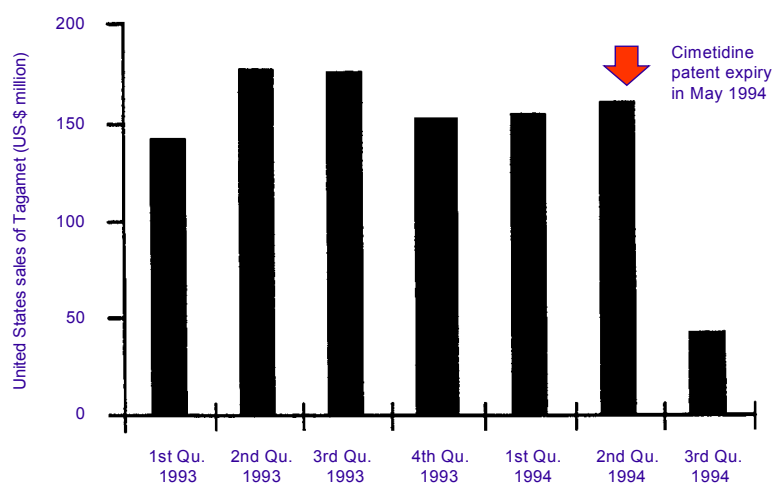


Figure 11: Tagamet (cimetidine) sales decline upon patent expiry

Quarterly United States sales data, by courtesy of SmithKline Beecham, 1995. Quoted from Schlander, 1998.

When discussing the role of health economics, however, it should further be borne in mind that only a small number of breakthrough products will produce such health economics benefits as have been found for Tagamet. Not only strategic considerations regarding relevant stakeholders and target customer groups will influence the usefulness of health economic evaluations. Often the profile of the product in question will determine whether or not pharmacoeconomic analyses can add real value (Tab. 2).

Table 2: Determining the need for an economic evaluation.

		Effectiveness		
		Lower	Equal	Higher
Costs	Lower	???	?	+
	Equal	-	-	++
	Higher	-	-	+++

In general terms, health economic assessments are not useful in the absence of clinically relevant features that differentiate the product of interest from its competitors. In that case price differentials and cost minimization calculations based on unit sales will provide the relevant answer. In contrast, economic evaluations will add helpful information if and when the new treatment has better effectiveness (a better efficacy / side effect ratio) than existing alternatives. In this case, the economic impact can be computed from the perspective of a given decision-maker or of society as a whole. Vice versa, the same models can be applied to calculate justifiable price ranges contingent on the perspective adopted.

Health economic analyses can help quantify the impact of clinical differences and translate that into monetary terms, but even the most sophisticated health economic models cannot substitute for clinical advantage of a new product. With price premiums in essence depending on clinical advantage, more than ever before effective research and development (R&D) will determine the prospects of research-based pharmaceutical companies (Fig. 12).

