

Drugs and Money

SEVENTH
EDITION

Drugs and Money

Prices, affordability and
cost containment

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A.H. Rietveld



EUROPE

Published on behalf of the World Health Organization
Regional Office for Europe by IOS Press

IOS
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C.P. de Joncheere et al. (Eds.)

IOS
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Amsterdam • Berlin • Oxford • Tokyo • Washington, DC

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ISBN 1 58603 334 4 (IOS Press)

ISBN 4 274 90582 9 C3047 (Ohmsha)

Library of Congress Control Number: 2003101613

Publisher

IOS Press

Nieuwe Hemweg 6B

1013 BG Amsterdam

The Netherlands

fax: +31 20 620 3419

e-mail: order@iospress.nl

Distributor in the UK and Ireland

IOS Press/Lavis Marketing

73 Lime Walk

Headington

Oxford OX3 7AD

England

fax: +44 1865 750079

Distributor in the USA and Canada

IOS Press, Inc.

5795-G Burke Centre Parkway

Burke, VA 22015

USA

fax: +1 703 323 3668

e-mail: iosbooks@iospress.com

Distributor in Germany, Austria and Switzerland

IOS Press/LSL.de

Gerichtsweg 28

D-04103 Leipzig

Germany

fax: +49 341 995 4255

Distributor in Japan

Ohmsha, Ltd.

3-1 Kanda Nishiki-cho

Chiyoda-ku, Tokyo 101-8460

Japan

fax: +81 3 3233 2426

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PRINTED IN THE NETHERLANDS

Introduction

Drugs and Money

During recent decades, society has attached great importance to improved health, and has witnessed a fast rising demand for health care. As a consequence of that development, most, if not all, countries have found themselves confronted with the problem of meeting growing expenditure on health care. That additional expenditure must either be financed or it must in one way or another be constrained; both approaches will probably have to be adopted in parallel. Increased public spending may meet with macro-economic difficulties, while increased private spending will give rise to equity concerns. The growth and the ageing of populations, the widening range and complexity of available medical interventions and changes in society's expectations regarding attainable health and desirable health care all put pressure on the budget available for health systems, whether these comprise prevention, curative services or the provision of care for the aged or infirm.

The very rapid growth of expenditure on medicines is of particular concern and it has attracted considerable political attention, in part no doubt because it is a concrete issue which at first sight appears readily amenable to economic control. That first impression has often proven misleading; despite the impressive variety of cost containment measures which have been devised over the years, drug expenditure has remained high and as a rule it has continued to grow.

One of the complicating factors in this particular field is that in so many countries a regulated, collectively financed health care sector coexists with a free and profit-driven marketplace. Both are widely regarded as desirable and defensible, yet it is evident that where the two interact conflicts may arise; a country seeking to contain pharmaceutical expenditure will soon find itself imposing restraints on those very industrial and commercial processes which it is so anxious to promote. The countries of Central and Eastern Europe, currently transforming their centralized economies into market-driven systems, and with their frontiers now open to western products at western prices, have experienced these conflicts in a particularly acute form. They have struggled greatly to strike a balance between the one-time ideal of free health care and current concepts of free enterprise.

In their determination to contain pharmaceutical costs, while at the same time aiming at improved care and equitable access to medicines, countries have often implemented a series of measures in rapid succession or even simultaneously, readily seizing on and adopting what appear to be promising policies developed in neighbouring countries. The result can be a bewildering, complex and dynamic patchwork of interacting approaches. In that situation it can be as difficult to identify the causes of failure as to explain whatever successes are attained; there is rarely anything in the nature of a controlled experiment in cost containment, and it has therefore become increasingly difficult for one member state to learn from the experiences of others. In some instances, too, the feasibility or otherwise of a particular approach is determined by purely national factors. It can for example be tempting, in a country where the bulk of drugs are supplied by national manufacturing firms, to impose limits on their promotional expenses or profits; such countries are today however few and far between, and where one is dealing largely with

multinational corporations one generally has neither the insight nor the implements which one needs to institute such methods successfully.

Health care systems in Europe are largely based on the principles of health as a human right, on equitable access to health and health services, quality of health care, on solidarity, and on the active participation of society as a whole. Because of the difficulties associated with rising costs, however, it is today vital to translate those ideals into achievements which are quantifiable both in terms of health and of expenditure; only with the help of such exact information can one hope to develop defensible policies which balance initiatives against resources. The 2000 World Health Report presented an approach to measuring the performance of health systems; it looked broadly at indicators in the areas of health attainment, of fair financing, of responsiveness of the system, and the efficiency with which these goals are achieved. Other publications have considered specifically the means which are available to assess the efficiency and costs of pharmaceutical care, a theme which is reflected throughout this book.

Many member states have over the years approached the World Health Organization for advice or information on the feasibility of (generally short-term) measures to control the growth of expenditure on medicines. Such calls for help led the Organization as early as 1983 to conclude that there was an ongoing need among member states for guidance in the development of their national policies with regard to cost containment in this field. In that year the Pharmaceuticals Unit (PHA), now the Health Technologies and Pharmaceuticals Programme, of the WHO Regional Office undertook a study under the title "Drugs and Money"; it culminated in a deliberately concise report, providing a critical overview of the effectiveness of older cost-containment schemes while also paying attention to innovative ventures. The report was widely used and repeatedly updated, with its sixth edition appearing in book form in 1992.

This present seventh edition aims, as its predecessors have done, to provide policy makers and regulators with a compact and practical review of the various approaches which have been developed and tested to date in an effort to contain the overall costs of pharmaceutical services and drug treatment. New measures, enjoying a greater or lesser degree of success, have continued to emerge during the 'nineties and the end is not yet in sight. In this small volume particular emphasis is again placed on those principles which may prove helpful in containing costs without introducing a disproportionate risk of adverse consequences. The true art of good housekeeping in this field is clearly to ensure that drugs continue to benefit society wherever they can, while eliminating every form of waste of public funds.

Unlike earlier editions of "Drugs and Money" this volume devotes considerable attention to the special problems of developing countries and those where the economy is currently in transition. While lessons learnt in one type of national environment may prove applicable in another, it is important to realise that the situation in western industrialized countries still differs substantially from that elsewhere. Although the nature of the problem of cost containment may be the same, transitional and less-developed countries do not find it easy to adopt many of the solutions developed by western-industrialised countries. Conversely, some of the approaches which have been developed in the developing world would not be applicable to industrial society.

Throughout the years the World Health Organization has taken the position that the question as to how to provide access to medicines while containing their costs must be viewed as an integral part of long-term pharmaceutical policies. More broadly it is a part of overall health care policy and, more broadly still, a component of the entire economic and social policy of a country. The problem of cost containment of pharmaceuticals cannot be viewed separately from such issues as equity, market structure or the quality of therapeutic care.

The book is structured in such a way as to provide the reader with a logical line of reasoning progressing from the scope and causes of the cost containment problem (Chapter 1) through the means which

exist to examining and quantify it (Chapter 2), to an extensive consideration of the principal solutions which governments use to cope with the problem (Chapter 3) and to measure the impact of whatever measures are taken (Chapter 4). Actual experience with the most prominent of the methods used to date is considered in Chapters 6 to 13. In the last two sections of the book, special attention is devoted to the situation in developing countries and those undergoing structural transition. Although the various approaches to cost containment are in this volume necessarily discussed separately, they are in fact inter-linked and complementary; some overlap and cross-referencing between the various sections of the book is therefore unavoidable.

Last but not least, although the title “Drugs and Money” may to some suggest otherwise, government influence is not limited to the financing of health care, but extends also to the organization, standards and delivery of health care in all its forms. Many regulations concerning the intrinsic quality of pharmaceuticals, the quality of prescribing and the proper use of medicines have been introduced over the last four decades, and their influence is complementary to that of measures designed primarily to have economic effects in this field.

Developments in this field continue and are bound to expand further. The massive human and financial challenges presented by the HIV/AIDS epidemic could not have been foreseen when the first edition of “Drugs and Money” appeared twenty years ago. Nor however could the ongoing worldwide response, encompassing challenges to the entire issue of drug pricing and patents. For all that, many of the methods currently in use to contain costs in the field of pharmaceutical care have essentially developed from those which were first conceived in the 'eighties, and with which sufficient long-term experience has been gained in different environments to assess their strengths and weaknesses. It is to be hoped that this review of what has been done and what can be done to provide affordable pharmaceutical care will again provide a helpful guide to all those faced with the issue.

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December 2002

Part I

Problems and approaches to a solution

Chapter 1

Scope of the problem

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1. Equity

Most countries strive for some degree of equity with respect to the financing of pharmaceuticals, recognising the gap between the cost of drugs to the average patient and his or her ability to pay. They have therefore adopted health financing policies, often involving third-party payers, which are designed to ensure that patients have access to the medicines which they need, although the actual apportionment of the financial burden between society and the individual may vary (Fig. 1). Prevailing notions of culture, tradition and general ethics influence the latter.

In the United Kingdom, for example, all residents are covered by the National Health Service (NHS) and access to drugs is subsidised directly, leaving only a minor role for private health insurance and a nominal charge to be borne by the patient. In the United States, at the other extreme, health insurance is voluntary and in the hands of profit-driven private insurance companies, leaving only a residual role

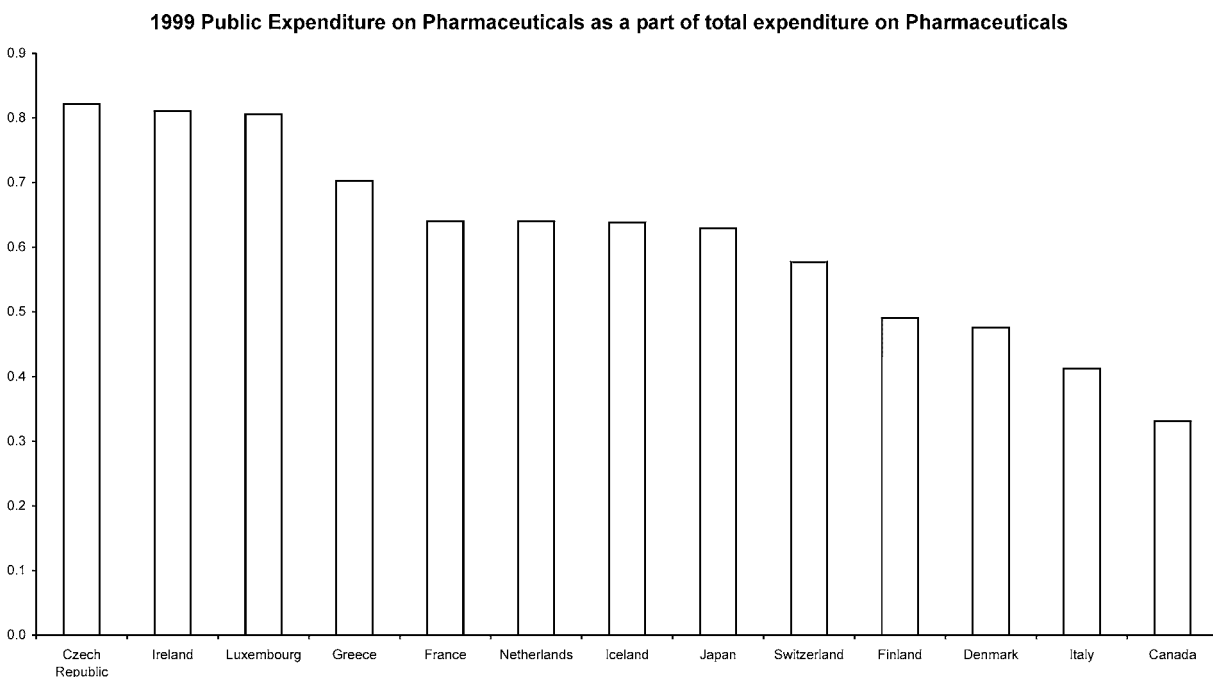


Fig. 1. Public expenditure as part of total pharmaceutical expenditures, 1999. Source: OECD data.

for public health insurance as a safety net for those not able to pay the insurance premiums. In effect, therefore, health insurance in the UK is government controlled while in the US it is market-driven with only minor involvement of government. By contrast one sees that developing countries, struggling with growing populations and diseases such as HIV-AIDS, often lack any form of health insurance; the financial burden of disease is carried by individual patients and their families, as a result of which patients commonly go untreated due to lack of money.

Despite these wide variations from country to country, a common element is the concern of the payer – public, private or individual – with the need to live within a limited budget; all budget holders increasingly demand value for money. Where funding is in the hands of an insurance system, whether it be public or private, one might in theory raise contributions or premiums to whatever level is necessary to meet expenditure, but in practice there is a serious risk that this will in its own way place an intolerable burden on the individual or the community. The end result may thus again be that the patient is deprived of necessary treatment.

The fact that both the prices of pharmaceuticals and the overall level of spending differ so greatly from one country to another fuels a continuing policy debate. Key discussions often relate to limiting the range of pharmaceuticals eligible for payment or reimbursement under an insurance system, and to proposals that even patients covered by an insurance system should be called on to carry some part of the financial burden themselves.

2. Cost containment

As a rule, patients have very little insight into the actual cost of providing them with health services. This is particularly the case where there is a system of collective financing; the patient is rarely confronted with the cost of whatever commodity or service he or she has received, and is inclined to believe that prices and payments are not his concern. On the other hand, the individual has considerable faith in innovation; new medicines can mean hope for many patients. The private sector responds by developing and bringing a continuous stream of new medicines to the market; it is often far from clear to what extent the prices of these new preparations really reflect the cost of their development, production and marketing, but it is clear that in many cases the manufacturer will attempt to set what is generally known in commercial circles as “the highest price that the market will bear”. In effect, where drugs are concerned, this usually means setting the highest price that the national insurance authorities are willing to tolerate. The negotiations to this end can be difficult and confusing, since the authorities commonly find it difficult to assess impartially in economic terms the ultimate benefit which the drug may provide, and they have little or no insight into the true costs which have been involved in developing the drug and putting it into production.

The market for pharmaceuticals is for various reasons not fully comparable to the normal competitive market in which other consumer products are sold, and in which the critical individual buyer is to a large extent able to ensure that he or she gets value for money. The inability of the individual to judge the merits of a drug, the fact that a patient's views may be governed by optimism rather than strict logic and the manner in which that choice is in any case largely entrusted to a third party (the physician) distort the market. The fact that governments find themselves obliged to intervene at many points distorts competitive market operation still further. In addition to specific safety nets intended to ensure access to drugs, countries have from the perspective of consumer protection introduced many regulations concerning the intrinsic efficacy, safety and quality of pharmaceuticals, as well measures to raise the

standard of prescribing and promote the appropriate (“rational”) use of medicines. These well-intended and necessary policies can nevertheless create on the one hand entry barriers for new market participants and on the other domain monopolies (e.g., for pharmacists and doctors). In addition, in seeking to contain the costs of drug consumption, countries impose price controls, limit reimbursement of drugs, de-list drugs considered non-essential, provide non-commercial sources of information, and interfere with wholesale and retail margins, and may even restrict the manner in which medicines are prescribed and used [1].

Some parties argue that it is largely the wide scope of government regulation which is responsible for the absence of price competition in the pharmaceutical market. These critics maintain that if this market were to be fully liberalized it would function properly like other consumer markets. This view seems to overlook the existence of the fundamental factors noted above which render the market in pharmaceuticals unusual; unhappy experience shows quite clearly that if this market is entirely unregulated the poor will be seriously deprived and both individual and community health will suffer. Nor is that view in line for example with the finding that, in particular when systems are based on equity, the absence of price control regulations is usually associated with high drug prices. In developing countries, where markets are usually less regulated, high prices of drugs are often a barrier to patients obtaining the drugs which they need, despite the fact that in theory a global industry should be capable of lowering prices selectively in poor communities in order to secure sales.

Price controls and other cost containment measures must therefore be seen as ways of coping with the problem of pharmaceutical expenditure. It is however not surprising, taking into account the progressive ageing of the population and the tremendous commercial pressures which are exerted (notably towards prescribers, but increasingly also towards the public) when new drugs come onto the market, that these official measures are not always as effective as governments would wish them to be.

3. Causes of cost increases

The reasons why the overall costs of pharmaceutical care tend to rise continuously have been well summarised by the National Institute on Health Care Management [7]. They are:

1. The replacement of older, cheaper medicines by newer, higher priced medicines.
2. Increases in the use of medicines
3. The introduction of new medicines for diseases for which hitherto no treatment (or at best a less effective treatment) has been available.
4. Increases in the price of existing medicines

Ad 1. The substitution of older, cheaper medicines by newer, higher priced medicines

It is estimated that in western industrialised countries about 70% of the annual cost increase of pharmaceuticals is due to expenditure on medicines introduced less than 5 years previously. These may be drugs for the treatment of diseases for which previously no pharmacotherapy existed (see above) but the great majority of new drugs do no more than provide an unexciting alternative to older (and usually cheaper) medicines. To give an example of these effects: if the treatment with a particular new medicine is ten times more expensive (which is the quite commonly the case) than the treatment with the older medicine which it is designed to succeed, the sum of money hitherto sufficient to treat ten patients will now suffice to treat only one. This phenomenon of artificial replacement is widespread; it is arguable,

Table 1
The Netherlands: Turnover of top 10 products in 1997

Product (Trade names in brackets)	Costs (mln dfl)	Increase (%)*	Increase in volume (%)	Price mutation (%)*
Omeprazol (Losec®)	292	19	25	(5)
Ranitidine (Zantac®)	90	(36)	(25)	(16)
Simvastatine (Zocor®)	198	24	27	(2)
Enalapril (Renitec®)®	97	0	11	(10)
Amlodipine (Norvasc®)	59	3	12	(8)
Budesonide (Pulmicort®)	75	0	2	(2)
Beclometason (Becotide®)	56	(10)	(7)	(3)
Fluticason (Flixotide®)	53	38	36	1
Paroxetine (Seroxat®)	64	37	37	0
Insuline (Mixtard®)	60	(1)	7	(7)
Total top 10 products	1043	6	11	(5)
Total costs reimbursed products	3902			

dfl = Dutch Guilders, approx. US\$ 0.50. Population: approx. 15 million.

*The price mutations in 1997 were predominantly negative because of the implementation of the Drug Prices Act in that year. This largely offset the cost consequences of the growth in volume during that year.

for example, that the great majority of patients with hypertension can today be treated adequately and safely with medicines which were available in 1970 or earlier, yet the machinery of persuasion provides an entirely different message. Since this process of replacement is continually taking place on a broad scale, the macro-effects on the growth of pharmaceutical expenditures are enormous; older medicines are crowded out by newer, and public money flows increasingly to the latter. In a sense, developing countries with their tight budgets are fortunately protected in part from this phenomenon, as a result of the “essential drugs” policies which continue to focus on what is good and necessary rather than on what is new. Industrialized countries enjoy this protection to a much lesser extent. Research in the Netherlands showed that in 1997 more than 25% of the total costs of pharmaceutical goods was attributable to the sales of only 10 products, the majority of these having been introduced fairly recently on the Dutch market (Table 1).

In order to contain the cost of pharmaceutical care, it is therefore necessary to control the influx of new medicines in the public system, as well as to control the reimbursement level and the prices of these products. New products should preferably only be admitted to the reimbursement system after a careful consideration of their added therapeutic value and the extent to which this justifies a rise in expenditure.

Ad 2. Increases in the use of drugs

Other things being equal, there is an almost consistent increase in the use of drugs in any population over time. That is due variously to growth in the size of that population, the ageing process, and changing attitudes towards the use of drugs. In 1996 in the United States individuals aged 25 to 44 filled an average of two to three prescriptions each year; those aged 65 and over filled approximately nine to twelve. While

the elderly represent only about 13 percent of the US population, i.e. about 34 million individuals, the US Senate Committee on Ageing found that they accounted for almost 35 percent of all prescriptions dispensed in the United States [10].

Increases in the use of drugs due to the expansion or ageing of the population are of course difficult to influence. However, there is also an increasing tendency in the population as a whole towards greater drug use. In part this may represent a spontaneous change in attitudes (e.g., a lesser willingness to tolerate illness or pain) but to a large extent attitudes both among patients and professions are clearly moulded by commercial pressures. There is heavy promotional pressure from the suppliers of pharmaceuticals, primarily on prescribers, but also on dispensers and users of pharmaceuticals.

As the primary aim of promotion is to increase the supplier's sales, it is evident that it has the potential to lead to waste, over-use and inappropriate use of medicines with a loss of quality in drug treatment as a result. Excessive or inappropriate use of drugs can undo much of the effect attained by even the strictest systems for setting prices and containing costs. Nor must one overlook the fact that considerable costs are involved in drug promotion. In the United States, pharmaceutical companies currently spend more than US\$ 11 billion each year on promotion and marketing. It has been estimated that \$8,000 to \$13,000 is spent per year on promotion to each physician [12]. Laing, using publicly available data in the US, found that "marketing and administration" costs greatly exceeded expenditure on research [2]. These costs will have to be paid for out of the turnover of sales and they therefore contribute to the high price level of drugs.

Commercial pressure on consumers was in much of the world confined until recently to the use of self-medication remedies, but there is now a movement towards direct promotion of prescription medicines as well ("Direct to Consumer Advertising", DTCA). The industry argues that communicating the facts to the public would improve the knowledge of the latter concerning the use of these products, thereby improving the quality of pharmacotherapy. There has however been powerful criticism of the content and style of such advertising both in the United States and New Zealand [3], and with good reason most other industrialized countries have been very reluctant until now to allow it, though a compromise may be engineered in countries of the European Union. As in the case of drug promotion directed at physicians, considerable costs are involved in DTCA, and these costs again contribute to the high prices of drugs. In 1999 some US\$ 1.8 billion was spent by pharmaceutical companies on DTCA, a rise of 38% over 1998 [8,9].

In order to prevent waste, over prescribing and inappropriate use, it is widely considered advisable to control the content as well as the form of promotion for pharmaceuticals. In any country there is need for an official set of enforceable standards, designed to ensure that promotion is truthful and that the information provided is both balanced and complete. This should be accompanied by public measures to promote the rational prescribing and use of medicines. Standard treatment protocols and treatment guidelines should be agreed and communicated to prescribers in an effective manner; in many countries these already exist – and provide an example to others – and it is striking how commonly the national associations of prescribers or general practitioners have played a role in their development and implementation. A high priority should be accorded to the development of drug information services to ensure that health professionals and the public receive reliable non-commercial information on medicines. The emergence of drug promotion and even drug selling through the Internet renders it even more necessary now than it was a decade ago to provide objective information as a counterbalance to the immense promotional pressures now exerted on doctors and patients to prescribe and use medicines in general and new medicines in particular.

Ad 3. The introduction of new medicines for diseases for which no prior or a less effective pharmacotherapy existed

Any true extension to the range and potency of drug therapy is in principle welcome, especially where a hitherto intractable illness or symptom becomes amenable to treatment. The introduction of anti-retroviral treatment for HIV-AIDS is an important and clear example. Every year a small number of breakthroughs in drug treatment, some more spectacular than others, can be recognized and will merit acceptance [6]. The challenge will be to distinguish these from the very many other innovations which, however forcefully they are promoted, have nothing significant to add to existing means of treatment and cannot be said to justify any increase in expenditure. At the same time, increasingly conditions are labelled as medically treatable, leading to additional pharmaceutical expenditures with often unclear outcome [5].

Ad 4. Price increases of existing medicine

In the absence of price control regulations or powerful large buyers (such a public health funds), the prices of prescription drugs tend to increase at a rate considerably greater than that of inflation [4]. In Brazil, following the abolition of price controls, the cost in dollars of each unit sold increased from \$4.68 in 1995 to \$6.26 in 1998 [11]. The number of units sold remained constant during the same period, indicating that the abolition of cost control had not improved the population's access to drugs.

4. Implementing cost containment programs

As pharmaceutical cost containment strategies touch upon the interests of many groups (industry, wholesalers, retailers, consumers, doctors, etc.), reactions sometimes amounting to forceful opposition are to be expected when such policies are proposed or implemented. Sometimes these reactions are based on misunderstandings which need to be countered with sound information. Fears as to the failure or possible adverse effects of a cost containment programme can for example often be allayed if it can be shown that similar measures have been successfully implemented, without doing harm, earlier in another country in a situation similar to one's own.

If support for such policies is to be obtained, and unjustified criticism defused in advance, a wide range of organizations and institutions need to be informed and invited to participate in the process. The best way to do so is to recruit them as participants at an early phase so that they can consider themselves in part responsible for the design and introduction of measures; at the very least they should be satisfied that their views have received a fair hearing.

In some countries *patient associations* and *consumers groups* are well established and their voices may prove to be an important political factor in the success or failure of cost containment policies. The *media* naturally influence and lead public opinion and their support too is very important for the success of the new cost-control program. In many countries professional bodies such as the *colleges of physicians* and *pharmaceutical societies* have over a long period been accorded particular functions in setting standards of professional practice and health care, or have in some other way become active players on the health scene; for such reasons their involvement and support are essential, and they can contribute creatively to the development and implementation of many types of new health-related policies. Greater credibility will also be accorded to any policy if it has been underwritten by prestigious *international organizations*, such as the World Health Organization and the World Bank.

The position of the *pharmaceutical industry* should be taken into account when the authorities plan to introduce new measures. It is clear that even fully justified policies may be criticized vigorously by industry if they impede its purely commercial interests, and that they will frequently have to be implemented in the face of such protest. On the other hand there are some situations in which caution is needed if one public interest is not to be sacrificed to another. While large multinational corporations are sufficiently resilient and flexible to adapt to restrictive measures, local firms in developing and transitional countries may much more susceptible. Industrial employment, income, exports and economic activity at large may be at stake, or even the continuity of supplies for essential medicines.

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Chapter 2

Data needed for developing and monitoring policies

Elias Mossialos and Monique F. Mrazek

To develop and monitor any aspect of drug policies – which naturally include cost containment – one needs to collect reliable and valid data on processes and outcomes. This chapter focuses on the data needed to detect and evaluate the impact of a drug policy on the different elements of drug management and delivery. Important variables relate to the various aspects of prescribing, dispensing and consumption, but also to the ultimate consequences in terms of health and finance. The types of data discussed in this chapter therefore include facts and figures on pharmaceutical expenditure, utilization, price, health and economics outcomes, as well as data on the pharmaceutical industry.

Since drug expenditure is determined largely by price, patient need and prescribing choice, data on expenditure can only be realistically monitored by taking these elements into consideration. The data needed in order to develop and monitor drug policies must therefore relate to a whole series of issues and actors. One needs to consider how these data can be obtained and examine some methodological problems that can arise in collecting and using them.

Monitoring alone will not explain the trend in drug expenditures, nor will it answer the question as to whether the level of expenditure is appropriate to meet reasonable goals in terms of health. It is therefore necessary to look beyond expenditure data and examine the changes in underlying trends in patient needs, prescribing choice and pricing. If we are to understand what factors create and modify a trend in drug expenditure, we shall need to look both at drug utilization and at prices. Expenditure data alone cannot, for example, differentiate a country with high unit consumption but low drug prices from one with high prices and lower levels of drug consumption.

1. Drug expenditure data

Monitoring pharmaceutical expenditure over a period of time makes it possible to determine the overall effect of cost containment policies (or other concurrent influences) on the size and growth of drug spending. Expenditure data can be expressed as a proportion of overall health care costs, as a percentage of national economic output (Gross Domestic Product = GDP) or as average *per capita* spending. When comparing expenditure on drugs as a function of total health expenditure, or as a *per capita* figure ratio, one finds wide variations between countries (Table 1). These relative expenditure levels and trends are used to make cross-national comparisons so as to understand better the relationship between structure and performance in different drug financing systems. It is particularly important to consider

Table 1
Pharmaceutical expenditure in selected OECD countries, 1997

Total expenditure on pharmaceuticals and other medical non-durables	% GDP	% Total healthcare expenditure	Per capita, US\$ exchange rate
Hungary	1.9 [†]	26.3 [†]	83 [†]
Greece	1.8 [†]	21.3 [†]	211 [†]
Norway	0.7 [†]	9 [†]	259 [†]
Portugal	2.1	26.9	216
France	2	20.9	482
Czech Rep.	1.8	25.3	92
Spain	1.5	20.7	207
Japan	1.5	20	492
Italy	1.5	17.5	296
Belgium	1.4	16.1	334
United States	1.4	10.1	406
Iceland	1.3	16.3	353
Canada	1.3	14.5	272
Germany	1.3	12.2	329
United Kingdom	1.1	16.3	244
Finland	1.1	14.9	259
New Zealand	1.1	14.3	188
Austria	1.1	12.9	272
Sweden	1.1	12.8	282
Australia	0.9	11.3	213
Netherlands	0.9	10.3	216
Korea	0.8	17	88
Luxembourg	0.8	12.6	311
Switzerland	0.8	7.7	284
Ireland	0.7	9.3	138
Denmark	0.7	8.5	225

[†] indicates 1996 data.

The consumption of pharmaceutical goods comprises both prescription medicines and self-medication products, often referred to as over-the-counter (OTC) medicines. The series includes the pharmacists' remuneration when the latter is separate from the price of medicines. Pharmaceuticals consumed in hospitals are excluded. The expenditure includes VAT and sales taxes where applicable. The amount of consumption in hospitals is included under in-patient care.

Source: [16].

drug expenditure data within the context of overall health care financing. Pharmaceutical services, like health care services generally, may be financed from public or private sources or from a combination of the two. Comparing trends in public versus private (including the over-the-counter market) drug expenditures gives an indication of the way in which the burden of drug financing is apportioned between individuals, society generally and different levels of government. Such differences in financing arrangements between countries should be taken into consideration when comparing trends; an apparent success in reducing public drug expenditure in a particular country is not necessarily praiseworthy if it proves to have placed an intolerable burden on individuals.

It is also useful for policy development to break down drug expenditure within the pharmaceutical service into its various components. Significant variations in drug spending between different groups within the service will sometimes (but not always) be attributable to population characteristics (services directed at caring for the elderly patients or the chronically ill will for example be expected to spend proportionally more on drugs). Again, different policy initiatives may have been directed to drug spending in in-patient care (hospitals) as compared with out-patient care (general practice physicians). Differences in the level of spending and rate of growth in each of these fields may be directly attributable to such specific policy initiatives [7] though one will always need to be alert to other concurrent influences.

1.1. Sources of data on expenditure

Ministries of Health or other government institutions in general report annually on national drug expenditure. Such sources, as well as those covering health expenditure generally, usually provide good coverage of the overall trend in public pharmaceutical spending. It is however often difficult to obtain complete data on drug expenditure which include (and differentiate between) in-patient and out-patient drug costs, prescription drugs and OTC, branded drugs and generic medicines, and spending in non-reimbursed and private pharmaceutical markets. National pharmaceutical industry associations often re-publish government data on expenditure in their annual reports along with other helpful figures. Commercial publications, such as *Scrip* and the *Financial Times*, occasionally publish national expenditure data.

One set of figures commonly used in making cross-national comparisons of drug expenditure in Europe is the OECD Health Database. The data generally cover both private and public pharmaceutical expenditure. However, as there is no cross-national agreement on statistical methods, the OECD data cannot be considered a standardised health statistic. The database is compiled from official government statistics. This limits its external comparability as variations between countries arise in terms of what is included in the calculations and how the categories are specified. Some countries are treated as special cases by the database because of variations in the characteristics of the population covered by the available statistics. In addition, limitations to the data arise because not all the information is up-to-date. At best, publication of annual expenditure figures usually takes a year. Figures from countries that have joined OECD only recently have not been fully integrated into the database. The quality and reliability of the data may also vary depending on what component of the data are being examined. For example, public expenditure data may be more accurate than information on private or out-of-pocket spending.

1.2. Methodological issues

The first methodological issue to consider when using expenditure data is how the figures have been calculated. Drug expenditure is dependent on both drug consumption and price. It is important to know whether expenditure figures include the consumption of both in-patient and out-patient prescription medicines, and whether they also include OTCs. Drug expenditure figures will also vary depending on where in the drug distribution chain the drug price and consumption volumes for the calculation were obtained; retail and wholesale prices are naturally higher than the manufacturer's price because of the intermediate mark-ups.

Three methods are commonly used to calculate drug expenditure. The first method derives drug expenditures from the *totality of receipts of pharmaceutical manufacturers or wholesalers* (excluding exports). Secondly, pharmaceutical expenditure can also be estimated from a sample of *prescriptions dispensed by*

pharmacies, provided we know the average price of a prescription. Finally, pharmaceutical expenditure can be estimated from the *sales of prescription drugs by retail pharmacies to the public*.

When comparing data over time, or between countries, it is important to make sure that they are measured in the same way. For example, data should be measured at the same point and time in the distribution chain, should comprise the same segments in terms of hospitals and out-patient care, prescription and self-medication, and should cover either total, public, private or out-patient expenditures. Again, when monitoring pharmaceutical expenditures over time, or between countries, the figures used should be real (constant-price) and not nominal (current-price). Studies of “real” pharmaceutical expenditure from year to year involve taking the costs for a baseline year and adjusting these for the subsequent effects of inflation on drug spending before making any comparisons with later years; this provides a true picture of the manner in which the cost burden on the community is changing. “Nominal” comparisons simply set the data for the baseline year alongside that for the years which follow, and therefore reflect both the effect of inflation and real changes in costs.

When comparing drug expenditure between countries a common measure needs to be used. One approach is to select a common currency unit. The problem with using a common currency unit is that bias may be introduced due to exchange rate fluctuations. What is more, exchange rates do not reflect the relative purchasing power between countries because they do not take account of the equalisation of prices of non-marketed commodities such as health care [12].

A similar degree of caution is needed when expressing pharmaceutical expenditure per capita using a constant dollar exchange rate. Here, although measuring pharmaceutical expenditure *per capita* provides a relative indication of consumption by adjusting for population size, the measure may be confounded by a number of factors including the purchasing power of the currency, and differences in the price at which a given product is sold in one country or another. Nor does this method necessarily provide a valid estimate of the changes in the burden borne by the individual as patients may have different combinations of private and public coverage, pay different amounts out-of-pocket, or may be exempt from all charges.

To eliminate differences in price levels between countries, pharmaceutical expenditure can be converted to a common currency using rates of currency conversion called purchasing power of parities (PPPs). PPPs convert currencies in such a way that the purchasing power in different countries is equalised to purchase the same basket of goods and services in all countries. The resultant comparisons provide a better picture of the real differences in the quantities of goods and services purchased. This is generally the recommended approach for cross-national comparisons. However, in using PPPs caution should be exercised as to their calculation: weak points are that the consumption functions for PPPs are in general only calculated every 5 years; what is more, health service costs are inevitably measured on the basis of a very small sample of prices and on weakly comparable volume indices [12]. Therefore, when using PPPs for international comparisons, not only may the composition of the baskets differ between each country particularly for health care, but in addition different values may be attached to the components of the basket in each country.

Pharmaceutical expenditure can be also expressed as a percentage of GDP, defined in the OECD Health database as the total domestic expenditure plus exports and less imports of goods and services. Monitoring pharmaceutical expenditure as a percentage of GDP provides a relative indication of how much a country is spending on pharmaceuticals as compared to its economic status. However, using GDP as a denominator introduces a bias because, as the figure is a ratio, there is a risk of confounding changes in pharmaceutical expenditure with fluctuations in economic growth. Again, GDP expressed in national currency units indicates only how much of the economy is spent on pharmaceutical goods, but says nothing about the purchasing power of a country.

Other common units of measure include drug spending as a percentage of total health expenditure; this gives a relative indication of resource use within the health sector. When examining this measure over time, it is important to distinguish rises and falls in health expenditure generally from rises and falls in pharmaceutical expenditure; the two may not run parallel.

2. Drug utilisation data

Drug utilisation research throws light on the medical, social and economic consequences of the marketing, distribution, prescribing and use of medicines [20]. Utilisation data are both quantitative and qualitative. Patterns of drug utilisation can be used to determine how variations in need, prescribing choice and price account for differences in drug use in different countries [10].

The consumption of prescription medicines in a given population is closely related to a number of factors: its demographic structure (notably because older people use more drugs), to the incidence and prevalence of disease, to its socio-economic structure, to the nature and extent of health care coverage, medical culture [17], marketing by the pharmaceutical industry, as well as prescribing and dispensing incentives and regulations. By examining population characteristics, epidemiological data, and figures on the frequency and severity of illness one can arrive at an estimate of drug consumption, and therefore what allowance should be made for drug expenditure in health planning. However, it is important to note that the calculated level of reasonable need for prescription medicines will not necessarily correspond to the actual level of demand. If a patient does not seek medical intervention, demand will be less than need, and the resources used will be less than those estimated in advance. Conversely, if people buy drugs for which there is no reasonable need, whether under the influence of commercial persuasion or any other factor, demand will exceed need.

2.1. Sources of utilisation data

In many situations, valid and reliable sources of utilisation data are not readily available. Sources of drug utilisation data include commercial and administrative databases, but only certain of these are designed in such a way that they capture the data needed for drug utilisation studies.

Data from commercial survey organisations such as Intercontinental Medical Statistics (IMS)¹ rely on sales figures as indicators of drug use. Figures are collected from manufacturers' and importers' records providing for a relatively complete coverage of the market. IMS also provides data based on samples of prescriptions from panels of pharmacists and physicians in each country. Analyses of sales data of this type have however primarily been designed for commercial purposes; various variables that are essential for assessing the appropriateness of drug use in a population are missing.

Administrative databases collect information on users of a particular system or sets of systems in order to meet the needs of health service providers. Typical examples of administrative databases include those compiled by bodies dealing with prescription payments or reimbursement schemes. These are increasingly complemented by databases that link diagnostic data with prescribing data (such as the General Practice Research Database in the UK, for more info on the database see <http://www.gprd.com>). By using such sources one can obtain extensive and detailed information on prescribing, dispensing, administration and the management of drug treatment in the public health service. One will find detailed figures

¹IMS is an organization that collects data on pharmaceuticals, chemicals and other healthcare matters in sixty-two countries. IMS has a near monopoly in the collection and distribution of international pharmaceutical sales figures, which are sold commercially to the pharmaceutical industry.

on the level of use of particular drugs and classes of drugs, the quantities and doses prescribed, the price paid, and as a rule some information on the type of patient or indication for which the treatment has been given. It is also possible to detect trends to switch from one drug to another within a given therapeutic category, such as may happen where a new compound has been marketed or where the recommendations in a formulary have been changed; as noted above, these can be matters of considerable financial significance.

There are, however, major caveats associated with the use of these large computerised administrative databases [18]. Data compiled on the basis of public insurance or reimbursement schemes often do not collect data on drug consumption funded by private insurance or by the individual. Problems may arise in the use of these large databases because of non-randomly collected comparison groups; they may also present problems because of incomplete or inconsistent reporting, under-coding or coding errors. As a result studies using these data must be critically analysed and cautiously reported.

2.2. Methodological issues

The reliability of comparisons made using drug utilisation data is dependent upon the use of a common drug classification scheme and unit of measurement. The WHO Regional Office for Europe has, since 1981, recommended the ATC/DDD system for international drug utilisation studies [19]. The Anatomical Therapeutic Chemical (ATC) system classifies drugs at five different levels of detail and provides for a unique identifier (Table 2); using this one can deal with a drug as an individual item, with all drugs having the same field of use, or with the entire therapeutic class to which they all belong. The Defined Daily Dose (DDD), which is the unit of measurement of drug use, is the assumed average dose per day for each active ingredient when it is used in its main indication for adults (it is based on an adult dose with the exception of preparations that are exclusive to children). This average dose selected for the DDD system is based on recommendations in the literature, the manufacturer's advice and experience with the product. The DDD does not necessarily reflect the recommended or Prescribed Daily Dose (PDD) for any individual patient or patient group, but using it as a utilization unit does provide the best means available for expressing consumption levels, particularly when making comparisons between prescribers, regions or countries.

Measuring the volume and the costs of drug use in terms of DDDs solves the problem of allowing for differences in prescription, duration of treatment or the potency of individual preparations. For example, it is possible to compare diabetes treatments between two centres, even though one may be using primarily (injectable) insulin with its potency measured in units and the other an oral antidiabetic drug dosed in milligrams; both types of drug have their own Defined Daily Doses and the number of DDD's used can be compared directly. It would not be possible to make that same comparison if the two drugs were

Table 2
Drug classification system. Example: Classification of Diazepam

AT		ATC	
N	Central nervous system	N	Central nervous system
N05	Psycholeptics	N05	Psycholeptics
N05A2	Tranquillisers	N05B	Tranquillisers
		N05BA	Benzodiazepine derivatives
		N05BA01	Diazepam

Source: [2].

to be measured in terms of common physical units (the number of packages, tablets, or injections) or the number of prescriptions written.

Consumption within a geographic region, expressed as DDDs/1000 inhabitants/day provides a rough estimate of how many patients receive a standard dose per day. Alternatively one can express annual consumption levels in an entire country in terms of DDD per 1000 inhabitants per year; Lecomte and Paris [13] used this measure to identify differences in overall pharmaceutical consumption in Germany, France, Italy and UK. Others have chosen to express their data in terms of DDD per average inhabitant per year, while when considering levels of in-patient drug use, DDDs prescribed per 100 bed days is a helpful measure. Provided one ensures that the same measures are used throughout a study, one can choose the form of DDD measurement that is most convenient.

Even when using the DDD, some caution may be needed in drawing conclusions regarding the data that emerge. A number of studies have for example found variations in the quantity and cost of prescribing between individual prescribers from different geographic areas (see review by Bradley [1]), and it is all too easy to assume that some of these physicians are over-prescribing or under-prescribing; in fact one will need to know more about the patient populations involved (e.g., their age and socio-economic breakdown) before jumping to such a conclusion. This particular issue of differences in use between age and socio-economic groups needs to be tackled critically. A crude means of standardising the populations concerned by giving weights to older versus younger patients has been proposed but it is not reliable. A more accurate adjustment for demographic differences may involve taking into account proven differences in drug needs between both the various age groups and the sexes [14]. The most important element to bear in mind however is that even such adjustments are only approximate, and that one should never draw conclusions as to the rationality of prescribing patterns from crude drug utilisation data.

3. Data on pharmaceutical prices

Drug prices differ, sometimes very substantially, between countries, even within the same economic area. Data on pharmaceutical prices can be compared both nationally and internationally. They serve both as a measure of the effect of different regulatory policies on the cost of pharmaceuticals, and as a reference for setting national drug prices. Here again however one has to be sure that the figures are reliable and that the comparisons made are valid.

The *reliability of the absolute figures* is generally not in doubt but one must ensure that they are measured at the same level and in a comparable manner (i.e. price may be expressed at the retail, wholesale or ex-manufacturers level, it may relate to smaller or to larger packages and in some cases a company may set one price for the private sector and another for a public health care system). Nor is it not unknown for the price charged at a particular level to be influenced downwards by a form of subsidy or upward by the imposition of taxes or duties.

The *validity of any comparison* will depend on one's taking sufficient account of the reasons why drug prices differ from one country to another. The manufacturer's own price-setting policy is obviously one determinant, and differences in price may in that respect reflect overcharging in some countries. However, government and insurance policies also play a role. The aim in negotiation may be to secure prices which are the very lowest attainable, or there may be some willingness to allow leeway for adequate input into research and development or to ensure sufficient income for retail pharmacists or dispensing physicians.

3.1. Sources of data on pharmaceutical prices

Data on drug prices from country to country often prove surprisingly difficult to obtain, though some of the figures can be extracted laboriously from sources such as National Formularies and reimbursement tables. Detailed pricing data are not readily available from government sources for use by researchers or other outside agencies, though in general, governments do publish average price data. In 1988, recognising the limited availability of drug price data, the European Community attempted to compile a data bank of drug prices and other basic product information from Member States. The data bank was intended to interface with a variety of national databases. That initiative led to the development of the European Community Pharmaceutical Information Network (ECPHIN), set up by the European Commission's Joint Research Centre. ECPHIN was supposed to provide a complete description of the medicinal products authorised by the European Union including price and reimbursement rates. This proved too ambitious, and by 2001 plans for ECPHIN had been abandoned.

Commercial database organisations such as IMS (see Section 2.1 above) collect detailed drug pricing data. Their information includes prices at ex-manufacturer, wholesale and retail price levels. IMS does, however, acknowledge that price data are audited and adjusted to represent the whole market. It is difficult to verify the reliability and accuracy of this database since it is one of the few sources of detailed drug price data.

3.2. Methodological issues

Any attempt to express the overall price level of drugs in a particular market must be based on figures for a sample of products. The validity of any overall conclusion or comparison regarding price levels is obviously dependent on how this "basket" of products is constituted. To be representative of the market as a whole, the basket should include a random selection of brand name, generic and OTC products. If international comparisons are being made, the samples for all the markets being compared should ideally be matched in terms of manufacturer, active ingredient, dosage form, strength, pack size and brand name. A standard unit of measurement and classification such as the ATC/DDD system described in the previous section should be employed.

Constructing a truly ideal product basket as a basis for international comparisons is unfortunately often impossible. The range of products available varies from one country to another. Even if the same product is available it may not be made by the same manufacturer in all the countries which are being compared, or it may not everywhere be supplied in the same pack size, dosage form or strength of active ingredient. It is also important to consider how well the products selected represent national consumption patterns in the countries concerned.

As noted earlier, it is also essential that comparisons be made between prices at the same level of distribution chain. As medicines move along the distribution chain from the factory, to the wholesaler, the pharmacist and finally to the consumer the price of the drug will rise to reflect the value added along the way. The consumer price of a pharmaceutical is generally composed of four parts: an *ex-factory price* paid to the manufacturer of the products; a *wholesaler's margin*, a *fixed tariff or margin for pharmacists*; and whatever *taxes* may be applicable. Variation in the consumer price of medicines in between countries in Europe is attributable to differences in the ex-factory price (ranging from 87.5 per cent of the consumer price in the UK to 49.9 per cent in Greece), the wholesaler's margin (12 per cent of the consumer price in the Netherlands but only 3.2 per cent in Sweden), the pharmacist's margin (33.4 per cent in Ireland yet no more than 5 per cent in the UK) and the value added tax (zero in Sweden, UK, Austria, Ireland but

20.3 per cent in Greece) [3]. These data illustrate how marked these variations from country to country are, even within this closely integrated economic area.

A further complication when one makes comparisons is that in particular situations the prices charged may differ from the norm. It has already been noted that a company may charge different prices in the public and private sectors. In addition special discounts may be offered to bulk drug purchasers such as hospitals and retail pharmacy chains, and such discounts may or may not be passed on to the ultimate payer. Where these practices are widespread they can significantly affect the actual figures, both as regards true margins and consumer prices.