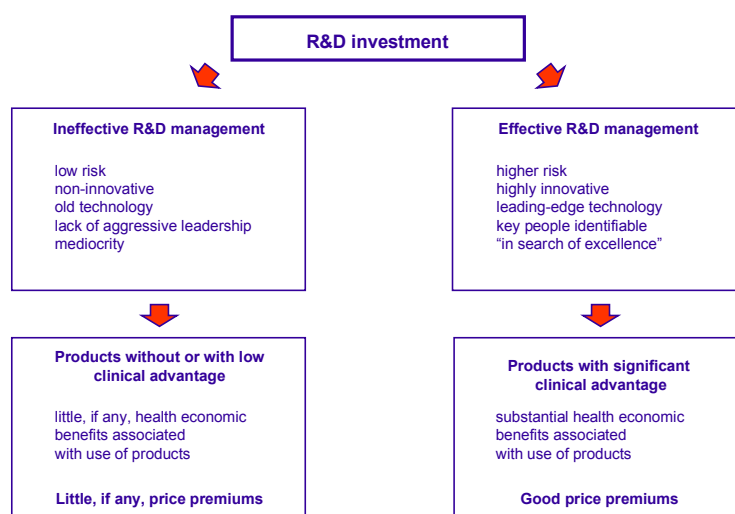


Figure 12: Effective R&D will separate winners and losers

The discipline of health economics can contribute to R&D portfolio management by assisting in the process of identifying therapeutic areas and projects with high commercial potential. In areas of large unmet medical need, the size of potentially emerging markets can be estimated on the basis of epidemiological data, the amount of unmet need according to type of cost - direct, indirect, intangible) incurred, and the anticipated willingness to pay for new treatments. This way, by quantifying the burden of disease and its various tangible and intangible components, health economic analyses will not only help increasing the effectiveness of R&D by better identifying and targeting commercial opportunities - rather the insights gained in the process of conducting health economic analyses will provide additional information as to the principle parameters of economic benefit to be documented throughout the

new drug development process. Beyond its contribution to strategy definition, health economics thus can provide practical guidance to clinical drug development.

Throughout the clinical development of a new drug candidate, economic analyses can be conducted, ranging from model development and the simulation of the likely economic impact based on the project hypotheses during phase I, feasibility studies during phase II, and the typical “piggyback” economic documentation usually done alongside phase III clinical trials (cf. Fig. 13).

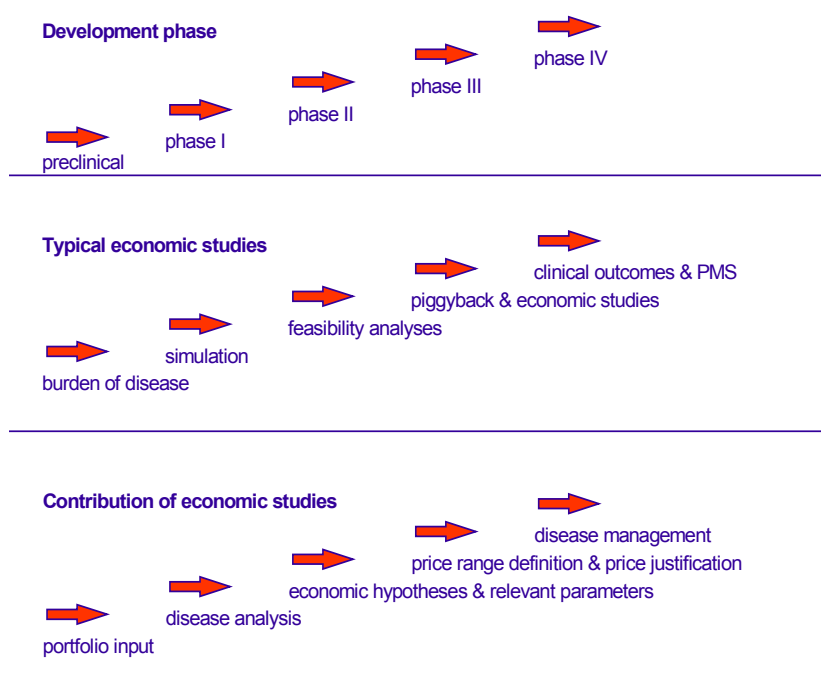


Figure 13: Economic assessments during clinical development of a new drug candidate.

The resulting contribution of health economics therefore includes five principle areas:

- effective R&D portfolio management;
- price range definition and price justification;
- highlighting opportunities associated with “disease management” concepts;
- strategic and tactical marketing support;
- helping management to influence (“enact”) its operating environment.