As with comparisons of expenditure data, when comparing drug prices between countries the position of any one country relative to others is likely to depend in part on how the comparison is made. Again one approach is to compare the *actual prices paid* in each country, transposing them into a common currency using current bank exchange rates. Such comparisons using a common currency unit are subject to complications of exchange rate fluctuations. They have the additional disadvantage that they provide no indication of the extent of the burden which these prices represent for the communities or individual concerned. For example, even a high absolute price may be relatively affordable in a country where earnings are similarly high. For this reason it can be more informative to compare price levels per country in terms of the actual PPPs.

When such studies are conducted over a period of time, it may be possible to detect trends in prices and to compare these trends from one country to another, again using a standard “basket” of representative products and applying a price index to it. For each country the index should measure the changes in the expenditure required to obtain the standard range and quantity of the drugs in the sample [4]. Using indexes alone to make comparisons between countries avoids the complications introduced by exchange rate conversions, and the local levels of inflation do not distort the comparisons. Consequently, it may be possible to conclude for example, that the burden of drug costs has risen less rapidly in one country than another. Again one must be aware that such a comparison requires that the pharmaceutical basket remains representative as time goes by, and this is not easy to ensure. Similarly, when constructing indexes it is difficult to take account of the effect of new drug introductions, the sometimes rapid change in the mix of drugs actually being prescribed, and developments in drug quality [11].

4. Health outcomes data

Data on health outcomes is required to develop, monitor and evaluate pharmaceutical policy. The types of health outcomes data commonly collected includes mortality and morbidity data, as well as data on health related quality of life (HRQL). Morbidity data can include both measures of actual and perceived disability.

HRQL is in general measured using multi-dimensional health status instruments, either psychometric or utility/preference instruments. Psychometric health status instruments measure health status along multiple domains and are either disease-specific (e.g., Skindex for skin diseases) or generic measures (e.g., the Sickness Impact Profile). Alternatively, preference weighting can be assigned to health states that reflect individual and population preferences for different health states. Quality weights can be assigned to health states using several methods: the rating scale, the standard gamble, and the time trade-off (TTO) are the most common techniques. Each health state is then combined with a time score in order to determine the number of Quality-adjusted-life-years (QALYs).

Deciding on the health outcomes to be measured depends on several things: potential differences in patient populations related to the main effects of the intervention; any side-effects or unintended consequences; and outcomes of interest depending on perspective taken (e.g., patient, third-party payers, society) [9, p. 84]. There may also be differences in the selection of health outcomes depending on whether our interest is clinical or economic. For example, health outcomes that are needed for economic evaluations may be final outcomes (e.g., rapidly of cure), while those of clinical interest may be intermediate outcomes such as changes in blood pressure. It may also be important to collect data on the frequency or probability of given outcomes.

4.1. Sources and methodological considerations of outcomes data

Outcome data can be routinely monitored and collected as indicators of policy performance. If outcome data are to be used as part of an evaluation it has been recommended that the primary data be collected from randomly controlled trials (RCTs) [6], but this represents an ideal which is not always attainable. Although the most unbiased evidence on outcomes comes from RCTs, these may lack precise data on some of the clinical end-points that are relevant to a given situation because they were designed to answer clinical questions rather than economic ones (e.g., efficiency may be a very different matter from effectiveness when conducting economic evaluations). RCTs clearly have a high degree of internal validity but it may not be possible to generalize from them to real world settings. It may simply prove impossible to collect from an RCT the data which are needed for monitoring and evaluating health outcomes associated with policy changes.

Alternatively prospective observational and descriptive studies can be used to generate data on outcomes. Both observational cohort and case-control studies can generate probability data of particular outcomes associated with an intervention; however, both types of observational studies are more prone to bias than RCTs (e.g., where patients are not randomly assigned, or questions of recall bias arise in case-control studies) [15, pp. 146–147]. Health outcome data can also be generated from administrative databases but the same caveats discussed earlier in this chapter apply.

5. Cost data on programmes or treatments

There are different ways of considering cost. In its basic accounting form cost equals the number of resources used multiplied by the unit cost. Costing in this way requires that all resources used by a particular programme or treatment be identified and valued. However, to economists “cost refers to the sacrifice (of benefits) made when a given resource is consumed in a programme or treatment” or in other words the opportunity cost [5, p. 54]. The value of opportunity forgone in the next-best alternative use of the resources do not necessarily equate to the market prices of the resources used (e.g., patient time). The total costs therefore comprise the sum of all expenditures or opportunity costs during a given time frame. It is difficult to make adjustments to costs that reflect the opportunity cost of the resource used; for that reason the pragmatic approach often adopted is simply to use the market prices for these resources.

Costs which may be measured should cover the *direct* costs incurred by the health care provider and (or) the patient (i.e. costs of hospitalisation, physician services, pharmaceuticals, etc.). *Indirect* costs to society of the productivity lost (e.g., due to the patient seeking care or costs resulting from disability or premature death). Data collected may also include *intangible* costs borne by patients in terms of pain and suffering; their inclusion is subject to debate [8, p. 189]. There is an ongoing debate on how to measure direct costs (i.e. marginal, variable, fixed, average, capital and shared costs), whether to included indirect

costs and what the best way may be to measure opportunity cost. (See Drummond et al., 1997, Chapter 4.) There is also debate over how to measure unrelated future costs [9, pp. 45–48]. The implications of these debates are discussed further in Section 2, Chapter 5.

The purpose and type of analysis undertaken will determine the categories for which cost data will need to be collected. For example, hospital costs may involve identifying costs of services, facilities and overheads, while community costs may involve costs associated with visits to GPs, nurses or other health professionals. From a third party perspective one may want to consider actual charges rather than costs because often third parties do not cover total health care costs. As regards patients it is important to place a value both on their time and that of their family, as well as to take into account any out-of-pocket expenses incurred. In such matters, however, it can be important to assess the relative importance of a cost item to the overall outcome since the cost of including some minor costs may not be justified by their significance in the total picture.

There is also a decision to be made about the precision of the cost data to be collected. Micro costing includes each component of resources used and a unit cost for each. Costs can also be collected according to the case-mix group (i.e. the type of case category or patient). Per diem costs can also be collected as an average of all categories of patients or for each disease category.

5.1. Sources and methodological considerations of cost data

The collection of cost data includes not only the collection the prices of the resources used but also the quantity of resources used. As with health outcome data, cost data can also be collected from Randomised Controlled Trials. The problem with obtaining costs from these RCTs is that, as noted above, they lack external validity and instead of reflecting costs associated with regular patient management and resource use, the costs obtained from RCTs may be protocol-driven.

However, in many cases cost data will be collected either from routine sources (such as administrative databases) or by acquiring specific primary data collection (i.e. in observational studies). Both data on prices and costs are often based on accounting costs or service prices. It is important to be aware of level data collection as for example, the retail price of medicines is often different than that obtained in a hospital setting. Cost data can be estimated from chart reviews, administrative databases or reviews of other hospital and medical records. Cost estimates for non-market items can be estimated using market wage rates (i.e. for volunteer time); for items which are difficult to value (such the leisure time enjoyed by the patient or his family) the estimate may be set at zero and then adjusted using sensitivity analysis (see below) to examine impact.

Alternatively cost data can be collected from other published literature. This is also useful for identifying key costs. The problem with these is that they can vary considerably between different settings. Practice variation in for example facilities or services used, nursing time etc. can account for a number of differences from place to place. Variability also arises in estimating future costs. To overcome such variability sensitivity analysis is used. Sensitivity analysis is the process of repeatedly using different values for probability and utility values in order to assess the degree of uncertainty associated with a result. Inferences are also made from other studies.

It may be necessary to ask patients directly for information (e.g., number and length of time of home visits by health professionals). Missing data can be estimated using meta-analysis to combine results from other studies. Alternatively assumptions can be based on expert opinion and then tested using sensitivity analysis. If data is collected from different sources then it will be important to use simulation models to combine the data and take account of the variation.

In collecting data it is important to define the time horizon (i.e. short-run constrained by fixed resources versus long run where all inputs are variable). Resources may change over time and data may be limited to certain time horizons. Often data is limited to the trial period and estimating future costs requires either calculating survival within a given period of the trial (usually set at 5 years or less) and then either discounting costs during the time of the trial or extrapolating events and costs beyond the period of the trial [8, p. 191].

6. Information relating to the pharmaceutical industry

Up to this point we have considered solely the data required to examine the efficient use of pharmaceutical resources within the health care system. It is however, also important to monitor and take into account data on the pharmaceutical industry, which in many countries forms a significant part of the manufacturing sector and as such contributes to a country's overall economy. Successful development and maintenance of a domestic pharmaceutical industry can have a very positive effect on a country's trade surplus, particularly in terms of foreign earnings and balance of trade. The interest of the health sector in regulating pharmaceutical expenditure, prices and profits may therefore have to be balanced judiciously against national economic interests. The latter will comprise the need to provide sufficient incentives and opportunities to preserve and develop an industry with a solid financial base, capable of effective innovation and sustained growth in the long-term.

Data are therefore required to calculate the contribution of this industry to the economy as a whole. This will include monitoring the industry's trade surplus, the volume of exports and the number of people employed. It is also important to monitor the investment of the pharmaceutical industry in R&D projects both in its own laboratories and externally at universities and clinics, or through other joint ventures such as those with biotech companies. Successful innovation can be monitored through the level of patenting and the success in commercialising innovative technologies. Finally, data on the environment in which the pharmaceutical industry is operating can be relevant; they will include figures and information on the availability of resources, the presence of related and supporting industries, and the availability of skilled labour. All these various forms of information will contribute to a view on the achievements and prospects of the national pharmaceutical industry, and the extent to which its interests should counterbalance those of containing pharmaceutical expenditure.

One of the best sources of data on the national pharmaceutical industry is usually the national industry association. National associations of pharmaceutical manufacturers publish in their annual reports numerous facts and figures which are intended to promote the industry, but which can be valuable in assessing its situation. Commercial databases such as Datastream or those compiled by the IMS contain company-specific financial and commercial data. Annual reports from individual companies are also useful. Other industry specific information available in publications such as the *Panorama of EU Industry* published by the Eurostat, the statistical office of the European communities, and reports issued by the European and International Federations of Pharmaceutical Manufacturers' Associations. However, with all of these aforementioned data sources, there is really no way to verify its validity.

7. Conclusion

This chapter has focused on the types of data needed to develop and monitor drug policies. Whether using data on drug expenditure, utilisation, price, health outcomes or on the pharmaceutical industry

there are a number of common issues which should be taken into consideration particularly when making regional or international comparisons. It is important to be on the lookout for those characteristics of the pharmaceutical scene that are inevitably unique to each country, and to take them into account so that they do not invalidate comparisons. As pointed out in Section 3 above, for example, comparisons should be made using a common unit of measurement, matched samples and data from the same point in the drug distribution chain. In the past, too, bias has been introduced into some comparisons because of the limited availability and dissemination of good quality data on prices, volumes and outcomes outcome data. It is important that these and other possible sources of error raised in this chapter be addressed if data are to be obtained and used effectively to monitor and inform future policy development.

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Chapter 3

Policy options for cost containment of pharmaceuticals

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1. Introduction

In providing universal access to health care, a sound basis for the structural financing of national health care systems is of utmost importance. Cost containment can be seen as an ongoing series of attempts by governments to spend their limited financial resources as efficiently as possible.

Essentially, there are three ways in which one can hope to control pharmaceutical expenditure:

- Controlling prices of medicines at various levels.
- Influencing demand by implementing financial measures, such as budgeting and reimbursement.
- Influencing demand by implementing professional measures.

In this chapter, an overview is provided of the different options available. The key features, strengths and weaknesses of the various initiatives are discussed. In the subsequent chapters examples will be given of selected experiences with different approaches.

2. Price controls

2.1. *Reasons for price controls*

Drug prices are high for four primary reasons. *Firstly*, rigorous standards to protect the public from poor quality, unsafe and inefficacious drugs require manufacturers to invest in expensive research and development programmes. Those drugs that pass the standards are priced so that a company obtains a return sufficient to cover its investment in the drugs themselves, the costs of the drug research projects that failed, the costs of promotion, investment in future research and development and still yield the shareholders an attractive dividend. *Secondly*, there are certain factors which tend to create monopolies. One such factor is the quality standard already referred to, which imposes significant entry barriers for new market participants. Alongside patent protection it allows pharmaceutical companies to build up monopolistic positions within important segments of the pharmaceutical market. Products that improve health are relatively inelastic commodities, and strong demand enables the monopoly holder to command a high price. *Thirdly*, third party payers, rather than the patient, pay for drugs, making the consumer less price sensitive. *Fourthly*, as with all products of which the consumer has no real understanding, he or she tends to judge the quality and perhaps also the efficacy of a drug on the basis of its price: a higher price

is thought to indicate better quality and, vice versa, a low price (as in the case of generics) is believed to signify a lower standard.

In the market for more typical consumer products, the “fair” price of an item is the result of an ongoing process of negotiation between the supplier and the user. The outcome of such a process depends on the strength of the parties involved relative to each other. In the pharmaceutical market, by contrast, there can be no real negotiation between the patient and the supplier of drugs. The patient is simply not in a position to enter into such negotiation, as he would (either individually or by contributing to market resistance) when buying another type of product.

Free pricing of pharmaceuticals is, as has been pointed out in Chapter 1, usually associated with high price levels. The retail price of a medicine is not determined by the real costs of its development, production and distribution, but as with any other commercial products by what the market will bear. From the perspective of safeguarding universal access to health care, it is however necessary that prices be kept at reasonable levels. Most European countries, even those that at one time maintained a system of free pricing, have therefore implemented some form of price control.

It should however be borne in mind that price control measures are just one of the instruments available to governments to contain the costs of the health care. A sound pharmaceutical cost containment policy comprises a mixture of the varying instruments and it refrains from interference whenever this is feasible.

It is not realistic to assert, as is sometimes done, that over-zealous price controls are generally likely to push prices down to levels that are too low to deliver a profit and to finance research and development. That may well have happened incidentally in the case of a particular drug in a particular market, but across the board the process is one of give and take; the parties put their cards on table, compromises result, and what a company loses on one drug it is likely to gain on another. Especially in the larger markets, companies are quite capable of standing firm to ensure that their earnings are adequate; if pressed beyond the limit in such a market a firm can always choose to withdraw a product from sale rather than trade it at a loss. There are however no signals that western countries have in fact pushed prices down to such low levels.

2.2. *Methods of price control*

Several alternative methods are used to contain the prices of pharmaceuticals. All these methods have in common that regulators attempt to calculate a price for pharmaceuticals which is “correct” or “fair” to the various parties concerned.

Prices can be controlled at different points in the chain:

- (1) At ex manufacturer level;
- (2) At ex importer level;
- (3) At wholesale level;
- (4) At pharmacist level.

Usually combinations of these approaches are used. Examples can be found of systems in which the ex manufacturer/ex importer prices are regulated while the maximum margins allowed to wholesalers and pharmacists are simultaneously fixed. One also encounters systems in which only the pharmacy selling prices are regulated, while manufacturers, importers, wholesalers and pharmacies negotiate with each other on their charges and margins.

The most difficult step in developing any price control system is the establishment of a “fair” price. As stated above, in a market for more typical consumer products, the “fair” price of an item is the result

of a negotiating process between the supplier and the user. Consumer markets are usually transparent and it is possible to obtain information on product characteristics and to compare prices. By contrast, pharmaceutical markets are often characterized by monopolies or oligopolies, while the user generally has insufficient insight into products and prices. If it is not possible to compare prices with those of other comparable products, it becomes very difficult indeed to know what a “fair” price is. However a number of methodologies have been developed to calculate fair prices; five such methods will be described below:

- (1) Cost plus calculations;
- (2) Profit ceilings;
- (3) Comparative pricing;
- (4) Price negotiations;
- (5) Pharmaco-economic calculations.

Again, combinations of the different methods are as a rule used.

2.3. Price control at ex manufacturer/ex importer level

2.3.1. Cost-plus systems

The cost-plus method usually involves complicated calculations with respect to the costs of production of individual products and, allowing a certain profit margin, thereby arriving at a justifiable price level for these products. The pricing authority needs extensive and reliable information about the costs and margins of companies. Regulators can demand such data, but they may well find the information supplied by companies difficult to verify. Costs and margins are not independent of company policies: the basic costs of production, research and marketing may vary considerably between companies. Where the company with which one is dealing is a daughter firm of a multinational concern, it can be well-nigh impossible for the outsider to obtain any reliable overview of where and how costs are being incurred and profits taken. Furthermore, there is the problem of allocating overhead and research costs to individual products.

Cost-plus systems are usually rather static, creating problems for regulators and companies, as the prices of individual products cannot be promptly adjusted to changes in market conditions. There are no incentives for companies to increase efficiency and introduce cost-saving innovations. In some of the former Eastern Block countries, the cost-plus method has had detrimental consequences for the local pharmaceutical industry due to the reluctance of regulators to compensate for their R&D and marketing costs, thereby weakening their competitive position relative to that of foreign producers.

In an environment in which economies are much more open and much less predictable, and where companies have to compete with other (foreign) firms such systems have become ineffective and administratively too complicated to apply (although some countries still maintain variants on the method).

2.3.2. Profit ceilings

In this method the pricing authority sets a ceiling on the return on capital (sometimes on sales) for the company as a whole. In Europe only the United Kingdom operates a voluntary profit maximization system, the so-called Pharmaceutical Price Regulation Scheme (PPRS), in which the government negotiates with individual pharmaceutical companies on the amount of profit that can be made through selling their products to the National Health Service.

Although profit control schemes are associated with the same problems as the cost-plus method, profit control systems can be more flexible as the profitability of a company as a whole is controlled, rather than the margins on individual products. The greatest difficulty, as with the cost-plus approach, arises with

multinationals and their far from transparent earnings and costs; it is significant that the British PPRS scheme operates in a country where a substantial part of the market is still in the hands of domestically based producers.

2.3.3. Comparative pricing systems

In comparative pricing systems the prices of identical or similar products marketed in certain other countries are compared to the prices of products on the domestic market. A growing number of countries (e.g., Portugal, Romania and The Netherlands) have implemented comparative pricing systems. Several methods are in use. Some countries compare price *increases* in drugs in order to determine permissible price increases for domestic products. Other countries require companies, when bringing new products to the market, to supply information on the prices for these products in selected foreign countries. A more comprehensive model involves comparing the prices of all (reimbursed) products on the market with the prices of similar or identical products in other reference countries.

Comparing prices of medicines between countries can be difficult due to methodological and data problems. *Firstly*, it may be difficult to identify entirely identical medicines due to differences in brand names, pharmaceutical forms and unit strengths. *Secondly*, the prices in different countries may be hard to compare due to differences in the margins allowed to wholesalers and pharmacies, differences in VAT and so on. *Thirdly*, there may be obstacles in obtaining accurate and up to date data on the prices of medicines abroad. *Fourthly*, depending on the type of comparative pricing system that is chosen, extensive computer hardware and software may be necessary to operate the system. However, experience shows that by using the right comparator one can solve these problems.

The system used for setting prices in The Netherlands is an example of an advanced comparative pricing scheme. Maximum permissible prices of pharmaceuticals are set by calculating an average wholesale price for medicines on the basis of the prices of comparable products in Belgium, Germany, UK and France. Medicines are considered comparable when they have the same active ingredient, the same unit strength and a comparable pharmaceutical form. Prices are compared at the pharmacy buying level, net of Value Added Tax (VAT). When this system was implemented in 1996, prices of pharmaceuticals on the Dutch market fell by on average of 20%.

2.3.4. Price negotiation models

In the pharmaceutical market the individual patient is, as already noted, in a too weak a position to enter into negotiation with the supplier of drugs. Furthermore, as it is the prescribing doctor who decides on the drug and since the patient usually has some form of insurance, the patient may not be very price sensitive. This lack of price sensitivity is further increased by the consumer's incomplete knowledge concerning drugs. Institutional buyers such as hospitals, health insurers, regional and national governments, on the other hand, have more technical expertise and information than do individuals and are, due to budgetary constraints, sensitive to the prices of drugs. Furthermore, due to their size and resources, they can exercise considerable bargaining power, and are capable of negotiating prices with the supply side of the market. Negotiation on prices is made easier for buyers when (generic) substitutes are available. In those cases where a pricing authority negotiates on behalf of a large group of people or for a major market, the bargaining power can be considerable. In most European countries, virtually no market for pharmaceuticals exists outside the social health care system and often pricing authorities can refuse to admit a drug to the reimbursement system if they consider that the price is too high. Negotiation can also take place in a decentralised manner, being handled by hospitals and other health care services, provided they have the organisation and incentives (e.g., budgetary constraints) to act in a cost conscious manner.

Some bodies, mainly in the public sector, use tender systems. This is often the case when vaccines are purchased for immunization campaigns or when drugs are bought for the armed forces or to provide a strategic reserve. In developing countries, tendering is commonly used to cover the needs of hospitals and primary clinics for essential medicines.

An example of a negotiation model can be found in France, where the government controls prices through direct negotiations before the launch of a product. In the United States, Health Maintenance Organisations (HMO's) negotiate on the prices of the drugs which they purchase. In varying degrees the element of negotiation can be found in most systems, since regulations usually allow some room for interpretation.

Even the bargaining power enjoyed by large public buyers naturally has its limitations. Especially in cases where the supplier has a monopoly due to patent protection and the product fulfils a health care need (e.g., the treatment of a previously incurable disease), the supplier is in a strong bargaining position to impose prices on the buyer. A good example of this is the market for HIV-AIDS drugs. Suppliers may also refuse flatly to accept low prices where there is a clear risk that a product sold at an exceptionally low price may "leak" into another market through parallel importation, thus undermining a company's consolidated income and profits. There is also the possibility of a spill-over of low pricing to other countries that have implemented comparative pricing systems.

2.3.5. Pharmaco-economic evaluations

Pharmaco-economic evaluations are new as a tool to control prices. In essence, regulators (or other purchasers) try to establish "fair" prices on the basis of complicated calculations, taking into account the costs of other treatments, the costs of disease for society and so on. The costs of a drug are thus set against its direct and indirect benefits, as compared with alternative drugs and treatments, and its possible disadvantages and risks. The essential question is how much the drug is worth to the community.

Currently a number of countries (Australia, Canada, Finland, Norway, UK, The Netherlands) are using pharmaco-economic evaluation, experimentally or definitively, as an additional tool in the decision-making process regarding the pricing and reimbursement of medicines; one of the most developed of such systems is that applied by the Australian Ministry of Health.

Although attractive as a theoretical model, the outcome of pharmaco-economic calculations seems to be rather dependent on the use and misuse of a drug when actually marketed. Various assumptions (e.g., about future use) have to be made when making these calculations. Although in some aspects promising, the science of pharmaco-economics must still be considered a developing field in which a lot of debate is going on [25]. The data needed and some of the methodological issues are discussed in detail in Chapters 3, 4, 8 and 9. Australia seems to have proven that one can operate a system like this if one has a first class group of experts. However, like other countries Australia is not immune from other pressures; recently strong political pressure, clearly resulting from the pressures exercised by pharmaceutical industry on politicians, has succeeded in undermining the composition and the work even of this eminent body of experts.

2.4. Price control at the level of the wholesaler and the pharmacy

2.4.1. Limiting distribution margins

The costs associated with the distribution of drugs consist of the mark-ups of the wholesalers and the pharmacies. Distribution margins are usually regulated, as they contribute considerably to the consumer price of drugs; these margins can represent more than 40% of the price ultimately paid.

Limiting wholesale margins

Limiting the wholesale margin can be achieved either (1) by allowing the wholesaler a maximum margin for its services, or (2) by setting a maximum for the price at which the wholesaler can sell a product to pharmacies. A combined approach can also be adopted in which a maximum is set for the total distribution mark-up; wholesalers and pharmacies then have to negotiate with one another for their share of this mark-up. An example is Romania, where a maximum is set for the total distribution mark-up, with subsidiary provisions setting a maximum margin for the wholesaler and a minimum margin for the pharmacy within this total mark-up.

Limiting pharmacy retailing margins

Systems of remuneration for pharmacies fall into two classes, the one being product-orientated and the other patient-oriented [15]. Many systems are in fact hybrid schemes, in which elements of both approaches are used.

Product oriented remuneration systems for pharmacies can be divided in three categories:

- (1) *Fixed margin systems*: a fixed percentage mark-up is added to the wholesale prices of all dispensed medicines. This principle is widely used in competitive retailing systems, both in the USA but also in more tightly regulated systems such as exist in Europe. In European markets, mark-ups are generally fixed and are re-negotiated periodically with governments. Retail mark-ups on prescription drugs vary but are usually around 30%. Most countries refrain from regulating margins on OTC drugs, since for these the rules of the free market apply much more clearly than for prescription drugs. A pitfall with fixed margin systems is that the pharmacist may negotiate discounts on the wholesale price of a drug, thus increasing his gross margin without consumers necessarily benefiting by lower prices (although in some countries – like the USA – part of such a discount is indeed reflected in a lower consumer price). Some countries have therefore introduced systems to recover these discounts (e.g., the “claw back” system in the UK and The Netherlands) to the benefit of the National Health Service or its equivalent. Other countries, such as Denmark, have simply forbidden wholesalers and pharmacies from offering or accepting discounts.
- (2) *Mark-ups may be maximised instead of fixed*. This variation is inspired by the thought that third-party payers may negotiate lower margins and consequently lower prices with wholesalers and pharmacies. The effect of this negotiation will however depend on the respective bargaining powers of the parties; in practice therefore, maximisation of the mark-up will not *per se* lead to a reduction in the consumer price. One of the arguments used against systems exerting such pressure on the retailer is the risk of lower quality service, such as a reduction in stock levels for high priced but essential medicines. In order to prevent a loss of service quality, countries may impose additional requirements on pharmacy operations (such as an obligation to deliver any drug within a given time frame).
- (3) *Mark-ups may be digressive*: here the percentage mark-up decreases as the price of the drug increases. Usually the main purpose of digressive margins is to make it less attractive for the pharmacist to dispense high priced drugs than low priced drugs. The structure of margin rates differs greatly among the countries which have adopted such systems. Usually the rate differences take into account specific domestic price structures and consumption patterns.

The *patient-oriented systems* for remuneration of the pharmacist can be divided into two categories, although combinations may be used:

- (1) *Capitation systems* in which the pharmacy receives a fixed sum per patient per year. This sum may be digressive depending on the number of patients per pharmacy. In capitation systems it

is usually necessary to ensure specifically that pharmacies do not place an additional mark-up on the drugs they dispense. As in other systems, combinations of approaches may be used, e.g., so that alongside a capitation fee an additional margin on dispensed products contributes to the pharmacy's remuneration.

The purpose of capitation systems is to make the remuneration of the pharmacist as far possible independent of the volume and the price of the drugs dispensed. Although in theory capitation systems for pharmacies are effective in achieving this, in practice (as with the fixed margin systems) pharmacies may receive discounts on the price of the medicines they buy. It has proved difficult to prevent this as discounts may take many shapes and forms and are therefore usually difficult to detect. Furthermore, if a pharmacy is involved in wholesaling or if a wholesaler owns a pharmacy, discounts may be transferred to the wholesaling operation. Some countries, notably Denmark, have responded to the problem by forbidding the offering and acceptance of discounts altogether. Other countries (The Netherlands and the UK) have introduced systems to "claw back" these discounts to the National Health Service or its equivalent, thereby using the bargaining power of pharmacies as a tool to attain additional price decreases.

- (2) *Fixed fees per prescription.* In these systems the pharmacy is paid for its activities by a fixed sum per prescription dispensed. As in capitation systems, the purpose of a fixed fee per prescription is to make the remuneration of the pharmacist as far as possible independent of the volume and the price of the drugs dispensed. Again, as in capitation systems, a fixed fee per prescription system renders it necessary to prohibit pharmacies by regulation from placing an additional mark-up on the drugs which they dispense.

3. Reimbursement measures

3.1. Positive lists

3.1.1. The concept of a positive list

A list of those medicines eligible for reimbursement is usually called a positive list. The opposite of a positive list is naturally a negative list, specifying those drugs which will not be reimbursed. The National Health Service of the United Kingdom maintains a negative list on which about 129 substances are placed. An important advantage of a positive over a negative list is that separate decisions have to be made to add new drugs to the list. In addition, because of pressures exercised by user groups, transferring drugs to a negative list is usually politically more difficult than maintaining a limited positive list to which only selected drugs will be admitted.

The existence of an approved list of reimbursable medicines is regarded as an important tool in improving the quality of care as well as in containing the costs of pharmaceutical care. Experience in many countries, both in Europe and the developing world, strongly suggests that limitation of the range of reimbursed drugs can be achieved without depriving the population of valuable therapeutic opportunities. Norway, for instance, had until a few years ago only 600 drug substances on the market, and achieved the same pharmacotherapeutic results as other countries with many times more registered drugs on sale. According to EU regulations, no restriction on the number of drugs on the market is permitted, and member states have therefore usually followed an alternative course by limiting the list of those drugs for eligible for payment under a national health service or public reimbursement system. From the therapeutic point of view, the selection of drugs available on the market is in most industrialised countries so broad that considerable limitations can be imposed without creating any real threat to patients' interests.

3.1.2. Global and national lists

Although there may be differences between countries with respect to medical culture and the prevalence of certain diseases, it is today well established that the drawing up of a uniform drug list sufficient to meet normal health needs is entirely feasible. The success of the model list of “essential drugs” agreed under the auspices of the World Health Organization is a case in point. Although its main purpose was not to support cost-containment – it has always been intended as a minimum list to meet the principal health needs of a community with very restricted resources – it has shown the way to the compilation of drug lists which reflect the needs of a population. It is striking that the WHO Model List has been so widely adopted, with only minor modifications from one country to another. Although in an industrialized country with a well-developed economy a somewhat wider range of drugs will generally be regarded as justifying payment from the public purse, the principle is the same; one is defining a common core of needs which will very largely be the same in different communities; alternative drugs or more recent drugs which offer no particular advantages but generally cost more, will have no place on the list.

3.1.3. Establishing a list

Each country has direct responsibility for developing and adopting a list of essential drugs, according to its own policy in the field of health; such variations as occur from one country to the next are likely to reflect the need to make special provision for regional or rare diseases, or differences of medical opinion as to the importance of minor differences between drugs. There are however some basic rules, regarding the list and the organisation around it, that should be applied in order to make the use of a positive list effective. In particular, the criteria for drug selection should be objective and transparent, their application consistent and the criteria should be laid down in a law or other form of regulation. They will tend to be similar to those developed by WHO in drawing up its model list of essential drug list, and laid down in the Organization’s relevant Technical Reports [29,30]. The *first* decision to be taken by any country is which classes of treatment are to be financed collectively: is the disease for which a particular drug or class of drugs is intended of such a nature that patients should have universal access to the treatment? Tuberculosis and rheumatoid arthritis clearly fall within the category of disorders for which the community should fund therapy; the common cold may well be considered to fall outside it. The *second* decision is which individual drugs or therapies for a disorder are to be paid for, out of the various alternatives available. As a rule of thumb one should be restrictive in reimbursing new, more expensive medicines that are meant for the treatment of diseases that can already be treated with existing products; new products which are not more effective and/or encumbered with fewer side effects than well-tried older drugs should not be reimbursed. Furthermore, where equally effective alternative drug treatments are available, the least costly alternatives should have preference for reimbursement purposes. Where new drugs appear to have advantages over existing drugs, a careful assessment is necessary as to whether these advantages are relevant. If the answer to this question is affirmative, the issue is whether these advantages merit the price difference with older drugs and consequently inclusion on the positive list.

A positive list should specify drugs under their generic names, and not by their brand or speciality names. Medicines intended for the treatment of minor, self-limiting diseases should in principle not be on the list; this rule will usually exclude from reimbursement products clearly intended for (and suitable for) self-medication, such as simple antacids and cough syrups. When drawing up the list, one would do well to concentrate in first instance on excluding such items, and on the elimination of those products that have already been criticised as useless or superfluous by official publications or by the medical profession itself. Well-known textbooks and bulletins on drug treatment will provide particularly useful guidelines.

Meeting the criteria for admission to the list should not lead automatically to reimbursement. The available budget and the financial consequences of a proposed reimbursement list will have to be set against one another before the list is accepted.

3.1.4. *Updating*

A systematic procedure for updating the list is necessary. This is likely to entail dealing with representations from the health professions, patient organizations, and commercial firms with new products, all of whom will be likely to present arguments for adding items to the list. As the decision on reimbursement should be based on the added value of a certain product, it is clear that the main criterion for addition will be true and useful innovation; an innovative product can only be added to the list if from the perspective of health care there is an objective need for such a product. As implied above, not every new product is sufficiently novel to attain this standard; merely presenting a new structure, a new mode of action, an improved dissolution time or a longer duration of action does not mean that the new drug is necessarily more reliable, safer or simpler to use than those already on the list. The question whether a given product is or is not covered by patents plays no direct role in its eligibility for reimbursement, though the fact that a patent brings with it a degree of monopoly is likely to be reflected in a demand for a high price, and it is this price which in turn must affect the decision for or against inclusion in the list.

3.1.5. *De-listing of drugs*

A problem frequently experienced, especially in western-industrialised countries that have already operated positive lists for a considerable length of time, is that the criteria for admission to the list are not applied consistently or with sufficient strictness, as a result of which expensive drugs are added which do not in fact offer real therapeutic or other benefits as compared to older items. At the same time the list becomes ever longer as new drugs are added, and since most of the additions relate to new and costly items the value of the list in containing costs tends over time to decline.

This necessarily raises the question of removing items from the list. From time to time a drug will cease to be eligible because it has in effect been supplanted by a better alternative at reasonable cost. This may be the case (as in the situation where drugs are removed from WHO's Model List of Essential Drugs) because a new generation of drugs is so superior to older products in terms of efficacy or safety that the latter have to be regarded as obsolete. It can however also happen that the price of a drug on the positive list is increased to a point where it is no longer commensurate with its merits; in that case, the authorities will need to insist on a return to a lower price, or to replace the product on the positive list. Not surprisingly, any attempt to remove an established drug from the list of reimbursable items is likely to prove unpopular, both with its manufacturer and with those physicians and patients who are accustomed to using it. When de-listing drugs, it is advised to follow the same principles as when creating a positive list: the criteria for de-listing drugs must be objective and transparent, their application consistent and the criteria should be laid down in a law or regulation; drugs should be de-listed by generic name. When de-listing drugs, it is again best to concentrate in first instance on elimination of those products which are widely agreed to be useless or superfluous.

Medicines which have been released for over the counter (OTC) sale, i.e. items likely to be used in self-medication, should as a principle be de-listed although exceptions may be made; listing should probably be maintained for a drugs which also retain important prescribed uses in the treatment of major diseases or where there is a substantial risk that de-listing will result in a shift in prescribing to more expensive or more potent drugs simply because these remain reimbursable. Such a shift could impair the quality of pharmaceutical care.

3.1.6. Structure and procedures

In order to structure the decision making process around the positive list efficiently, a formal advisory committee can be established. It should consist of medical and pharmaceutical experts, and have ready access to internationally recognized experts in the field of clinical pharmacology who can be consulted when necessary. This committee will on request provide advice as to whether particular products meet the criteria for reimbursement. The committee may also be accorded the task of periodically revising the drug list and make proposals for deleting obsolete items.

Companies should apply to the Ministry of Health for medicines to be entered on the list of reimbursable drugs, submitting a motivated and documented request. The Ministry of Health will then request the committee to examine the submission and to advise the minister, who will take the ultimate decision, in the light both of this advice and of the available budget.

3.2. Reference price systems

3.2.1. Principle of reference pricing

Contrary to what the name suggests, reference pricing is not a form of price regulation: it is a means of setting limits to the reimbursement level of a drug by making use of the existence of equivalent drugs on the market [16]. In this respect, a consensus seems to be emerging that if a price is to be accepted as eligible for full public payment or reimbursement, it must be closely comparable to those of the cheapest therapeutically equivalent drugs on the market. In the light of the current prices of similar drugs, a single "reference price" is fixed, which the authorities regard as acceptable for funding. If the price of any product is higher than the reference price, public payment or reimbursement will only be granted up to the level of the latter, and the difference between this and the actual market price will have to be paid by the patient ("co-payment principle"). The means adopted to fix a reference price are considered later in this section.

In practice one usually finds that within a given therapeutic group several closely similar drugs are available. Particularly where the market includes generic products or where there are parallel imports the choice is likely to be a wide one. Unless the prescriber or patient has a very strong preference for a highly priced item, treatment can be provided using one of the drugs sold at or below the reference price and co-payment can be avoided.

The reference price system provides a strong stimulus to the physician to adopt low-cost prescribing and to the patient to accept it. In addition a strong stimulus is given to companies to lower the prices of their products to the reference price level so as to retain market share. In that way they will avoid loss of sales as patients shift to cheaper products in order to avoid co-payments, and the lower price may actually lead to an increase in unit sales and market share. Thus price competition between companies is fostered.

In summary, reference price systems generally serve three purposes. *Firstly*, they are a tool to induce doctors and patients to choose cheaper medicines within a therapeutic group, thus decreasing the costs for society. *Secondly*, they stimulate the suppliers of the more expensive medicines within a group to lower their prices. *Thirdly*, they make both prescribers and patients more aware of possible alternatives to the drugs which they might in the first instance be inclined to choose, thus increasing the transparency of the pharmaceutical market. For such reasons, reference price systems are nowadays widely used, usually in combination with positive lists, and as a rule based on the ATC-classification. Various different pharmaceutical forms can often be considered as essentially similar and thus grouped together.

3.2.2. Grouping of medicines

The first question to be answered when introducing a reference price system is how to classify medicines into more or less homogenous groups of closely similar products which can be regarded as interchangeable in treatment. This is essential. The entire system will fail if opponents can validly demonstrate that the various products within a group are not in fact closely similar, one being superior to another or having different uses, and that it is improper to apply a single reference price to them all.

The simplest approach is one in which each category comprises no more than alternative brands or versions of the *same generic drug substance*, available in the same form and the same dosage strength. This can be useful in some areas. A benzodiazepine tranquillizer, a long-established anti-inflammatory compound or a corticosteroid is likely to be out of patent and available from many sources. Provided all the alternative products have passed the regulatory system and are thus known to be of adequate quality, the homogeneity of such a group cannot be challenged.

It is only a small step beyond this to compile a group of drugs based on closely similar but not chemically identical substances, used for the same purpose. To take the same example: a group of benzodiazepine tranquillizers, of anti-inflammatory drugs or of corticosteroids can readily be recognized within which all the products are interchangeable (provided one takes account of some variations in potency and thus dosage) and to which a single reference price can fairly be applied. Another small step is to bring together within a group different brands or products which do in fact differ to some extent in their form of administration (e.g., tablets, capsules, rectal or transdermal forms of administration) but which are still interchangeable when one comes to treat the patient. The system in The Netherlands uses these approaches, bringing together in a group a series of products with the same therapeutic properties despite the fact that they may be based on different generic substances and pharmaceutical forms, provided there are considered to be no significant differences in wanted and unwanted effects between them.

A more ambitious and more difficult step is to group together as reference price units a series of drugs which, although they differ in their form, nature and mechanism of action, are all used for the same purpose and are all similarly safe and convenient in use. This approach could, for example, involve bringing together in a group a series of quite different types of agent for treating hypertension. Here one is likely to encounter challenges, sometimes rightly so, if the imposition of a single reference price on an excessively broad group would mean that many patients are likely to be treated with a drug which is not in fact suited to them, merely because it is cheap. Whether countries should opt for the simpler versions of a reference price system or the more advanced versions is, among other things, dependent on the country's wealth, its ability to maintain complex systems and its own national policies in the field of health and health financing. Clearly the most important single element in a reference price system is to ensure a reasonable degree of homogeneity in the reference price groups, however they are constituted. In this respect, several countries use the ATC (Anatomic, Therapeutic, Chemical) classification of drugs, developed and maintained under the auspices of the World Health Organization for the purpose of drug utilisation studies only, as it provides a classification of drugs at various levels of detail ranging from very broad therapeutic classes through sub-groups of similar agents down to individual drug substances. Various national drug reference price systems use the ATC and data on dose-equivalence in establishing the groups to which reference prices are to apply.

3.2.3. Fixing the reference price

Once a group of interchangeable drugs has been defined, a reference price for the group has to be defined. This reimbursement level can be based on the average price of the medicines within the group: drugs with a price lower than this calculated average will be fully reimbursed. The alternative option is simply set the reference price at the level of the price charged for the cheapest medicine in the group.

This second option is usually adopted in simple reference price systems where each category of drugs comprises only products based on the same generic substance.

3.2.4. Levels of payment or reimbursement

Where the reference price for a category of drugs is based on an average, rather on the cost of the cheapest, one will usually find that several products are available at this level or below it. All these will be eligible for full reimbursement. As noted above, patients who choose for a more expensive drug within a group are entitled to it, but they will only be reimbursed up to the reference price, and at the pharmacy they will have to pay the difference between the reference price and the actual price of the product chosen. Doctors should be encouraged to inform their patients about the reimbursement status of equivalent products.

3.2.5. Pitfalls and limitations

The challenges which arise to any definition of a broad category carrying a standard reference price will have to be faced. Valid objections will need to be respected, but provided drugs have been carefully selected for their equivalence and interchangeability in medical practice the category will be defensible.

A phenomenon to which one should be alert is that, while the manufacturers of expensive drugs may lower their prices to meet a reference level based on a calculated average, the manufacturers of low cost drugs may actually *increase* their prices up to the reference level in order to increase their income. If this happens on a large scale, overall costs to the public purse may actually increase. The only adequate answer will lie in complementary approaches, such as a system to require official approval of price increases, which will only be granted on reasonable grounds.

Finally, a reference price system will clearly not be applicable to certain highly innovative drugs which are unique in nature and cannot be said to belong to any pre-existing therapeutic group of products interchangeable with them, so this drug will form a class of its own. To ensure fair pricing of such products one will clearly have to adopt other approaches.

3.2.6. In summary

On theoretical grounds, but also in practice, reference price systems appear to be successful in stimulating low-cost prescribing, price reductions by manufacturers and importers, and price competition in the drug market generally. They are applicable over a large area of the pharmaceutical market, but are not helpful in containing the prices of highly innovative and unique products having no true equivalents. Their successful operation depends in great measure on the definition of clusters which comprise reasonably interchangeable drugs and for which reference prices can be set.

3.3. Co-payments

3.3.1. The principle of co-payments

The notion of co-payments has been referred to briefly above in connection with reference pricing systems. It is however of broader application. All that it means is that a system of public health financing has chosen deliberately to limit its commitment to pay for pharmaceutical care, shifting a part of the burden onto the patient himself or herself. In some or all instances, the patient will be obliged to make a co-payment before a drug is dispensed.

Co-payment systems usually serve three complementary purposes. *Firstly*, they oblige patients to finance part of the costs of their medication thereby decreasing the financial burden on society. *Secondly*, they make patients more aware of the costs of health care. *Thirdly*, they discourage patients from using too many or excessively expensive medicines. Co-payments are generally used in combination with a

positive list and can be built into reference price systems, but they can also be imposed as an alternative to the latter. There is a conceptual difference between co-payment systems as such and co-payment within reference price systems; as noted under 3.2.1 above, co-payments within reference pricing schemes can generally be avoided by choosing lower-priced drugs; in a co-payment system, by contrast, the payments are universal and generally unavoidable, except in certain well-defined situations which justify exemption from charges. Reports on the effectiveness of co-payment systems in lowering pharmaceutical expenditure have up to the present been contradictory: this may be due at least in part to differences between the various systems in use, and between the national systems of health care within which they operate.

3.3.2. *Alternative structures*

Co-payment systems can variously be based on: (1) the imposition of a fixed “prescription charge” for each prescription dispensed (2) introduction of a variable prescription charge representing a percentage of the total cost of a prescription; (3) combinations of fixed sums and percentage charges; and (4) the setting of an annual minimum level for drug expenditure per patient, below which no reimbursement will be granted (“annual deductible” system).

3.3.3. *Safety nets and exemptions*

It is important to build into any co-payment system certain provisions to ensure that it does not deprive individuals of essential treatment or expose the community to epidemic risks (e.g., by inducing patients suffering from infectious diseases to forego treatment). Access to essential but expensive drugs can be preserved by a system of charges which protects the patient against burdensome levels of co-payment for these items; the level of co-payment may for example be set to reflect the therapeutic value of a drug (e.g., with a low co-payment for a drug of great therapeutic value). Vulnerable groups, such as children or pregnant women, will generally be granted exemption from co-payment, as will patients suffering from epidemic diseases (such as tuberculosis) or conditions demanding life-long treatment (such as diabetes). There is often much pressure from society to create widespread exemptions from any co-payment system for additional population groups, involving for example the elderly, pensioners, the disabled or government employees. Exemptions must however be kept in hand if the system is not to become excessively complex or expensive in operation, vulnerable to massive litigation and ultimately ineffective.

3.3.4. *Organization*

As a general rule, co-payment systems should be transparent for the patient and should be kept as simple as possible. In particular the pharmacist, who in most instances is the agent charged with collecting co-payments, will cooperate most readily with co-payment schemes that are simple, efficient and easy to implement.

3.3.5. *Pitfalls*

The need to avoid adverse consequences of co-payment schemes, and to limit exemptions and complications, has been outlined above. In addition one must beware of introducing well-intentioned special provisions which can be misused or manipulated. If for example the level of co-payment for an valuable but expensive drug is deliberately set at a low level so as preserve its accessibility, whereas a low-priced item in the same therapeutic category carries a high co-payment, one may thereby create a “perverse” incentive; the prescriber and patient who would ordinarily have chosen the low-priced drug may move to the expensive item in order to evade the high co-payment, resulting in a greater cost to the public purse. Similarly, when implementing a system of flat rate co-payments (for example a fixed sum per prescription) one should also implement measures to limit the dispensed volume per prescription. Experience

teaches that patients may otherwise try to minimise co-payment by asking the doctor to prescribe drugs in greater quantities for longer periods, thus again in some cases raising total expenditure rather than lowering it.

Any system of “annual deductible” ceilings for individual contributions is particularly tricky to operate. While they may, as intended, stimulate patients to request cheaper (e.g., generic) medicines so long as they are below their ceiling and are thus paying all costs themselves, it can happen that, once the ceiling has been or is about to be passed, particular patients who are heavy users of drugs may create stocks for the next year by obtaining additional prescriptions which will be covered from the public purse. In addition, a “deductible” system is complex to administer since it usually applies to all health services and not merely to drugs; a patient may have reached the ceiling by using other health care services and therefore obtain all drugs without co-payment.