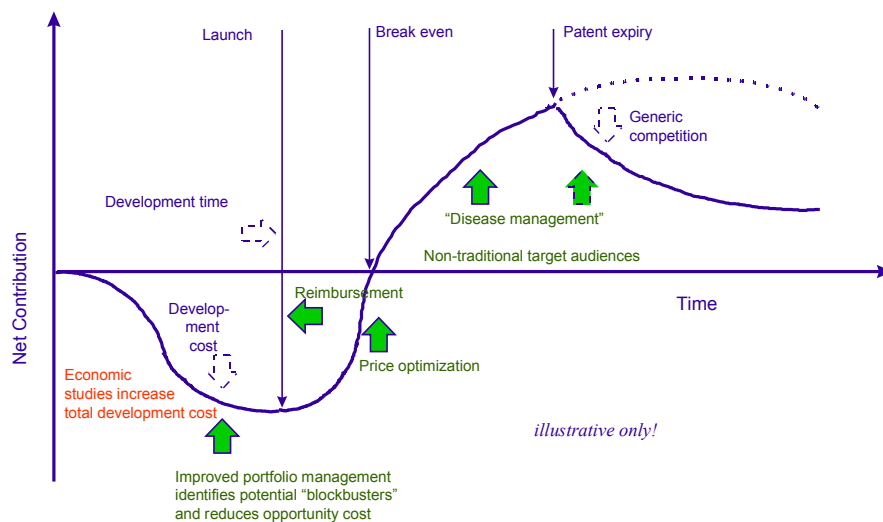


Figure 14: Health economics and the product life cycle.

Thus health economics can be expected to help maximizing the product life cycle from project definition through optimizing the development strategy, gaining reimbursement to marketing support (cf. Fig. 14). Further, at the corporate level and via industry associations, economic arguments need to be put forward to show the value of pharmaceuticals to society and thereby attempt to counter attacks on grounds of its perceived profitability.

Integrating Health Economics

In a recent study of twelve leading pharmaceutical corporations, conducted by Stemeroff et al. (1997), three models for implementing a health economics function were identified (cf. Fig. 15). As described above, most of the companies surveyed had started with a small department with tasks limited to the demonstration of “value for money” for existing products (“model A”, Fig. 15). These product-related data were intended to serve the purpose of defending presumably high prices.

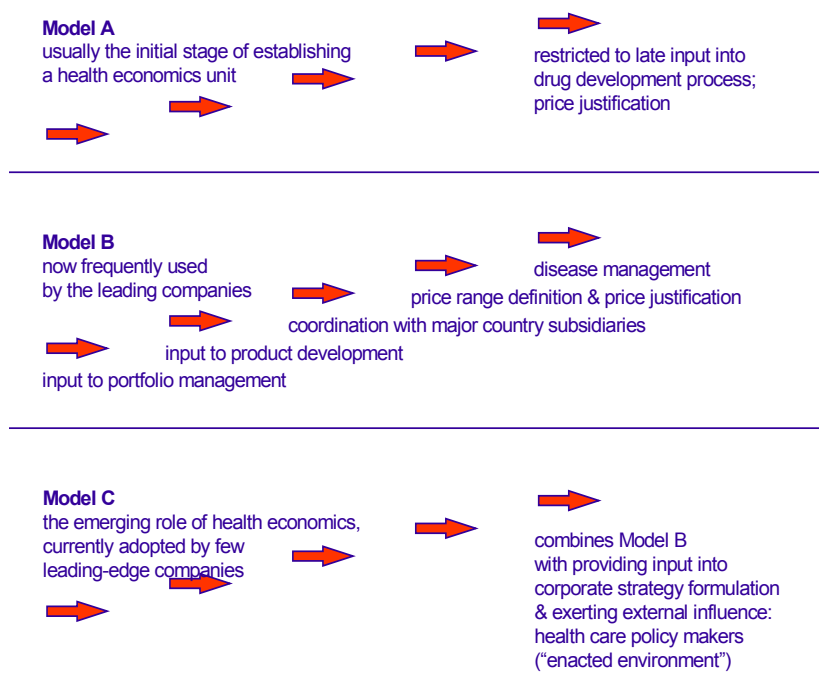


Figure 15: Contemporary approaches to establish a health economics function.

Most of the leading-edge pharmaceutical companies by now have proceeded to expand the responsibility of their health economics function to provide input to the portfolio management and new drug development process (“model B”, Fig. 15). To date, only very few companies have gone one step further and pro-actively involve their health economics departments in corporate strategy formulation and the definition of corporate positions in external health policy issues on a routine basis (“model C”, Fig. 15).