Finally, it is necessary to find ways to be fair to the individual who has particular difficulty in making co-payments. In some systems, patients may have to contribute to the cost of other health care services and not merely to that of pharmaceuticals, resulting in an intolerable burden. In one way or another such cases of hardship have to be identified and relief provided, e.g., by limiting the totality of co-payments by an individual to a fixed sum.

3.4. Generic substitution and parallel imports

3.4.1. Generic substitution

Generic substitution is defined as the process through which governments seek to reduce costs by stimulating the prescription and dispensing of generally cheaper generic medicines instead of their more expensive branded equivalents. The opportunity for generic substitution arises wherever the patent protection on the original branded drug has expired, enabling other manufacturers to produce it at a competitive price, either under the generic (international non-proprietary) name or under brand names of their own. Although unpopular with research-based companies, the situation is generally regarded as fair. During the period of patent protection the inventor has had many years to recoup investments and make a profit, and after this time the community should be able to benefit from the price reductions resulting from the introduction of competition. The savings to the public budget can on the one hand be used to benefit health care generally or on the other hand to render possible the purchase of newer high-cost drugs which expand the scope of drug treatment.

The argument has often been advanced by research-based manufacturers that the “generic” equivalents of their products are likely to be deficient in quality. In the past there have been problems regarding quality with some generic suppliers (just as there have been problems with brand-name drug manufacturers) but nowadays generic products and their manufacturers, like the original specialities and their sponsors, are legally obliged to go through the process of regulatory approval.

3.4.2. Parallel importation

As noted earlier in this volume, the price of a drug supplied by a multinational manufacturer may vary considerably from one country to another. As a rule the sale of the drug in a particular country is channelled only through an agent appointed by the manufacturer, and the price charged is that which the manufacturer has set for that country (subject to whatever government permission is required). In practice, however, small firms and even individual pharmacists or traders in a high price market soon identify means of obtaining the drug in bulk in a foreign country where the sales price is much lower and importing it independently in “parallel” with the official agent. Even after the costs and overheads

involved have been paid and profits earned, it often will prove possible to sell this “parallel” version of the original drug at a considerably lower price than that charged by the official agent.

In theory the constitution or quality of a manufacturer’s drug may prove to be somewhat different in various countries, and manufacturers objecting to the “parallel” importation of their products have sometimes made his point; in practice, however, any differences which exist relate only to particular excipients or colouring agents or to the language of the packaging text. It is now in any case common practice for “parallel” products to be examined and approved by the regulatory authorities to establish the fact that they are indeed identical to the version imported officially.

3.4.3. Experience with substitution

Over a period of some 25 years, the trade in both generic equivalents and parallel imports has greatly expanded, and their availability has resulted in considerable cost savings both to the health services and to patients. While adverse publicity by the original speciality producers has engendered some distrust of these products, both among health professionals and the public, this has largely been overcome, particularly by provision of objective information and in view of the savings which can be achieved. These savings may be sufficient to render superfluous more complex and more unpopular cost containment measures, such as de-listing of reimbursable drugs.

3.4.4. Implementing substitution

An essential starting point is the implementation of a requirement that both generic drugs and drugs imported in parallel must go through the usual national regulatory approval process so that their equivalence can be guaranteed. If the labelling is in a language not generally understood in the importing country, or if there is a difference in the name of the product, regulatory approval may be subject to the provision of appropriate stickers and package inserts. If the regulatory authorities register these products, buyers can safely assume that there are truly no differences in quality between regular imported branded medicines, generics and parallel imported drugs. Governments and/or third party payers can consequently promote generic substitution and parallel imports, thereby reducing pharmaceutical expenditure by substituting more expensive drugs by cheaper, similar (or identical) drugs.

The best way to promote substitution is to stimulate the prescribing doctor to specify only the generic (international non-proprietary) name of a medicine on his prescription instead of a particular brand name. In practice this is sometimes difficult to achieve. Many physicians are less familiar with the generic names of drugs than with the heavily promoted brand names. The generic names of some drugs, in particular when they are combinations of different substances (as in the case of most oral contraceptives) can be complex and difficult to remember. There may also be a residual degree of distrust or doubt regarding the equivalence of generic or parallel items. One step which is permissible in most countries, is for the doctor to specify, alongside the speciality name, “. . . or equivalent” (the exact term to be used depends on the prescribing and dispensing regulations in force) so that the pharmacist is free to substitute a parallel or generic version of the same drug; conversely it may be possible to introduce the more drastic rule (subject to its conformity with international agreements on patents and copyright) that substitution by the pharmacist will *always* be allowed unless the prescriber has explicitly indicated his desire to use a particular branded speciality.

Measures regarding doctors need to be complemented by measures concerning dispensing pharmacists. Regulations need to be drawn up and promulgated permitting pharmacists to substitute branded medicines by generic or parallel imported items, either at their own initiative or where the physician has specifically indicated his approval. Where the physician has prescribed generically, the regulations on

dispensing should at least entitle the pharmacist (and preferably oblige him) to issue a low-cost item in the spirit of the prescription.

Finally, some form of incentive may be developed to encourage the dispensing of low cost equivalents. An example of a financial incentive can be found in The Netherlands where the pharmacist may retain, at public expense, one-third of the price difference between the drug prescribed and the cheaper drug actually dispensed.

3.4.5. Educational measures

For reasons already touched on above, both health professionals and the public need to be educated and reassured if cost-containment initiatives based on substitution are to have maximum effect. The residual distrust in this area needs to be countered by reassurance, for example as regards the quality guarantees inherent in national regulatory approval. Minor though insignificant differences between the original speciality to which the patient is accustomed and the equivalent product which he is offered at the pharmacy may reawaken the distrust: minor differences in colour, taste or packaging need to be explained and the reassurance repeated that the product being supplied is in no sense inferior to or different from that which it replaces.

3.5. Prescription controls and limits on the duration of prescribed drug treatment

Many a medicine has a range of indications; it is prescribed for a wide variety of patients suffering from various disorders present in varying degrees of severity. The authorities or third party payers may deem it unnecessary to reimburse such a drug when it is prescribed for one indication (e.g., a minor self limiting disease, such as use of aspirin for an incidental headache), but entirely proper to do so when it is used for some other purpose (e.g., long-term use of aspirin in chronic rheumatoid arthritis). Such a differential approach is feasible; it involves introducing the principle that medicines may only be reimbursed when certain conditions are met. It may similarly prove necessary to attach specific conditions to the reimbursement of a particularly expensive item or where the drug is such that extensive misuse can be expected (e.g., stimulants).

Actually implementing such conditions can however be problematical, because of the difficulty in recognizing situations in which the conditions for reimbursement are indeed met. A prescribing doctor might for example bend the rules to some extent so as to enable a patient to avoid paying for his or her medicine. Where conditions are imposed they should be simple and they should apply only to a small number of medicines where they are unavoidable, otherwise severe problems in implementation and control will arise. The same advice applies to a system in which prescribing doctors and patients have to seek written permission from the authorities (government or health insurer) for the prescribing and use of a given drug.

Devising and implementing conditions for the reimbursement of particular drugs is nevertheless feasible, using well-recognized textbooks and bulletins on drug treatment as guidelines. Again, as in the case of creating a positive list, a formal advisory committee should be established. Composed of medical and pharmaceutical experts, it could well be the same committee as that advising on the positive list for reimbursement.

In the case of exceptionally expensive drugs which have to be used very selectively, one option is to limit their prescribing to specific locations, e.g., certain specialized hospitals or clinics. Patients with a disorder for which these drugs are likely to be needed can there be assessed by clinical specialists and, if appropriate, a prescription for the drug in question can be issued. Again it must be noted, however, that

the system must be manageable; this will only be case where the number of patients likely to be eligible for such treatment is small.

One other option is to limit the quantity of any medicine that will be reimbursed. The limit can take the form of a maximum total quantity which the physician is allowed to prescribe for a patient, or the imposition of a maximum duration of therapy that can be reimbursed (e.g., medication sufficient for one week when prescribed for the first time or for three months during follow-up treatment). As many patients prove to discontinue their therapy before they have used all their medication, limitation in the quantity prescribed at any one time will often prevent waste without impairing treatment.

Where a tariff system based on capitation with dispensing fees is introduced for pharmacists, one should be alert to any subsequent increase in the number of prescriptions dispensed, as pharmacists may find it more profitable to break down a single prescription into two or more dispensing acts, each of which will earn a fee.

3.6. Budgeting

Governments may opt for financial ceilings on health care expenditures. The global budget is then broken down to provide budgets for the individual sectors in health care and these may be split further, resulting for example in the calculation of a further ceiling for the total costs of goods of pharmaceuticals and the costs associated with the distribution by pharmacists. In such a situation it will be necessary to introduce sanctions for those firms, individuals or practices exceeding the budget, e.g., compulsory price reductions or a the lowering of tariffs.

When rationally devised, overall budgets in health care prove to be an effective means of containing the costs of health care. There are indications that insurance-based systems (Germany, Belgium, The Netherlands, France, Sweden) encounter more difficulties in setting budget limits than do tax-based systems (UK, Denmark, Italy). This may be due to the fact that in insurance-based systems more parties are involved, rendering the process of negotiation complex and difficult to manage.

3.7. General Practitioner fund holding

Setting a budget for individual general practitioners provides a global approach to issues of spending, involving both price and volume questions but also the allocation of resources between services. The greatest experience with this approach in Europe has been gained in Germany and the United Kingdom.

The primary motivation to reduce prescribing costs by budget holders is essentially financial, and the latter may be subject to financial sanctions if they exceed their permitted budget. Fundholding practices seem to be prone to limit their prescribing expenditure, although there is also evidence suggesting that these effects may be transitory [11]. There is however a general lack of evidence as to whether prescribing cost economies obtained through a fundholding system are really in the best interest of the community; there is for example no evidence of the consequences in terms of long term morbidity or patient satisfaction. Furthermore, general practitioners seek to ease pressure on their budgets by earlier referral of patients to second line health care, which so far as the overall health service is concerned is likely to raise costs. Last but not least, the concept of GP-fundholding appears to have suffered from the fact that budgeting has taken place at too low a level; if standard budgets are set for all practices, despite the fact that the financial needs of practices differ, some such practices (e.g., those treating a population in poor health) will find their permitted expenditure reduced in all too drastic a manner. This risk can be largely avoided by setting budgets further upstream e.g., at the level of the insurer or the regional government, so that these genuine differences in need are averaged out.

3.8. Pharmacy Benefit Management (PBM)

In the United States, where the health system is market driven, a system of managed care through Health Maintenance Organisations has been established. Various definitions of managed care exist, but common to all is the active management of utilisation of services by controlling access, costs and or quality through direct intervention before, during or after service delivery. Pharmacy Benefit Management (PBM) schemes were set up within this system to provide drug-related administrative services and to manage pharmacy costs. PBM's often provide an integrated package of cost-containment measures based on formularies, generic substitution, co-payments and utilisation control, sometimes combined with use of purchasing power to obtain reduced drug prices from manufactures. PBM's are typical of a primarily market driven health system, where coverage of health care costs is delegated to private insurance companies and private HMO's, supported by private PBM-companies. European and other countries have followed with interest American developments in managed care and PBM's. One should be aware, however, of the basic differences in health system on the two sides of the Atlantic; the US system is inherently based on differences in access to care, while in European and other countries equal access to adequate care is the primary objective. The disadvantages of profit-driven HMO's and PBM's have been well defined by critical reviewers. Profit driven HMO's are stated to deliver a lower quality of care [14], while patients' prescription information has been used to advertise a new drug without patients being aware of it [20]. PBMs often have alliances with drug companies, a fact which casts doubt on their objectivity. A more detailed description of experiences with PBM's in the US is provided in Chapter 12.

4. Professional interventions and strategies for influencing demand

It is feasible to influence demand by educating prescribers and users. The objective here is not *primarily* to contain costs, but to influence demand and optimise rational drug prescribing and use. The relevance for expenditure is that by optimising rational prescribing and drug use one will commonly prevent direct waste (overuse of drugs) and render treatment more cost-effective. An overview is provided here of the different options available to influence prescribers or patients, with some discussion of their effectiveness in actually changing the pattern of drug use.

4.1. Prescribers

The key principle in professional interventions is to provide prescribers with the information and education needed to make medically sound and cost effective drug choices. This involves continuous effort. The pharmaceutical sector is dynamic and it is strongly influenced by socio-economic circumstances. Traditionally, education is the realm of the medical profession itself, but in the face of rising costs the health authorities have in recent decades become more involved, particularly in providing a counterbalance to the slanted prescribing information emanating from the pharmaceutical industry. The industry invests heavily in inducing prescribers to make use of its products, and there is ample evidence that prescribers are sensitive to these promotional efforts which often lead to extravagant prescribing [28]. The profession itself has, in general, not invested resources in seeking to counter the promotional efforts of the industry, for example by developing continuous medical education in this field. On the contrary, programmes for continuous education have in many countries depended heavily for their maintenance on financial support from the pharmaceutical industry. In order to ensure the availability of objective information health authorities have to become involved.

4.1.1. Drug formularies and drug bulletins

The first step is to provide the prescriber with practical, objective and evidence based information on drugs and prescribing, and to keep him up to date. Drug formularies (or formulary manuals) and drug bulletins are now widely available. The term formulary can be confusing since it is used in different senses. Here the term is used for a reference book providing summary drug information on individual drugs including for each the generic name, indication(s) for use, contraindication(s), dosage schedules, side effects and warnings. Such a drug formulary is intended as a handy reference guide, covering most (but not necessarily all) of the drugs on the market. In some formularies, therapeutic assessments of all drugs are included as well as cost comparisons, culminating in advice as to which drugs within a group should be regarded as products of first choice. Clear examples are the British National Formulary (BNF) and The Netherlands "Farmacotherapeutisch Kompas", both of which provide evaluations, advice on choosing between drugs and cost comparisons. In general, formularies would benefit if they were to provide in addition information on the reimbursement status of drugs, as well as relevant patient charges or co-payment levels.

Specialised types of formularies include those limited to reimbursed drugs or to drugs in the public health system; there are also smaller formularies providing a selection of a limited number of first-choice drugs within a drug group (drug based formulary), or first choice drugs for treating selected common clinical problems (indication-based formulary). These specialized formularies are more condensed than the general type; the selective indication-based formulary is particularly helpful to the prescriber because it is limited to the most relevant information and is easy to use. Its value and acceptance naturally depend on the expertise of the people responsible for selecting the first choice drugs, and the transparency of the process of compilation. The best of these selected formularies are those which are demonstrably based on a process of evidence-based drug choice. From a public health perspective, the cost of treatment should be one of the selection criteria. The newly formed NICE mechanism in the UK has added affordability to the traditional criteria of safety and efficacy, thus establishing a better basis for prioritisation of resources (DoH, Faster access to modern medicines 1999).

4.1.2. Industry-sponsored formularies

Particularly in countries where the public health authorities have failed to step in, the pharmaceutical industry has itself sponsored formularies, such as MIMS (The Monthly Index of Medical Specialities). The disadvantage of these commercial formularies is that they tend to provide incomplete information (for example, about adverse effects), or provide only information on drugs produced by the firms which have sponsored the publication. As a rule they also contain advertising and their contents are heavily weighted towards specialities rather than generic equivalents.

4.1.3. Therapeutic guidelines

Whereas formularies provide drug centred information, therapeutic guidelines centre on each disease in turn and its most appropriate treatment. The best of such guidelines are fully evidence-based and systematically developed on the basis of wide consensus; they provide valuable assistance to prescribers in deciding on appropriate treatments for specific clinical problems. In their most complete form, guidelines also provide give information on diagnostic procedures and set out clear, diagnostic criteria for starting or adjusting treatment, as well as proposing the treatment of first choice. They are extensions of indication-based formularies in providing more extensive information about the entire treatment process. Guidelines are the most practical form of information for the doctor, because they provide support on decision-making in practice and do not focus only on drugs.

Most guidelines have been developed by the profession, as for example in The Netherlands, where the College of General Practitioners has developed individual guidelines for a series of diseases, and in Scotland with the so-called SIGN guidelines. In other countries, the health authorities have taken the lead, such as in France. In many developing countries Standard Treatment Guidelines (STG) for different levels of care have been developed, for example those in Uganda or Malawi and those recently developed for East Timor which are attuned to the special problems of the many clinics which are headed by a medical assistant or a nurse because so few physicians are available.

4.1.4. Structures and techniques

The responsibility for formularies and guidelines may lie variously with the public health authorities, health insurance institutions or scientific organizations within the medical or pharmaceutical professions. Ideally, the information provided should be evidence based, the decision making process transparent, and the choices such as to reflect optimal treatment. The extent to which this is attained may be influenced by the source of the publication. One could argue that private health insurers, such as third party payers in the US, run the risk of leaning too heavily on cost driven decisions. Formularies and guidelines developed by the medical and pharmaceutical professions' (scientific) organisations have the advantage of being the most acceptable and credible for the prescribers, particularly if they involve opinion leaders prominent in their field. The responsibility of public health authorities is to ensure the development and distribution of objective formularies and guidelines, preferably by the medical and pharmaceutical profession. When that is not feasible, the public health authorities should initiate the development of and establish a (national) formulary and guideline committee, consisting of prominent physicians and pharmacists on order to ensure quality as well as credibility and acceptability to the field.

Since most principles of evidence-based medical care and drug treatment are universally applicable, one might in theory expect that formularies and guidelines would be developed for international or regional use. Some such international publications do indeed exist, but most formularies and guidelines are in fact produced nationally or even locally. This reflects the fact that national or local circumstances (such as the economic environment, the standard of professional training and the range of drugs available). Considerations of cost will have to weigh relatively more heavily in poorer countries than in richer countries. Moreover, there is always an element of assessment and interpretation of the different elements of evidence when set against national/local circumstances. In addition to the fact that national and local formularies and guidelines can be tailor-made to fit the circumstances of the community, it seems clear that the fact that where they reflect consensus attained in the community or profession this is an important element in their acceptance.

Information technology facilitates the use and the impact of formularies and guidelines. In industrialized countries. the use of computers in the consultation room is spreading fast; practical decision support systems are becoming available. Whatever techniques are used, it is important that the material is readily accessible to prescribers and other users; that is most likely to be the case if printed publications are distributed free of charge to all who need them.

4.1.5. Updating and the significance of bulletins

There is a constant risk that formularies and guidelines will become outdated as new information and drugs become available and concepts of treatment change. Formulary and guideline development is therefore a continuous process, and not a 'once-only' effort; the best of such publications appear at least once annually. Again the primary role of the health authorities is to see that this is the case. More detailed information about the development process can be found in 'Managing Drug Supply' [23].

Drug and prescribing bulletins, though generally independent of formularies and guidelines, play in effect an important role in updating them as new drugs and new facts appear. Often published monthly or even fortnightly, bulletins may emanate from drug regulatory authorities, professional organizations, consumer organizations or independent foundations. In some cases, bulletins produced independently enjoy a financial subsidy from the authorities in order to enable them to be distributed without cost to the professions, as well as to libraries and students. As with formularies and bulletins, there is an absolute need for an objective and transparent approach if a drug bulletin is to attain and retain credibility. A large number of drug bulletins now collaborate in the International Society of Drug Bulletins, resulting in a wide international exchange of data, draft texts and experience (see <http://www.isdbweb.org>).

4.1.6. *The choice and effectiveness of interventions*

The provision of information is an important and necessary step for increasing knowledge and competence. However, it is generally not enough to change existing prescribing patterns. To that end, the concept of formularies has to gain acceptance with the health professionals; a good distribution system for the drugs listed in the formulary has to be in place to ensure their ready availability and intensive strategies have to be adopted to ensure the formulary's selection of drugs actually becomes the basis for day-to-day prescribing. A wide range of approaches to implement change in medical practice have been used, separately or in combination. In the present chapter a general outline is given, while in Chapter 13 the issue is dealt with in-depth. The principle methods of professional approaches used to implement change are listed in Table 1.

The choice of interventions intended to influence the prescriber needs to be carefully considered and should be based on the available evidence of success for particular strategies, otherwise projects may waste scarce resources on ineffective approaches. Evidence about the effectiveness of different approaches on different medical activities is accumulating [4,5,10]. As is the case with other areas in medicine, modest improvements are found in general in prescribing behaviour [10]. Table 2 provides an overview of the effectiveness of the different approaches to change prescribing behaviour. Most of the studies reviewed (81%) were conducted in the US, often relating to interventions in hospital care; generally modest improvements in performance were found following after interventions. Effectiveness

Table 1
The professional approaches used to implement changes include

-
- Distribution of written educational material.
 - Conferences or educational meetings.
 - Interventions that involve locally deriving consensus recommendations.
 - Educational outreach visits and academic detailing that take place at the prescribers' location.
 - Exploiting the influence of local opinion leaders.
 - Patient-mediated interventions in which information given to or received from patients is intended to influence professional practice.
 - Audit and feedback, where physicians receive summary information on their performance over time.
 - Patient mediated interventions in which information, given to or received from patients, is mobilized to influence doctors' practice.
 - Reminder systems where doctors receive specific reminders at the time of prescribing decisions (decision support systems), either computer generated or by hand-written reminders.
 - Marketing, in which physicians are targeted by public interventions similar to those, used to market commercially specific desired prescribing choices.
-

Adapted from EPOC [5].

Table 2
Effectiveness of professional interventions to optimise prescribing

	No. of interventions	Positive findings	%Positive interventions	95% CI
Distribution educational materials	7	3	43	13–78
Audit and feedback	33	17	52	34–66
Outreach	4	2	50	10–90
Patient mediated	8	5	63	30–90
Conferences	1	1	100	–
Marketing	0	0	0	–
Multifaceted	43	21	49	20–80
Overall	96	49	51	41–61

Source [10].

seemed to be greater in the case of interventions carried out in other countries (mainly Europe and Australia) where there was a greater focus on primary care, but it is still not entirely clear how effectiveness differs from one health care level to another. It is clear that the health care tradition and cultural context modify the success of implementation strategies. For example, a local consensus strategy on asthma treatment, involving small groups of general practitioners and combined with audit and feedback techniques, was successful in The Netherlands and Norway, but proved inapplicable in Germany because of differing views on asthma and different expectations regarding education [26]. Few studies have looked at the effect of computerised decision support on prescribing, though there is reason to believe that improvement is attained as regards decisions on drug dosage [17]. In some countries nevertheless, decision support systems in using guidelines or formularies have been implemented nationwide (UK, NL).

Passive dissemination of information, e.g., by simply publishing formularies and guidelines is generally ineffective unless it is supported by other measures. The frequent use of multifaceted approaches is creates the problem that since various complementary approaches are necessarily used at the same time it can be difficult or impossible which has made a contribution to change.

4.1.7. The situation in developing countries

In their review of approaches to improving rational drug use in primary care in developing countries, Laing [19] found that most of the interventions identified had some form of education as at least one of their components. Workshops and training as well as community case management strategies were the most frequent types of approach. Community case management is a multifaceted technique primarily encountered in developing countries; typically it involves the training of community health workers in the appropriate diagnosis and treatment of a key health problem, often involving care of children.. This approach is often combined with community sensitisation and education, active community based case finding and parallel training of facility based health workers.

Community case management for acute respiratory infection (ARI) and diarrhoea were clearly successful in reducing mortality; their overall effects on the appropriateness of drugs choices, especially in the case of ARI, have however not been well studied. Other approaches that may yield moderate to large improvements were audit and feedback (or group processes), and audit combined with supervision. As in the industrialised world, the simple dissemination of printed educational material (clinical guidelines, prescribing information) had no impact. Experience in Zimbabwe underlines the relevance of

active and continuing programme implementation; when the activities were discontinued, irrational drug use increased again.

4.2. Interventions targeting consumers and patients

Where overuse of drugs is demonstrable, the patient or consumer is sometimes in part responsible, insisting that the doctor write a prescription for him. Misconceptions about drugs in general, or about specific drugs in particular, commonly play a role in this matter; the misconceptions may be of long standing, or they may have been fostered by pharmaceutical marketing of a type which can only be said to comprise misinformation. Conversely, a patient may be so afraid of a drug or so ignorant of its proper use that he takes it improperly or not at all; inadequate “compliance” with agreed therapy is a widespread problem, one consequence again being waste of resources, either because the drug remains unused or because illness is unnecessarily prolonged. While “intelligent non-compliance” by the patient provides him with some opportunity to correct irrational prescribing when he recognizes it, the ideal to aim at is clearly one in which the patient and his doctor agree on what therapy is to be chosen, prescribed, and taken.

Public education regarding drugs involves an approach to the entire community (i.e. including healthy people not using medicines) and aims to promote awareness of irrational drug use, and possibilities for change. Communication channels may include printed materials (posters, leaflets, textbooks), mass media, interpersonal encounters with health workers, schoolteachers, or folk media community theatre, singing groups, puppet shows etc. In some countries, such as France, general teaching about drugs has long been part of health education in schools. There are many indications that public education can be successful, but there is a general lack of good evaluation of the impact of the various activities and approaches on the rationality of drug use, nor are data available which could render possible a proper cost-benefit analysis [9]. A systematic review of the effectiveness of mass media campaigns on health service utilisation does seem to show how use of these media can have a positive impact [12].

Quite apart from the possibility that public education may result in economies, one should also realise that it is wise to enlist the understanding of the public when contemplating cost containment measures. Some such measures have encountered opposition from the public which has proved to be generated in part by lobbying from interested parties. It is particularly necessary to create understanding among the public of the value and significance of a positive list; the misunderstanding should not be allowed to arise that such a list limits treatment unduly or results in the use of medicines of lesser quality. A new communication channel is the Internet, where a massive and confusing volume of information on medicines – objective and commercial, scientific and nonsensical – is to be found; it is very necessary that reliable official guidance, recognisable as such, also be represented in this medium. To date, the positive or negative impact of public education on rational drug use is still completely unclear with only anecdotal information available, advanced both by proponents and opponents.

Product information for patients, in printed form and dealing with individual drugs, is likely to be influential and widely popular. While the task of the physician and pharmacist in informing the patient about a drug and its proper use is beyond doubt, this form of information needs to be supplemented by others. Drug compendia, providing the officially approved information on all marketed drugs, have existed for many years as a source of reference for doctors, but in more recent years they have proved helpful to patients as well. In Denmark and various other countries the current Drug Compendium is always available in the pharmacy where patients can consult it when coming to collect their medicine; in some other countries, the Compendia also appear in shorter patient-orientated editions for home use.

Patient Information Leaflets (PIL's) – officially approved printed patient information sheets describing the drug and providing instructions on how to use it – have proved a very necessary, efficient and highly appreciated means of informing the user. After a long period during which some countries made no provision for such package inserts (and others had package inserts which were written primarily for the health professional) provision of PIL's has become standard practice in the member states of the European Union and many other parts of the world. Such inserts need to be well written with effective graphic designs, large print size and clear layout to enhance legibility. Pictograms may overcome linguistic or literacy barriers.

Many countries cannot as yet afford to provide Patient Information Leaflets for all medicines and to all individual patients, yet simple instructions for the most commonly used drugs, printed on inexpensive paper and handed out by the pharmacist at the time of dispensing are within reach of most countries.

Other interventions to assist patients to follow their prescriptions – primarily developed in industrialised countries and for chronic diseases – include well thought-out programmes designed to increase user-friendliness, to promote patient empowerment through self-management and self-monitoring (for example in asthma, or hypertension), and to provide reminders regarding compliance, reinforcement of information or rewards for improved adherence. There is little evidence that such complex approaches consistently improve medication adherence; the results suggest that there is still a need to develop innovative approaches that can be applied with the resources usually available in clinical settings [13].

Prevention of misinformation is a complementary and very necessary approach to guiding the public. The provision of reliable education and information, considered above, naturally enables the public to protect itself to some extent from misleading influences, but in some matters there remains a considerable risk that misunderstandings will be fostered. For many decades it has been the case that advertising for prescription-only drugs has, at least in most western industrialized countries, been directed only to physicians and pharmacists, who are assumed to be capable of adopting a critical attitude to it when necessary. Within the last decade, however, a move has arisen to permit direct advertising to the public of products of this type; the practice emerged first in the United States and then in New Zealand. Recent proposals of the European Commission open up possibilities of pharmaceutical companies offering information to patients with AIDS, diabetes or asthma directly. This proposal is viewed by many as a first step to allowing direct marketing to patients, although the EU Commission has denied this [27]. From the side of large pharmaceutical companies it has been argued that this comprises a new and useful form of public information, but from the content of such advertising it is clear that it is designed to induce the user to pressure his or her physician to prescribe new drugs. This practice has two seriously adverse consequences for the public purse; on the one hand the turnover of new and expensive medicines is unnecessarily increased, on the other hand the heavy promotional expenditure is inevitably, though indirectly, financed by the community in terms of high drug prices. In 1996, \$600 million was paid for televised commercials for prescription drugs in the United States, and the commercial results have induced advertisers to increase their promotional budgets further [23]. In 2000 the amount for DTC was estimated at US\$ 2.5 billion [21].

The authorities need to be similarly alert to the indirect public dissemination of commercial information on prescription drugs. Use of the Internet opens this possibility; in the recent past, the Bristol Myers Squibb concern was found to have breached the UK code of practice for advertising by maintaining a promotional website for health care professionals which could be accessed by the public [2].

Finally, in this connection it should be pointed out that some commercial companies have exerted an important effect on public opinion by the manipulation of patient groups. It has for example been shown that belief among the US public that the condition known as "Attention Deficient Hyperactivity

Disorder” in children is a biological defect requiring drug treatment, reflects in part the heavy financial support provided to the organization of parents of these children by a drug manufacturer.

5. Conclusion and recommendations

Experience so far with different professional interventions targeting prescribers has provided us with effective tools for improving the rationality of prescribing and preventing the waste of public funds resulting from overuse and inappropriate use of drugs. This is the case in both industrialized and developing countries. The next challenge is to make wide use of such tools, and in that respect many countries still lag behind. The same has to be said as regards the health education of the public in these matters; we have learned how to achieve success, but we do not always apply the lessons. Up to the present both prescriber-oriented professional interventions and public education remain under-utilized approaches in the quest for effective and efficient drug use. Patient information has been rather more widely developed, in particular through the use of patient package inserts. If that advance is not to be undermined, it will be important to avoid the error of introducing “direct to consumer advertising” for prescription drugs, which is all too likely to promote overuse and misuse.

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Chapter 4

Methods for monitoring and evaluating processes and outcomes

Monique F. Mrazek and Elias Mossialos

1. The notion of monitoring

When any form of policy – economic or otherwise – is intended to have an impact on pharmaceutical care, it is important to measure its intended (and possibly unintended) effects. The present chapter will consider methods that can be used to monitor those effects on both process and outcomes. Monitoring *process* involves a regular review of the activities that make up drug management and delivery programs, and that are intended to achieve policy objectives as regards to both health and expenditure; it is sometimes more clearly known as “internal” assessment. Monitoring the results, i.e. the *outcomes*, will show whether these policy objectives are being achieved; this is sometimes termed “external” assessment.

Monitoring initially involves selecting particular *indicators* that can serve as measures of policy performance. Indicators of both process and outcomes are initially measured and then followed over the course of time. The information obtained can be compared against a predetermined *target* for each indicator providing a basis for the evaluation.

2. Linking monitoring to policy goals and objectives

2.1. Components of policy

Any long-term policy needs to have a clear overall *goal*, as well as a set of specific *objectives* which one intends to attain and a list of the *outcomes* which can be anticipated. These three components need to be set in advance when the policy is planned and adopted. One will also need to devise a system to measure progress as the policy is implemented.

The ultimate *goal* of drug policies must be to improve the well-being and health status of the patient population. However, given the inevitable constraints on funding in this area, an associated goal would be to ensure that drugs are managed, delivered and used in a cost-effective manner. A competing goal in setting drug policy may be to foster or sustain the contribution of the R&D based drug industry to the domestic economy. Where a balance is struck between competing health and industrial policy goals will depend on the weightings of the domestic interests.

The *objectives* of a policy are detailed end-points that need to be attained and steps that need to be taken over time. Objectives are commonly defined by an analysis of the population’s clinical needs and demands to be met.

Finally, one will have to define at the outset the *outcomes* that can realistically be anticipated, i.e. the specific effects in the field, at the level where the community is affected by the policy.

The monitoring of policies will thus need to be based not only on internal feedback from within the administrative structure (to check on measures taken and other aspects of implementation), but also on external feedback from the field (to determine the attainment of objectives and the effects as the population experiences them). Monitoring will have to reflect all aspects of the execution of the policy, but in particular the goals, objectives and outcomes which have been defined in advance, should wherever possible, be concrete enough to render possible the measurement of progress. The methods of measurement are considered under Sections 3 and 4, below.

While all these concepts are straightforward, one can run into problems when putting them into practice. It might for example be said that the level and pattern of drug utilization is an outcome measure, but quite apart from the difficulties which can arise when measuring utilization (see Chapter 2) it may be far from clear what its significance is. The level of drug use does not necessarily equal the level of clinical need, since there may be over-use or under-use as well as inappropriate patterns of use. Nor is the level of clinical need necessarily an indication of the level of demand, for as pointed out earlier in this volume the latter may be unreasonably high and sometimes (e.g., because of lack of money) unreasonably low. Levels of utilization, clinical need and demand therefore should be tracked separately. Each of them varies from country to country according to epidemiological, demographic and cultural factors, while the availability of resources (such as personnel, technology, institutions and finance) to meet needs will vary between health care systems. It follows that the goals and objectives of drug policies are likely to be country- and health care system-specific, and that the measures of progress that can be used in those policies will similarly be specific to the situation.

2.2. *Setting priorities*

Because some of the various interests reflected in a policy may inevitably conflict with one another – especially in terms of vying for financial resources – priorities will have to be set at the outset. Criteria that are well recognized for evaluating the allocation of health care and pharmaceutical resources are *effectiveness, efficiency, equity* and *quality*. As the policy is implemented, the feedback attained through monitoring may indicate the need to revise or adjust the policy or some of its components, and this can mean a rethinking of priorities and a reallocation of resources. For example if a cost containment plan for drugs proves to be producing disproportionate hardship for the elderly (inequity) or causes a worsening of outcomes (ineffectiveness), or even increases costs rather than reducing them (which will point to increasing inefficiency unless there has been no commensurate increase in effectiveness) these problems should show up in the course of monitoring and the priorities may have to be revised.

2.3. *Setting objectives*

The point has already been made that progress towards meeting objectives must wherever possible be measurable and it is therefore necessary that objectives should be expressed in concrete rather than general terms [13]. Objectives should be set at both micro and macro levels. Micro level objectives concern effects on individual patients, physicians or institutions. At the macro level objectives will typically relate to the operation of the pharmaceutical service, the overall health care system or the wider social, political and economic environment in which government decisions are taken; examples of the latter might include the objective of securing a change in the system of university medical education or amendments in the tax system relating to drug imports.

2.4. *Effectiveness as a criterion*

Drug cost containment policies should not significantly impair effectiveness in terms of improvements in health outcomes, and wherever possible effectiveness should be enhanced [1]. Better health outcomes should be expected if the process of drug use is made more effective. Whether drug management and delivery truly has become more effective will depend on the quantity, quality and appropriateness of the drugs prescribed, dispensed and consumed, relative to a patient's clinical need. This is true at both the micro and macro levels. Patient needs can be assessed using a consensus of expert opinion as to what ought-to-be provided, based on the clinical facts and the epidemiological situation. Improvements in the effectiveness of the process of drug management and delivery can be detected in terms of health outcomes in the patient population.

2.5. *Efficiency as a criterion*

Efficiency relates health outcomes to the resources used to produce them. Drug policies should aim to maximize health gains subject to equity constraints (i.e. equity-efficiency trade-off) while keeping the costs to society as low as they can reasonably be. At the *macro* level it is important to achieve both production efficiency (producing services at the least cost) and efficiency in the allocation and application of those resources (maximizing health gains given limited resources). Maximizing efficiency at a *micro* level implies among other things that effective pharmaceuticals should be supplied at a price reflecting the contribution of the drug to improving health status as compared with alternative treatments. In other words, this means maximizing the use of cost-effective drugs. Efficiency at all levels is thus a necessary element in improving economic outcomes.

2.6. *Equity as a criterion*

Equity is concerned with ensuring that the benefits and burdens of pharmaceutical care are fairly distributed. Applying the principle of equity is complex and can be confusing. Equity in terms of finance means that patients, society, the professions and the industry should each make a reasonable contribution to the cost, commensurate with their means. Distributing access and delivery fairly will involve ensuring that all population groups are treated equally, with no deprivation as a result of their location, age, sex or other characteristics.

It is simple to propound these general principles of equity, but in applying them one is inevitably faced with the difficulty of deciding, in specific situations, what is "just" and "fair". If, to take an extreme example, a group of individuals live by choice or necessity on a remote outlying island, far removed from any pharmacy or specialised prescriber, will it be "fair" to expend the same percentage of our budget per household on them as on city dwellers, despite the fact that less resources can be purchased for the same amount of money for the islanders as compared to the city dwellers? Or should one, to be equitable, allocate more of our budget and hence resources to the islanders in order to attain an urban level of service, despite the fact that the city dwellers will in effect be shouldering a disproportionate burden to the benefits received?

Multiple definitions of a fair or just distribution have been used in health care, reflecting variously quality of utilisation, distribution according to need, equality of access and equality of health (see [6,16]). Each of these definitions relies on value judgements which differ (see [1]). When evaluating the effect of a drug policy in a particular health system it is therefore important to know which definition of equity has been adopted. A system adopting an egalitarian approach (distribution according to need and financing

based on ability to pay) will have different objectives than a libertarian system (entitled to what they get provided it is acquired justly), and therefore cannot be evaluated using the same definition of equity.

2.7. Quality as a criterion

All the criteria so far discussed are certainly important but it is also crucial that what is provided meets the patient's reasonable expectations with regard to quality in the broad sense [10]. The meaning of quality at one level may be to equate it to effectiveness, but the definition of quality certainly goes beyond a reflection of how patients perceive the effectiveness of the services they receive. The definition of quality is also likely to differ depending on cultural expectations and values, as well as the nature of the health care system through which pharmaceutical services are delivered. For example, a US patient may equate quality to freedom of choice, while a patient in the UK may equate it to shorter waiting times or to reduced variations in services across the system. Expert definitions of quality include the dimensions of access, appropriateness, and technical and/or interpersonal excellence as measured by the health outcomes achieved [3,10]. Therefore access to pharmaceutical services (i.e. availability of prescribers, pharmacies and medicines) should be appropriate to what patients need and delivered in a manner that displays good levels of professional practice.

Minimum quality standards must certainly equate to the minimum standards governing licensing of professional health practitioners. Drugs for example may be overprescribed, or prescribed and used inappropriately suggesting poor quality of professional care. This may be associated with the risk of increased illness and again indicate a poor quality service. Monitoring quality may require that data be collected on the behaviour of individual prescribers which is certain to be met by some resistance particularly if individuals are to be singled out amongst their peers for poor performance. However, if the quality of individual professional performance is to be evaluated and changes made, than these efforts need to be done with the co-operation and participation of the professional staff or there is likely to be resistance to change [3].

Effectiveness, efficiency, equity and quality are naturally inter-linked. Improving clinical effectiveness (for example by increasing the use of medicines of proven effectiveness) may improve quality. Increasing effectiveness while controlling for costs may increase efficiency. In increasing efficiency, new opportunities can be created for improved effectiveness and equity. However, there may have to be trade-offs between these laudable ideals. For example, maximising effectiveness and efficiency will not necessarily result in a more equitable distribution of pharmaceutical resources or better quality pharmaceutical services. The costs which the community is prepared to assume may increase in order to improve quality, effectiveness and equity, but they may decrease if the community is determined to push for efficiency at the expense of other criteria. Therefore, it is important to find a balance between these different criteria.

3. Types of indicators

To determine the effect of drug policies one will have to find and select suitable indicators (i.e. measures). Indicators that will prove helpful in measuring the effects of a cost containment policy will relate variously to *internal* process (i.e. implementation of the policy) and to the policy's actual effects on drug management and delivery in the field (*external* indicators) as measurable in terms of health and economics.

3.1. Internal (“process”) indicators

In the administration of health care programmes, both governments and hospitals routinely collect process data. Input variables include the numbers of doctors and pharmacists; output variables include the volume of drugs prescribed and dispensed. Measures of process generally relate a quantity of input to some meaningful denominator; commonly used denominators include population served (e.g., drugs dispensed per thousand population) or patient population actually served (e.g., costs per patient day).

To assess the efficiency of the process in the delivery of pharmaceuticals, indicators have been developed that relate cost along various dimensions including input or output. Pricing indexes are a measure of process that can be used by policy makers to monitor the change in drug prices over time, though the figures may be distorted by changes to the product basket (see Chapter 2). Process data can also be used to develop prescribing indicators to monitor whether drug choice is appropriate, effective, safe and economical; a national insurance fund is for example likely to have very detailed data on prescribing in individual practices and for individual patients. Effectiveness can be monitored using process indicators of quantity, quality and appropriateness associated with variations in drug utilisation data. Indicators of the use of pharmaceutical services, relative to patient need, can be used to assess equity in terms of access. Indicators of the process of drug delivery such as availability (distribution of prescribers and pharmacies), organisation (types of facilities) and financing (co-payment arrangements) can be used to monitor equity in terms of potential access and the freedom of choice.

Improvements in process indicators do not necessarily signal better health or economic outcomes. A given input does not guarantee a given output, and an output may be affected for better or for worse by factors quite divorced from the input. There may also be a considerable time lag between changes in process indicators and associated indicators of outcomes. For such reasons it is not sufficient to monitor policies solely in terms of progress in implementation on the one hand or observed outcomes on the other; both are needed.

3.2. Outcome indicators

As implied above, one will always need to test the ultimate effect of policies in terms of what actually happens in the field where they are supposed to take effect. For example, the cost-effectiveness of drug interventions and programmes can be assessed using economic evaluations. Health status should be measured both at the individual and population level. At the individual level health outcomes focus on measuring clinical or physiological changes. The health status of populations can be monitored using epidemiological data such as mortality, morbidity, disease prevalence and incidence, as well as measures of social and economic productivity [12]. All the time one will need to beware of the pitfall noted under Paragraph 3.1. above, i.e., a known output may not have resulted from the known input, or from that factor alone.

4. Developing indicators for monitoring

Success in monitoring process and outcomes depends on the reliability of the indicators which are used. Five criteria should be considered when selecting indicators: *usefulness*, *clarity*, *measurability*, *reliability* and *validity* [18]. Issues relevant to the quality of indicators will be briefly considered here.

First of all, the indicators developed should be *reliable*, *practical* and *useful* to decision makers, helping them to improve the processes and outcomes of pharmaceutical care. Concrete issues directly related

to policies and for which suitable indicators have to be found include drug expenditure, consumption, prescribing and pricing, as well as health and economic outcomes. The indicators developed should be able to detect the effect of a policy in terms of effectiveness, efficiency and equity criteria. Some indicators, for example prescribing figures from a well-managed reimbursement system, are obviously reliable and relevant; others may well need to be field-tested and the results discussed with decision-makers.

An indicator must also be reasonably amenable to *measurement*. Just what one measures is likely to depend on the facilities one has, and which types of figures are most likely to be complete, representative, accurate, rapidly available and statistically valid [23]. Some types of data can be (and often are) captured in large administrative data bases; however these, as pointed out in Chapter 2, may have been designed for uses other than cost containment and policy review, and lack precisely the variables which one now needs. Data from such an information system may therefore prove disappointing when one puts questions which the system was not designed to answer. If one has any reason to doubt the reliability of the data in such a system, some form of peer review at the source will be advisable, for example to ensure that data are being entered consistently and in line with prescribed procedures.

In a cost containment programme, quantified data (especially costs) are obviously likely to be of most use, but qualitative data can also be very helpful. Qualitative indicators are generally based on “yes” or “no” answers to survey questions and are particularly useful in monitoring attitudes and preferences. Prescribing can for example be monitored both quantitatively in terms of the number of prescriptions written but also qualitatively in terms of changes in physician knowledge or attitudes regarding the prescribing decision.

Special studies such as randomised control clinical trials or observational studies can be used to gather data that are not collected by routine monitoring systems; these however involve additional costs and it may prove very difficult to maintain them consistently over a long period. Sentinel reporting systems, which collect data on a carefully selected sample, are useful for monitoring the short-term impact of policy implementation, particularly in order to detect unexpected or unintended outcomes [18]. Time pressures, the availability of financial resources and the willingness of staff members to comply with requirements will influence the type of monitoring method selected.

Establishing indicators for international comparisons is more difficult. As noted elsewhere in this chapter and earlier in this volume (Chapter 2), variability can be expected in the manner, types and extent of data collected between countries. In addition, ongoing policy implementation and reform can make it difficult to identify and maintain compatible indicators over a period of time. However, certain indicators for international comparisons of national drug policies [4] and indicators of drug use [26] have been defined and they are worth examining if it is proposed to compare policies across borders.

5. Setting monitoring targets

Just as each objective needs indicators, so each indicator needs targets in time. If for example one *objective* of a cost containment programme is to reduce the well-documented over-prescribing of antidepressant drugs, an *indicator* can be the quarterly prescribing level for five major drugs of this type as documented by national insurance payments, and *targets* could be a 20% reduction by December 2003 and a 50% reduction by December 2005.

Explicit targets for indicators should be incorporated at each stage of the policy, planning and budgeting process. At the policy stage, to take the same example as above, it may be decided that the over-prescribing of antidepressant drugs represents an unhealthy trend in mental health and brings with it

heavy expenditure as well as a risk of dependence. At the planning stage, consideration of what is known about the true levels of clinical depression in the population may lead to the conclusion that prescribing at one third of the current level is desirable and attainable; examination of the national insurance records will confirm that these provide a reliable indicator for the turnover in the principal antidepressant drugs. The budget will explicitly incorporate a projection for reduced prescribing costs, but also provisions for professional and patient re-education regarding depression. The targets will then be set in terms of achievements anticipated by 2003 and 2005. Defining and setting clear indicator-linked targets at the beginning of the policy process thus helps to ensure the objectivity of evaluation in later stages.

6. Techniques for evaluating projects and programs

6.1. Economic evaluation

Economic evaluation is an important tool for assessing the micro efficiency and effectiveness of pharmaceutical programs in terms of costs and outcomes, as well as cost/effect relationships for individual medicines. In seeking to maximise both effectiveness and efficiency despite constraints on resources, governments and industry have increasingly used economic evaluations to compare alternative courses of action in terms of both their costs and health outcomes. Economic evaluations generally draw upon decision analytic models so that the cost and health consequences of alternative treatment and probable pathways can be simultaneously analysed. Decision trees are useful tools for calculating and comparing the expected cost per patient outcome of alternative treatment strategies. Using a decision tree, an analyst is able to model and compare the costs and outcomes of a medical intervention (e.g., drug therapy) against that of alternative forms of treatment and (or) other medical or surgical interventions. This type of evaluation can simultaneously take into account the alternative means of delivering pharmaceutical care in terms of method, place, timing or quantity, at all phases of treatment [20].