In light of its cross-functional nature, as laid out in this paper, pharmacoeconomics will be best located centrally, i.e. at corporate headquarters: the new discipline is influencing research and development, strategic marketing, local marketing and sales, and ultimately also corporate strategy formulation, and it is - or will increasingly become - critically involved in pro-actively enacting the operating environment of pharmaceutical companies. Vice versa, it requires input and expertise from all these fields (cf. Fig. 16), plus market research and pharmaco-epidemiology. With its strong commercial orientation and its consequences for business strategies, a health

economics function will be best placed in close contact with the board of international firms. At Janssen, this has been resolved by establishing a dual reporting line of the Health Economics & Pricing group. Other, in particular smaller companies are experimenting with different approaches, such as establishing a decentral health economics unit at local operating company level. Given the different focus of local as opposed to international management, however, local health economic expertise - while no doubt required - can only supplement a central group, but will not be able to replace it given its broad involvement in strategic decision-making to be effective.

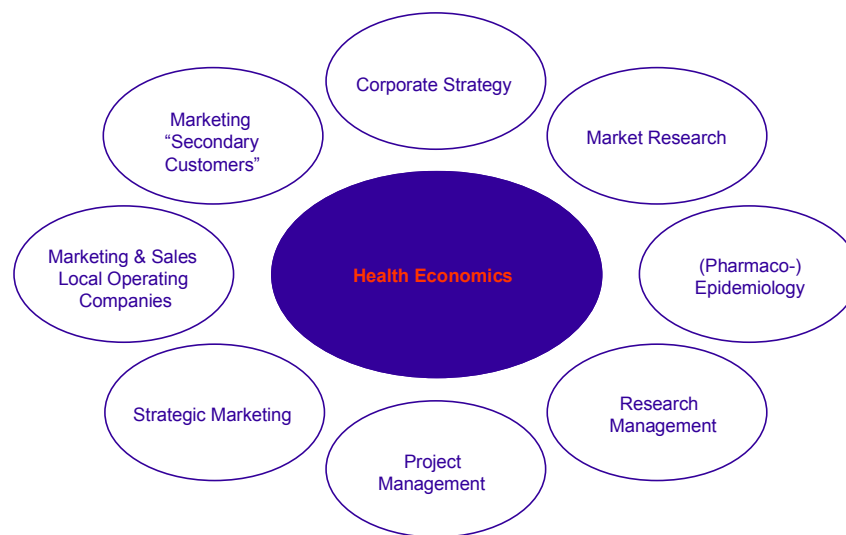


Figure 16: Health economics in relation to other organizational functions.

The impact of health economics on strategic decisions of virtually all critical functional areas will also lend justification to its integration in a high-level group responsible for strategic marketing, as it is, for instance, the case at the German company Merck KGaA. In particular, international strategic marketing departments have often been established to bridge the gap between research and development on the one side, and local more operationally orientated marketing & sales on the other side. As long as pharmaceutical companies have not found ways to effectively overcome their traditional functional organization by implementing horizontal, business unit and process oriented structures, while at the same time preserving their

core competence centers, integration of health economics into strategic marketing is likely to be the optimal approach.

Recommended Further Reading

Danzon, P.M. *Pharmaceutical Price Regulation - National Policies Versus Global Interests*. Washington, DC: The AEI Press, 1997 (107 pages).

Getzen, T.E. *Health Economics - Fundamentals and Flow of Funds*. New York, NY: John Wiley & Sons, 1997 (467 pages).

Johnson, N.E., Nash, D.B. (eds.). *The Role of Pharmacoeconomics in Outcomes Management*. Chicago, IL: American Hospital Publishing, 1996 (97 pages).

Schlander, M. *The Contribution of Health Economics to Market-Oriented Pharmaceutical Research & Development*. Witten, Germany: Universität Witten/Herdecke Verlagsgesellschaft, 1998 (240 pages).

Sloan, F.A. *Valuing Health Care. Costs, Benefits, and Effectiveness of Pharmaceuticals and Other Medical Technologies*. New York, NY: Cambridge University Press, 1996 (273 pages).