There are essentially three basic types of economic evaluation: cost-benefit analysis (CBA), cost-effectiveness analysis (CEA) and cost-utility analysis (CUA). The debate is still on going as to which of these approaches is to be preferred.

Cost-benefit analysis (CBA) measures both cost and benefits in monetary terms as it seeks to identify interventions that will bring about potential improvements in welfare. This technique involves the need to place a monetary value on items such as health benefit. A number of means of doing this exist (e.g., the human capital method or measures of an individual's willingness-to-pay such as revealed preferences or contingent valuation), but to some extent the figures are unavoidably artificial. For example, the human capital approach does not measure the individual's willingness to pay for their own health and survival [21]. Although revealed preferences and contingent valuation do attempt to measure willingness-to-pay, the former involves an uncoupling of the valuation of consequences from the context [14], while the latter is still considered experimental.

Cost-effectiveness analysis (CEA) again measures costs in monetary units but it expresses effectiveness using a biological yet quantifiable unit of effect such as the number of lives saved or life years gained. CEA assesses the incremental costs and incremental effectiveness of one medical intervention relative to another. Unlike CBA, CEA ratios must be compared to an external standard and outcomes common to both alternatives are needed in order to judge relative desirability. A special form of CEA known as cost-minimisation analysis is essentially limited to comparing costs between alternative forms of treatment where the effectiveness of each has been demonstrated or can reasonably be assumed to be the same.

Cost-utility analysis (CUA), like CEA, is concerned with incremental analysis. CUA, however, quantifies effect in terms of “utility”. Utility in this sense represents subjective values (i.e. quality weights) given to their overall health status; over a period of time one may express the health status in “quality adjusted life years” (QALYs) or “health related quality of life (HRQL). These quality weights have the merit of combining both the positive and negative effects of a treatment into a single summary score that usually ranges between 0 (equal to death) and 1 (equal to perfect health). It is possible to compare health outcomes in different diseases using the elicited values. Combining health state utilities with cost information renders it possible to calculate cost-utility ratios for alternative treatments.

In spite of advances made in carrying out such measurements, the application of CUA is currently limited by problems associated with the determination of utility values and QALYs. In many instances, for example, utility scores cannot be obtained from patients themselves for such reasons as severity of illness, mental capacity or age, and they have to be derived by the observer from other groups in society. But this may be a good thing, as many observers believe that in systems where the public pays for health care, QALYs should be elicited from a random sample of the population.

Conducting an economic evaluation requires data on costs (i.e. unit costs or prices of resources), physical quantity of resources consumed (by the treatments being compared) and outcomes (i.e. defining comparative treatment effects and how treatment affects quality of life) [7]. The basic data requirements for both health and economic outcomes were discussed in Chapter 2. The data needed to conduct an economic evaluation will depend on the perspective or viewpoint used to determine the range of costs. Commonly chosen perspectives for economic evaluations are those of the health care provider, the patient, the community and society generally. The societal perspective includes all costs born by patients, insurers or other parties, while the patient perspective includes only those costs born by the patient. Therefore, changing the viewpoint will affect the range of costs considered and could affect the choice of programme or treatment being evaluated.

The data needed also depends on the time frame used. The time frame used for collecting data on costs and outcomes should not be misleading and bias the analysis in favour of one intervention over another. If costs are followed over a lifetime then it is standard practice to discount these future costs to present values. Methodological debates surrounding economic evaluations and how they are used by decision-makers is discussed in Chapter 5.

6.2. *Evaluating quality*

Several methods exist for evaluating the quality of pharmaceutical care provided from prescribing through to delivery. The narrowest of these is the Drug Utilisation Review (DURs). DURs are used to evaluate the level and pattern of drug use. They were originally motivated by concerns about excessive or inappropriate prescribing [8]. DURs can be used to document the association between inappropriate prescribing and its adverse clinical and/or economic consequences. Appropriateness of drug use can be assessed on three levels:

- (i) whether any medication is warranted;
- (ii) if indicated, which drug would be the agent of choice;
- (iii) whether the chosen drug is used in an appropriate manner (dosage, duration, type and frequency of monitoring and the risk of drug interactions) [5].

However, it is not always easy to make such an objective assessment at any of these three levels. To determine acceptability one will have to set the identified pattern of use against some recognised standard

which is applicable to that particular therapy (for example as defined in an authoritative therapeutic guideline). This can be time-consuming [11] and even controversial but necessary.

A second common method of evaluating quality is that of audit. Audit is used to determine whether an optimal quality of service is being achieved within the resources available. The evaluation can be used to uncover areas of problem or concern to prescribers and their patients, to determine whether there is an effective use of resources to achieve desired outcomes or to address equity considerations in terms of geographical, social or ethnic differences in service use and prescribing patterns in relation to population needs. There are two main types of audit; *medical audit* evaluates the quality of medical care, including procedures used for treatment, the use of resources and the resulting outcome and quality of life enjoyed by patients [22] while *clinical audit* focuses on the quality of professional care by doctors, nurses, pharmacists and other health care providers (e.g., in the delivery of pharmaceutical services). If the findings are indeed favourable, health providers and users can be reassured; if not, changes will be needed. Adjustments to service made in the light of medical audit findings can lead to improved patient outcomes, better quality of life and the more cost-effective use of resources. A prerequisite to audit is the availability of accurate patient information [2]. The main disadvantage of audit is that it takes a considerable amount of money and professional time.

Finally, quality assurance provides a systematic approach to evaluating health and pharmaceutical care. A WHO working group [25] defined four components of quality assurance in health care: patient satisfaction with services provided; professional performance (technical quality); resource use (efficiency); and risk management (the risk of illness or injury associated with the service). Quality assurance evaluations of prescribing for example have focused variously on *prescribing patterns* to assess physician competence and appropriateness in prescribing (i.e. performance) [15], on *drug utilisation* to evaluate different strategies to contain costs (i.e. resource use) [17], on *compliance* with prescribing guidelines to monitor the continuum of quality use of medicines between in-patient and out-patient care [19], and on the *monitoring of preventable adverse outcomes* (risk management). Important in performing a quality assurance assessment will be appropriate and valid indicators as well as a meaningful time-frame. For example, one study that was evaluating adherence to prescribing guidelines found that indicators evaluated at an individual patient level give differing results to aggregate data, and self-reported instruments were found to overestimate adherence [24].

6.3. Production and cost models

The extent to which efficiency has been achieved can be assessed using production and cost models. These models apply production and cost functions to any production process; they determine the particular mix of inputs which will result in the lowest costs for any given level of output and the optimal size of the production if costs there are to be kept to a reasonable minimum. These models have been applied to physician, hospital and insurance services to determine the extent to which production efficiencies have been achieved and how they can be further improved [1].

6.4. International comparisons

In an attempt to gain a perspective on the macro efficiency of the drug system, helpful comparisons can be made to other politically and economically similar countries. One must however beware of possible pitfalls in making international comparisons because of cultural, demographic and political differences between countries, as well as, methodological issues associated with the data used in the comparisons; the matter has been previously discussed in Chapter 2 and is touched on again in Section 7 below.

7. Limitations of monitoring and the use of indicators

The use of monitoring and indicators is not without problems. Some specific pitfalls have been noted above, but there are also more general difficulties. While for example performance, as judged on the basis of a single indicator, may have improved, it is important to put this indicator back into the wider policy context and consider whether the overall policy change which brought about this improvement was on balance beneficial. It is particularly important to consider whether using the selected indicators may have introduced perverse incentives that shift problems from one area into another that is not monitored. Making an effort to meet indicator targets can mean that other important issues get neglected, a dilemma known as Goodhart's Law of government policy indicators [9]. According to Goodhart's law, if some variable is made the focus of measuring policy performance, then people and institutions will devote a disproportionate amount of time and effort to meeting this target at the expense of other aspects of their performance which are not subject to the same level of scrutiny. The result can be disbalance with negative effects. This phenomenon is familiar: for example, although the objective of a negative list may have been to reduce drug costs, it could be that obliging physicians to prescribe other products will result in cost increases in unexpected areas (e.g., because of adverse reactions resulting in hospital admissions). The obvious solution would be to monitor more variables. However, if too many indicators are selected the evaluation may be rendered so complex or the measured outcomes may prove so contradictory that the findings are difficult to understand and act on. Finally, introducing too many indicators can render the entire process excessively costly and labour-intensive, the phenomenon that has been termed an "audit explosion".

A further risk is that in selecting indicators there is sometimes a tendency to choose an indicator or target that is not relevant to a particular policy context or health care system. The indicators may not be relevant despite being simple to understand and may have been selected because they were likely to suggest a favourable outcome. This tendency to isolate clusters from their context is known in epidemiology as the Texas-sharpshooter fallacy, referring to the story of a Texas sharpshooter who shoots at the side of a barn and then draws a bull's-eye around the bullet holes.

It is important not too adopt policies from abroad too rapidly merely because an audit carried out there has indicated that they are successful. Even if the foreign audit seems methodologically sound, the same policies implemented in one's own country may prove disappointing when the results are assessed, because of differences in the medical and organisational context or other difficulties pointed out in earlier sections.

It is important too that any results arising from evaluations be disseminated and action taken so that necessary changes are made. Results should be disseminated to the appropriate decision-makers in a timely manner. Strong leadership and governance principles can be useful to ensure that appropriate changes are made in a uniform manner at a macro level and where applicable at local levels. Problems associated with the dissemination of evaluations are discussed in more depth in Chapter 5 of this book.

8. Conclusion

Before planning any policy evaluation one needs to consider carefully how the pharmaceutical service is structured, how it functions (i.e. its dynamics) and how the goals and objectives of intended policy measures (whether related to cost containment or not) could affect it. Policy priorities will have to be set in advance and means identified of assessing progress. Cost containment policies can themselves be

costly as well as time-consuming, and only with good planning, the setting of clear priorities and careful assessment over time can one ensure that they are worthwhile and will do more good than harm.

The assessment of progress may well lead to the need to adjust, extend or even abandon particular policies. Since both the policies themselves, and any amendments to them as they are implemented, can have widespread implications for local structure and resources, health service managers should be involved in setting the agenda for the evaluations. In addition, the ultimate recipients of service – patients and professionals – should also be involved in assessing the effects of policies in the field. Most important of all, these ongoing measures of progress need to be studied, regularly and promptly, by the policy makers themselves, so that whatever policy changes are called for can be introduced without undue delay.

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Chapter 5

Making use of economic evaluation

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1. Introduction

Although awareness of pharmaco-economics has increased greatly, its practical use in decision making is, as we have seen in Chapter 4, at best opaque. Some of the issues will be considered in Chapter 6 in the context of the Australian experience in assessing matters of subsidy or reimbursement. This present chapter focuses on identifying barriers and potential solutions to increase the use of economic evidence in the decision making process.

Increasingly the pharmaceutical (and device) industries are using economic evidence as part of their submissions to the authorities for determining the reimbursement price of a pharmaceutical or its inclusion in a drug formulary. In part this has been a selective marketing strategy to promote the value added of a specific intervention, but more recently several countries including Australia, Canada, England, Finland, The Netherlands and Portugal have begun to introduce systems which formally link cost effectiveness to reimbursement decisions for new pharmaceuticals and, in some cases, other clinical technologies. Systems of this kind are known in the pharmacoeconomics literature as *fourth hurdles* or *cost-effectiveness hurdles*, because in effect they require pharmaceutical firms to demonstrate cost effectiveness before launch, in addition to quality, safety and efficacy, the first three hurdles ordinarily imposed by licensing authorities. Furthermore health technology assessment agencies have been established in most developed countries to provide further information on the clinical effectiveness, and in many (but not all) instances, on the economic impact of a technology [18]. Table 1 provides an overview of the situations in which economic evaluation should be expected to be helpful to decision makers.

Welcome though these developments are, evidence of the actual systematic impact of economic evaluation data on decision making remains limited [8,24]. More recently, the EUROMET study examined the use of economic evaluation in Europe and found that few decision makers made use of economic evidence [13]. A similar lack of evidence was reported in a recent European study of evaluations of health care interventions, although some *ad hoc* evidence of impact was observed [18]. A number of

Table 1

Economic evaluation as an aid to decision making

- Development of treatment guidelines
 - Decision making in health care organisations
 - Approval decisions
 - Reimbursement decisions
 - Pricing decisions
-

Adapted from Johannsen [4].

barriers against increased use of economic evidence by decision makers and practitioners are outlined in Section 2, together with some possible ways of promoting greater use of economic knowledge and tools in this field.

A second important reason for the apparent lack of impact of economic evidence on the decision making process in health lies in the methodological difficulties in measuring impact. This is beyond the scope of this chapter but it should be remembered that, even where economic evaluations *do* influence a decision making process this is notoriously difficult to confirm – for instance one consequence of using economic evidence may be to *do nothing*, i.e. not to change current policies or practice. Further research into impact assessment is required.

2. Barriers to the use of economic evaluation data

2.1. Inadequate links between knowledge producers and decision makers

Links between the various bodies that may produce economic knowledge and those involved in decision making may be weak. An additional impediment seems to be a fragmented decision making process. Guidelines developed at the macro level may fail to play a role in decision-making at the lower levels for many reasons including inadequate dissemination, lack of professional support, lack of financial incentives or failure of political will [1]. Regardless of the management hierarchy in any country's health care system, using economic knowledge better in decision making demands a multi-dimensional approach tackling a number of different obstacles.

Increasing the sense of ownership that decision makers have over knowledge has been shown to increase the use of such knowledge in the decision making process [15]. Elsinga and Rutten [10] demonstrated that close co-operation between researchers and policy makers in The Netherlands had promoted the use of economic appraisal in health care decision making at both the micro and macro levels. Involving decision makers in a study means that it is more likely to be relevant to their needs. A decision maker who has commissioned a pharmaco-economic study or served on its advisory committee is less likely to ignore its conclusions than if he has merely experienced it from the outside. In addition, involving these decision makers may help to ensure that the results are more widely disseminated.

Ideally all stakeholders should be involved from the outset, i.e. not just in the process of conducting the study, but also in framing the study. Researchers can be guilty of framing studies to answer research questions of limited policy relevance, whereas decision makers in commissioning research may seek answers to questions which are unlikely to be delivered within the time frame of the study; there is therefore every reason for them to work together from the planning phase onwards. One approach to that, which also builds a joint sense of ownership in the work, is to be seen in the Policy Synthesis Programme developed by the Canadian Health Services Research Foundation [4]. This programme brings researchers and policy makers together from the outset, to develop a common approach to a research question. One way in which this process seeks to overcome barriers is including both researchers and policy makers in mixed groups from the outset, rather than have both groups naturally clustering together and adopting more entrenched positions.

2.2. Lack of receptor capacity

Evidence from economic evaluation is often presented to decision makers and practitioners in a form which may be impenetrable for an individual without a background in health economic appraisal. Reports

may be very long, highly technical and fail to set out clearly the policy implications of a technology or procedure. Decision-makers neither have the time nor in many instances the technical expertise to digest such reports sufficiently. This barrier may be overcome in part by producing short reports, e.g., with a single page for the main message, three pages for the executive summary, and 25 pages for the report itself [3]. One should also try to create a cadre of knowledge brokers who would act as a conduit between the worlds of research and policy making. Such knowledge brokers would possess skills in economic evaluation and communication, they would also be comfortable in a policy making environment. Their job would be to interpret economic knowledge and present it in an appropriate form to policy makers and practitioners in order to facilitate the translation of evidence into practice. The knowledge broking process goes in both directions and it places much emphasis on the reinforcement of messages, to counter the non linear nature of knowledge transfer and assimilation. It must be remembered that economic evidence is only one of the various forms of knowledge that will reach policy makers, who will also be confronted by various myths, anecdotes and truths through other media; knowledge brokers again can filter such information and help to put it all into perspective.

This is not mere theory. As well as being used by the CHSRF to help develop receptor capacity in Canada, the Swedish Health Technology Assessment Council (SBU 2001) have for many years employed such knowledge brokers as roving ambassadors to take the Council's message – and other information – to practitioners throughout the country. These knowledge brokers can also help play a role in tackling some of the myths commonly held in the medical community about health economics, notably that it is a tool for denying individuals access to effective treatment interventions. Providing medical undergraduates with some teaching in health economics has also been advanced as a means of creating more comprehension of its relevance [17], and in the UK a leading charity, the PPP Healthcare Trust, is now funding a chair in health economics with the express remit that health economics training be provided within a medical school.

2.3. Limited acceptance of external data

Within a given country or region, there may be a shortage of researchers or funds, making it necessary to rely on economic data produced elsewhere. Such data naturally relate to the place where they were produced, and they may or may not be applicable in an area where the situation differs, for example as regards clinical practice, local health service delivery or relative prices. Judgements about whether or not they are likely to hold will be based on what are thought to be underlying similarities or differences in both biological factors and clinical treatment patterns. More often than not, it will be impossible to generalize from them, because of the marked differences between countries in their health care systems and treatment costs. Economic evaluations therefore require adjustment to take account of local treatment costs and practices; this is more valid than using multinational average cost data. To some extent economic cost data can indeed be adjusted, provided that the economic analysis has clearly distinguished between treatment costs and resources used. However this requires access to accurate local costing data, which itself may be problematical. In a recent analysis, the transferability to the French health system of foreign economic evaluations of adjuvant therapy for breast cancer was examined. None of the studies identified in the systematic review could be transferred, as costing data were not reported in a transparent manner [25]. As a result the authors recommended the international standardisation of data requirements in published economic evaluations.

Adjusting for treatment patterns is perhaps more complex. For example, a new intervention may have less clinical impact in a country where the condition is already treated intensively and greater impact

in a country where no alternative therapies are available. One way of dealing with uncertainty over the effectiveness of a treatment, particularly if research capacity and resources are limited, is to use a meta-analytical approach. Meta-analysis has been used in an attempt to overcome the problems in generalizing from a single Randomised Clinical Trial (RCT), especially because of a small sample size or other features of the protocol. Pulling together statistically the results of independent RCTs with the help of meta-analysis can provide a single estimate of effect for a treatment. An effective meta-analysis demands a strictly systematic review of the literature, ideally avoiding any language biases which could affect conclusions.

2.4. Methodological barriers

Most economic investigation in this area takes the form of cost effectiveness analysis, in which the costs and clinical outcomes of an intervention are compared. The incremental costs and effectiveness of one intervention compared to those of the next best alternative can provide decision makers with information on where one can most efficiently allocate scarce resources between different health care interventions. Decision makers also of course need to consider a range of factors including equity, budget impact and political preferences. However, even if efficiency alone were to be considered, it may not be reliable to rank therapies according to their incremental cost-effectiveness ratios. The dimensions of cost effectiveness analysis are sensitive to change, making comparisons of the ratio between models difficult. Where the numerator and denominator in the ratio cannot be assumed to be independent of one another, testing for statistical differences is difficult and requires the application of methods such as bootstrapping. When two treatments have equal medical costs, problems of interpretation arise, particularly when outcomes show only marginal differences or a mix of positive and negative benefits. Another problem is that most economic evaluations are based on efficacy studies carried out prior to marketing rather than on real post-marketing work in the field. An intervention may be shown to be cost effective in a trial, but if actual practice differs from the assumptions made, this product may not achieve the anticipated levels of cost effectiveness in practice. (It could of course be even more cost effective.)

When economic evaluation deals with a particular population, it may fail to provide a breakdown for each sub-population. Even where the cost/effectiveness ratio is poor for the total population, it may nevertheless prove to be favourable for a particular sub-group. Patient preferences for different interventions may also need to be addressed. Inconsistency in the inclusion/exclusion of indirect costs (such as those for informal caregivers) and societal costs will also affect these ratios.

While therefore cost/effectiveness analysis (CEA) is readily accepted as logical by clinicians, it remains a tool of limited usefulness for policy decision making, particularly since only interventions which have common clinical outcome measures, and similar study designs can meaningfully be compared. Cost utility analysis (CUA) overcomes this problem by estimating outcomes in a single outcome measure, quality of life, using one of a number of disease specific or generic instruments such as the EuroQOL [12] or the Health Utilities Index [27]. All the same, it remains difficult to transfer quality of life estimates from one specific context or population to another. Cost benefit analysis (CBA) measures both outcomes and costs in monetary terms, therefore allowing an intervention to be compared not only with another health care intervention, but also with any other publicly funded project. Theoretically this approach considers all costs and benefits to society as a whole, and is the most appropriate for resource allocation. However methods used in practice to elicit monetary outcomes, such as willingness to pay or accept costs, remain controversial. The validity of the actual estimates has been questioned, and clinicians are in any case particularly reluctant to accept evaluations in which health outcomes are expressed in financial

terms. For such reasons, CBA is not currently recommended in various national guidelines for economic appraisal (see next section).

2.5. Limitations of economic guidelines

The variety of economic evaluation techniques available and the inconsistency in the collection and use of both cost and outcome data, can readily confuse both decision makers and practitioners, especially when they are presented with apparently contradictory conclusions from different studies of the same intervention. The standardisation of methods in economic evaluation through the use of well accepted guidelines is one way in which greater harmonisation in economic appraisal can be ensured, making it less difficult to determine whether differences between studies are due to real factors or methodological differences. This is particularly important if studies are being carried out in different settings or may be internationally biased. Standardisation may also help non-specialist decision-makers judge the quality and correctness of a published study and draw valid implications for their own environment.

The evidence on the effectiveness of guidelines is however at best weak and international harmonisation of economic guidelines has some way to go. In recent years there has been an explosion in the number of guidelines available, but differences in the approaches which are recommended remain. This is evident from Table 2, which highlights key recommendations from Australia, Canada and England.

The guidelines differ particularly in their choice of analytical technique and outcome measures. Most strikingly, cost benefit is a preferred measure in Canada, whereas it is explicitly excluded in England and positively discouraged in Australia.

Regardless of the differences in guidelines, their development has been an important step in reducing the potential of bias in industry-sponsored trials [9]. The credibility of groups performing economic evaluation may sometimes be undermined by a lack of transparency in techniques used, or by their organisational structures, i.e. they may be seen as too close to either government or industry [6]. There is often little or no accountability or quality control for economic evaluators other than academic peer review. It has been argued that introducing some form of quality auditing may help to improve the credibility and consistency of these evaluations [16,22]. Monitoring would include an assessment of the methodological competence and appropriate choice of data. It would consider the choice of assumptions, data and analytical techniques as these can bias and pervert resource allocation decision. Simply relying on passive dissemination and uptake of guidelines without policing may result in poor methodological quality and bias.

2.6. Timing of economic evaluations

Another significant barrier to the use of economic evaluations by decision-makers has been the difficulty in gaining access to relevant studies in a timely manner. When decisions about the introduction of a technology are being made it is better to provide timely data on costs and benefits rather than to disseminate this after the event [8]. This can be helped by international co-operation. In an effort to help meet the needs of decision makers, the Cochrane Collaboration was established as an international network committed to preparing, maintaining and disseminating systematic reviews of research on the effects of health care. The reviews are available electronically on the Cochrane Library. A useful website to identify other such resources is *Netting the Evidence: A SchARR Introduction to Evidence Based Practice on the Internet* available at <http://www.shef.ac.uk/~scharr/ir/netting/>. Despite these initiatives to prepare,

Table 2
Comparative treatment of key methodological issues in national guidelines

	Australia (Commonwealth of Australia 1999)	Canada (CCOHTA 1997)	England (NICE 2001)
Viewpoint of analysis	Societal; show impact on the drugs budget	Societal; disaggregate by other relevant viewpoints. Can also undertake financial impact analysis	NHS and Personal Social Services. Also undertake financial impact analysis
Comparator	Most frequently used alternative	Existing best practice and minimum practice	Most frequently used alternative
Source of medical evidence	Effectiveness rather than efficacy	Effectiveness rather than efficacy	Any source, but must be justified
Analytic technique	CEA encouraged, CBA discouraged	CUA or CBA preferred, although CEA acceptable	CEA or CUA only
Outcomes	Can be intermediate or long-term	For CUA include one instrument from each of three types, disease specific generic, or preference based measurement. For CBA must use a contingent valuation method, e.g., willingness to pay	Long term clinical effectiveness measured in mortality and morbidity
Incremental analysis	Required	Required	Required
Allowing for uncertainty	Sensitivity analysis required	Statistical analysis if applicable, multivariate analysis encouraged	Sensitivity analysis Required
Discounting	5% per annum for all costs and outcomes	5% per annum for all costs and outcomes	6% per annum for all costs and 1.5% per annum for benefits
Presentation of results	Structured format	Report results in disaggregated as well as aggregated data.	Use International Conference on Harmonisation guidelines, include risk estimates and sub group analysis where appropriate. Reports costs and resource use separately.
Equity	N/A	No equity weights should be used, but results should transparently indicate any equity issues	Provide information on the clinical and social status of patients most likely to benefit

maintain and disseminate systematic reviews, many trials completed by pharmaceutical companies are not published and are therefore not included in systematic reviews of the evidence.

As well as timely data collection, the timely dissemination of economic evidence is also crucial. Results of economic appraisals should be disseminated sufficiently early to be capable of influencing deci-

sions. The results of a study are likely to have greater effect if dissemination is attuned to the budgetary planning cycle. In addition, those producing evaluations should be aware of current policy issues with relevance to a specific technology [11].

2.7. Providing incentives for use of economic evaluation

As well as tackling some of the barriers to the use of economic evidence, positive incentives and mechanisms can be used. Most notable of these at the policy making level has been the increase in the use of explicit fourth hurdles in a number of countries, which explicitly link reimbursement and access to health technologies to cost effectiveness. Even where guidance was theoretically voluntary but strongly encouraged, as was the case with NICE in England [21] monitoring bodies can be used to encourage implementation. A Commission for Health Improvement now assesses whether NICE guidelines are being enforced locally; this body indeed has the power to take over the administration of local bodies if their performance is unacceptable.

Financial incentives may also be used to increase the uptake of evidence at the local level; rates of influenza vaccination in Denmark were for instance increased following the introduction of targeted payments to patients, whilst in the UK cervical cytology screening became more widely employed following the introduction of additional performance related payments based on the level of uptake achieved [19].

3. Conclusion

The facilitation of the use of economic evaluation knowledge in the policy making process is complex, and as yet there is little evidence to demonstrate that economic evaluation is used systematically in a decision making arena. There is a need to address the imbalance between research and development, but also to concentrate more resources on the active dissemination and implementation of knowledge.

There are enormous interests at stake, pharmaceutical companies are increasingly expected to continue to fund analyses of cost effectiveness as part of the reimbursement process. Yet in many instances decision makers do not have the skills (or access to researchers with skills) to objectively assess this economic evidence. This gap between knowledge producers and knowledge consumers might be met through the development of local receptor capacity, e.g., knowledge broking. The ability to assess objectively and inform the policy making process is of particular relevance given the inconsistencies in the use of economic evaluation within and between countries. Such inconsistencies extend to guidelines themselves, with several well known guidelines holding very different opinions on the role of cost effectiveness and cost benefit analysis. One possible vehicle for overcoming these difficulties may be the establishment of an international clearing house for economic evaluation, which would identify methodological differences and help to facilitate the transfer of such knowledge between different settings. These methodological issues are far from being resolved; the debate and disagreement may indeed become even more intense [23]. Furthermore there is a need to invest more resources into research and collection of data on impact assessment, since it may be the case that economic evaluation has had a significant impact in decision making. Again increasing the involvement of decision makers in the knowledge production process may increase their willingness to provide data on how decisions are made in practice. Without evidence that investment in such evaluation does help to facilitate change, there remains a danger that enthusiasm for the conduct of evaluation may wane, increasing inequities and inefficiencies in the allocation of health care resources.

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Part II

Selected experiences with policy options

Chapter 6

Measures relating to use of drug subsidy lists and to regulation

A.S. Mitchell

1. Terminology

This chapter is contributed primarily from the perspective of a country – Australia – in which the pattern of public payments for drugs is built largely around the compilation of “drug subsidy lists” – i.e. lists of those drugs considered eligible for such payment. In other countries the terminology is a little different but, as pointed out in Chapter 3, the notion of establishing positive (or negative) lists for this purpose is widely accepted.

2. The systematic use of economic evaluation

In the last decade or so, there has been increasing interest in the use of economic evaluations of drug treatments in order to provide a firm basis for the value-for-money judgements that are inherent in drawing up or amending drug subsidy lists. The relevant form of economic evaluation is an incremental analysis. This can be defined as an analysis of the change in costs as compared to the change in outcomes that will occur when one intervention substitutes for its comparator [4], for example when one chooses to treat hypertension with a newer angiotensin II receptor antagonist or calcium channel blocker rather than with an older diuretic. This approach recognizes that there is always an alternative approach to treatment (even if it is merely the choice of “no active intervention”). The changes in costs and the resulting changes in outcomes must be quantified as accurately as possible.

Decisions to change the subsidy status of a drug are mostly made “at the margin”, i.e. they relate to a particular new drug [7]; they are not part of “global” decisions in the sense that the subsidy status of all currently subsidised drugs in the therapeutic class is under review each time a new drug is considered. Rather the considerations focus on the comparative merits and costs of the proposed new drug as compared with its nearest competitors.

3. The decision-making framework

The first basic requirement is a decision maker. The administrators of many large drug payment systems seek advice on clinical – and increasingly on economic – matters, usually from an independent committee. In these instances, actual decision-making is usually shared between the committee and the administrators. The cardinal issue in each decision is usually whether a new drug should or should not be

added to the existing lists. An incremental economic evaluation of the proposed drug can provide useful and relevant information to help in making such decisions. However, incremental economic evaluations are even more useful if the drug subsidy system has the capability of restricting drug subsidies to specific patients and specific indications, or of negotiating prices. Targeting the subsidy to patients likely to benefit most and/or lowering the price can both improve the cost-effectiveness, or value for money, which the drug provides [8].

The second requirement is a process by which timely and relevant information is provided to the decision maker. There are three basic approaches. Firstly, the commercial sponsor of the drug may initiate consideration, by lodging an application for subsidy. This is attractive because sponsors know when new drugs are becoming available, have the incentive to seek listing and have access to most of the necessary information. In addition, it leaves the onus of proof with the sponsor to meet any requirements of the decision maker. Secondly, other interested parties outside the scheme (for example a patients' organization) may lodge a similar application; this can be more difficult where the requirements of the decision maker are onerous, requiring the submission of medical and economic evidence which the interested party may not have available. Thirdly, the drug subsidy system itself can initiate consideration, for example where it feels that new published evidence calls for a re-evaluation of therapeutic preferences. In practice, all three approaches are used, but the first is the most usual.

The third basic requirement is for the information needs of the decision maker to be clearly made known. This is important to promote consistency in applications and thus in decision-making. This is best achieved through the promulgation of guidelines. Australia was the first jurisdiction to release guidelines that requested economic analyses. The current Australian Guidelines date from the November 1995 edition [3]. These are the only set of guidelines to have been revised by a decision maker in order to reflect insights and experience and, in particular, to indicate the basis on which the decision to list a drug could be negative as well as positive. The province of Ontario in Canada released its guidelines in 1994 [9]. The province of British Columbia accepts submissions that follow either the Ontario guidelines, or the guidelines of the independent Canadian Coordinating Office of Health Technology Assessment [2]. The French government released guidelines in 1995 [10]. The Sickness Funds Council in the Netherlands released Guidelines which entered into effect in 1999 [1]. Guidelines fall within a wide spectrum which ranges from the purely clinical at the one extreme to the purely financial at the other.

The fourth basic requirement is that one must be able to appraise independently and critically the submissions received according to the Guidelines. The Australians have instituted a two-step process to appraise submissions: an in-depth review by evaluation teams comprising skills in clinical epidemiology, biostatistics and health economics; and a concise overview by an independent technical committee comprising individuals of national standing from the same three skill areas. The integration of the three skills is deliberate. The appraisal restricts its comment to the validity, relevance, strength and interpretation of the evidence. It leaves the value judgements inherent in the decision-making process to those delegated to making the decisions. The Ontarians have lists of clinical and economic experts who provide advice on submissions according to a set format. Advice from a clinician is routinely sought for new drugs. When thought necessary, economic advice is separately sought. Each expert is asked to recommend a course of action to the decision-makers. The British Columbians have two separate teams, one to review the clinical evidence and another to review the economic evidence. Both teams prepare recommendations to the decision-makers. The French do not appear to have established an evaluation process. This seems to have contributed to the decision of the key committee (*la Commission de Transparence*) to indicate in 1997 that it no longer wished to receive submissions according to its guidelines.

4. Experience with and potential offered by economic evaluation

Little material has so far been published which provides any real insights into the experience gained in using economic evaluations in a systematic manner. Most of what has been learnt lies with the Australians, although the Ontarians are currently reviewing their experience. The Australian experience suggests that the underlying clinical evaluation is pivotal [5], and hence has focused on the scientific basis of the clinical evidence. Even under this regime with clear guidelines, underpinned by strong legislation, problems arise frequently during the conduct and interpretation of the analyses [6]. Economic evaluation is intrinsically complex and genuine differences of opinion on how to interpret the results of clinical trials complicate matters further.

The problem most commonly encountered relates to means of determining the therapeutic outcome when comparing different drugs. It is possible that this focus could become the basis of future harmonization of the preparation and appraisal of economic evaluations around the world. Key issues would include methods for rigorously applying high quality clinical evidence across different contexts and integrating appropriate inferences from this evidence into economic evaluations. Based on a careful and rigorous evaluation of the experience in Australia so far, Hill et al. [6] warn that any agency or organization that wishes to make formal use of pharmacoeconomic data should realize the rigorous appraisal process that is needed before the raw data can be used as a basis for taking decisions. Published pharmaco-economic analyses usually do not provide enough detail to assess the accuracy of the underlying data.

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Chapter 7

Experiences with budgets

Christine Huttin

1. Introduction

In many countries, as described in previous chapters, governments today use financial measures to contain drug costs. This chapter will review some major examples of concrete measures with which experience has been gained. They range from imposing an overall ceiling on national drug expenditure (France) to professional measures such as budget holding for physicians (implemented in countries such as the UK, Germany and Sweden in Europe, as well as in Israel).

2. National ceilings on drug expenditures

Some governments opt for financial ceilings on the various forms of health care expenditure and set sanctions which can be imposed if these ceilings are exceeded. Drug expenditure is likely to be a component in several of the areas of health care for which ceilings have been set. In France since 1997 a national target for annual health expenditure (ONDAM)¹ has been set by the government, subject to approval by the parliament. The overall maximum level of expenditure is set in terms of four ceilings: for ambulatory care, for public hospitals, for private clinics and for other types of health care organizations, such as health centers for the elderly. The ceiling for primary health care expenditure is then split into three more specific ceilings: one for general practitioners, one for specialists and one for other services (e.g., dentists). These ceilings cover physicians' fees as well as drug expenditures, tests and diagnostic examination. In 1997, for instance, the ceiling for primary health care expenditure was as follows (Source: Loi de Finances, 1997):

General practitioners	143 billion FF
Specialists	68 billion FF
Others	56 billion FF

Within the first two categories, the expenditures for fees and other services (prescriptions, exams and tests) were in 1997 as described in Table 1. Sanctions and other types of measures accompany such national ceilings and can be implemented where the ceilings are exceeded. Physicians or pharmaceutical companies, for instance, may be required to pay back part of the overspent budget.

¹ONDAM: Objectif National des Dépenses d'Assurance Maladie (National Target for Health Insurance Expenditure).

Table 1

General practitioners		Specialists	
Fees	29 billion FF	Fees	42 billion FF
Prescriptions and other acts	114 billion FF	Prescriptions and other acts	26 billion FF

Source: Loi de Finances, 1997.

3. Professional measures

Instead of (or in addition to) national budget ceilings, some countries favour a series of financial measures involving health professionals, particularly physicians and pharmacists, to make them cost sensitive. This section will consider the approach whereby individual physicians are called upon to act as fundholders, i.e. to manage a health care budget (as for instance in the UK or in Germany), as well as certain measures designed to influence pharmacists via different systems of remuneration.

Fundholding: The theory of fundholding as developed in the 1980's reflects the argument that incentives rather than mere financial mechanisms have to be designed if one is to address inefficiency and cost-control approaches effectively. Budgets can cover different types of health services, various types of organizations and different professional groups (e.g., physicians, pharmacists and nurses). Unlike pricing policies or reference price systems, a budget addresses global issues of spending, taking into account questions of price and volume, but also the allocation of resources between services. The most extensive experience in this field in Europe has been gained in Germany and the UK.

The United Kingdom implemented its system of individual budgets in general practice in 1989. Physicians could originally opt to enter a budget holding system or not. Since April 1999 however, the "New NHS" has set up new organizations for primary care, the so-called PCG's (Primary Care Groups), and a predetermined budget has now become mandatory for all general practitioners who receive a group budget, a group normally comprising some 50 GP's. Since the UK has experienced ten years of budget holding for physicians, numerous studies have assessed the impact of such measures [7]. In early evaluation studies, there was increasingly strong evidence that fundholding practices did limit prescribing cost more efficiently than did practices that were non-fundholders [3,5,8]. The Bradlow study, for example, provides an estimate of cost increases following the NHS reform of 1991 among different types of practices. A large proportion of the fundholding practices made savings in their drug budget at the end of the first year of fundholding, ranging from 2.9% to 10% measured as the net ingredient cost (NIC) for medicines, whereas among non-fundholders expenditures increased by 18.7%. Concerning the NIC increase among fundholders, the study shows that the effects differed between those practices which had dispensing rights and those which did not.

As for reference pricing, scientific research designs models, such as experimental longitudinal designs, are not widely used to provide scientific evidence as to the impact of fundholding on prescribing; outside Europe, only Israel has opted for such a design and has done so on a limited scale.

Factors determining response: There are not many data on the factors which determine the reduction in prescribing costs. However, Whynes et al. [11] suggested that GP's who were total fundholders spent less time on management than did non-fundholders. In addition, a higher proportion of fundholders operated on the basis of a partnership agreement, in which all the partners had agreed on a protocol for patient management and operations. Moreover, fundholders possessed superior systems for dealing with

information and patient management systems. The motivation to reduce prescribing costs was mainly the fact that fundholding practices could reinvest budgetary savings, so as to improve diagnostic facilities and raise the standard of patient care.

Health related effects: As there is no quality assessment of prescribing policies among overall fundholders as compared with non-fundholders, it is not possible to determine whether prescribing cost economies obtained through the fundholding system are really in the community's best interest. There is, for example, no evidence of the effects on outcome measures such as long-term morbidity or patient satisfaction.

The effects of fundholding on prescribing patterns and costs may have been transitory, since more recent studies show no differences in the reduction of prescribing costs between fundholders and non-fundholders (e.g., [9]). One can also argue that drug manufacturers may have adjusted their UK marketing policies to face the new reality of medical fundholder managers. Research into the impact of fundholding on referral patterns [4,10] suggests that financial pressures have had little effect on general practitioners' referral decisions. Neither of these two studies found any evidence of change in the proportion of referrals between the two types of practice groups, i.e. fundholders and non-fundholders, following the National Health Service reform.

A major issue related to the fundholding system refers to the differences in access to secondary care according to the bargaining powers of fundholders versus non-fundholders or among different types of fundholders. If there is a stringent rationing of health services, then this negotiation power between different types of practices may support the strategies used by primary care services to facilitate access to secondary care for their patients (e.g., in the queuing system).

A fundholding system usually provides greater accountability to primary care physicians; it may for example empower the practices to provide extended community services. The terminology may become politically sensitive, particularly since creation of drug budgets at this level can be regarded as comprising a relative transfer of power to primary care physicians in the decision-making process on prescription drugs. This is the case, for instance, in the new NHS in the UK, where other concepts, such as Primary Care Group or Trust, with wider areas of accountability than budgets and forms of dynamics other than competition have been in place, especially in relation to drugs.

Though a fundholding system may appear as a power shift from national health fund agencies towards the medical profession, it may nonetheless be considered, at some stages of health care reform, as part of a hidden political agenda, where physicians feel they become "scapegoats". The fundholding system is at all events an important instrument to modify the power relation between or within the medical profession and other stakeholders. Much depends on the implementation process (in stages) and the comprehensiveness of the system in determining whether the introduction of these changes will lead to a fragmentation of the professions' power or will actually shift more power to physicians' organizations. The levels of fragmentation may be split between primary care physicians and consultants, or fundholders and non-fundholder physicians. By contrast, the fundholding system provides a larger power basis for collective decision making in organizations governed by clinicians. The implementation of fundholding in a health system may need to proceed in incremental steps in order to determine through experience the right organizational sizes for the grouping of primary care physicians.

Germany first implemented a national budgetary approach, thereafter introduced budgets at the provincial (Länder) level and then debated individual budgets for physicians. The UK, first experimented with partial fundholding (only one proportion of the general practitioners of the nation signed fundholding contract). Then, through the introduction of Primary Care Groups, it adapted the first concept of fundholders into a system concerning the whole profession, within larger collective organizations than the first

generations of fundholders. In relation to drug budgets, these larger organizations nonetheless had roles quite similar to the former fundholders. The forms of implementation may therefore partially depend on political options for centralization/decentralization of health care reforms. The US has experimented various types of Primary Care Groups, but the experiences appear not to have been very successful in terms of control over drug budgets. Little research has been performed so far to see whether within the context of a universal health system, such as Britain's NHS or the German system, drug budgets may achieve their targets more successfully than in a highly competitive environment.

If a fundholding system is voluntary, only larger practices or more entrepreneurial physicians will embark on contractual fundholding agreements. Yet if it is made mandatory in order to avoid some of the inequity effects, then more discipline is introduced in the grouping of physicians and some doctors are obliged to join collective organizations against their will. This represents a management challenge for fundholders and can be addressed with incentive mechanisms.

Fundholding is a way to increase the accountability of the professions and it can become quite important, in the context of a growing empowerment of patients (e.g., as they become better informed, in part from direct sources such as websites, as to their conditions and treatment options).

Recent developments in fundholding such as the UK experience, tend to combine the approach with the implementation of clinical governance, which facilitates an increased leadership by physician-led organizations vis-à-vis the stewardship by health care organization managers. Managers employed by physician groups usually share responsibilities, and clinical governance "leads" to sharing of key decisions in such organizations, for example as regards trade-offs on the cost and quality of primary care services (in particular drug interventions). Another recent development tends to extend the competence of primary care organizations with budgetary powers over drug budgets beyond the borders of health care services. Such approaches may lead to some forms of integration between primary care and social services.

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Chapter 8

Experiences with reference pricing

Christine Huttin

1. Definition

Reference pricing is not a form of price regulation; it is a means of limiting expenditure on the reimbursement of drugs by making use of the existence of equivalent drugs on the national market and setting a reimbursement tariff (called reference price) for groups of drugs which are considered to be “interchangeable”. In many therapeutic fields one encounters a series of alternative marketed products which, while not identical, essentially serve the same purpose. Nevertheless, the prices of the drugs in the “interchangeable” group may vary very greatly, with the newest products often being considerably more expensive than the others. Rather than agreeing that public funds should cover the costs irrespective of which product in the group a physician prescribes, a reference price system sets an acceptable price level. This may be the mean of the various prices, or may reflect the price of one of the lowest-cost items in the class or an average of various low prices; alternatively it may be the price of the product considered to be the most cost-effective in its category. If the physician wishes to prescribe a more expensive drug within the group, he may be called upon to provide special justification or the patient may be required to cover the extra costs.

Reference pricing as defined above, and as discussed further in this chapter, is based purely on a comparison of prices in the home country. However, there is also an alternative type of reference pricing which can be applied, in which the prices charged for drugs in other countries are also taken into consideration. Where a country has a system requiring official approval for drug prices, a comparison with prices in other countries is often used in determining the price which can be charged nationally. In that situation, lower prices encountered in other countries can be also used as references for setting reimbursement prices.

2. Use of national reference pricing

2.1. *Development of national systems*

The use of national reference pricing has been the subject of much debate within governmental institutions and with major stakeholders such as industry, the medical profession and patient groups. In Europe, the system has been adopted in countries such as Germany in 1989, Denmark in 1991, The Netherlands in 1993, Italy in 1995, and Spain in 1999. It is not used in large markets such as France and the UK, though in the latter country the setting of acceptable prices for generics follows a similar approach. Reference pricing has also been widely adopted in Central and Eastern European countries

(CCEE). Historically, the use of national reference pricing in Europe first attracted countries with high drug prices, a large generic competitive market and large price differences between the various versions of multi-source drugs – a set of factors which rendered this approach both necessary and feasible. In recent years countries with lower drug prices have also adopted the approach (e.g., Spain and CCEE). Outside Europe, reference price approaches have been applied in British Columbia (Canada) since 1995, and in New Zealand. The possibility of adopting the system was also discussed in Japan in 1998.

In countries, such as some of the member states of the European Community, where social health insurance funds are the largest purchasers of drugs, national reference pricing can have a considerable effect on corporate strategies for R&D and on marketing policies.

Setting a National Reference price system involves four main decisions:

- defining the number and scope of each class of “interchangeable” drugs for which a reference price is to be set;
- determining the way in which the reference reimbursement level is to be calculated for each individual class of drugs;
- establishing a procedure for defining the classes and setting acceptable reimbursement levels;
- setting mechanisms to permit exceptions where these are justified.

2.2. Definition and scope of drug classes

In order to implement such a system, one must define the various classes within which drugs are considered “interchangeable”, and one must define the market segment within which the system is to be implemented. Several options exist: one can for example limit the system to certain drug categories, usually those representing a major share of a drug budget; one can apply different criteria to the various classes in order to decide on the degree of interchangeability of the drugs within each; and one can choose to introduce the method gradually, experimentally or incrementally, perhaps in order to arrive ultimately at a comprehensive reference system.

Criteria used to define drug classes vary country by country and according to the market segment which is considered for reference pricing. A class may simply comprise drugs having the same active ingredient (as is the case of Germany for level I drugs), or it may extend to drugs with ingredients which are pharmacologically and therapeutically closely similar (Germany for level II drugs and British Columbia); in the broadest approach, a class may comprise all drugs with a similar therapeutic indication (The Netherlands).

The following are some country examples on the definition and scope of drug classes for a national reference price system.

Germany was the first country in Western Europe to introduce a reference price system, initially based on classes of drugs having the same active ingredients, and later moving to classes with therapeutic comparability. The system was designed to apply both to research-based and generic drugs, which were to be included three years after patent expiration. The length of this period was judged sufficient to ensure that generic competition would allow a fair representation of market prices.

Three types of drug classes were then defined:

1. Drugs having identical active ingredients (Level I).
2. Drugs having therapeutically comparable active ingredients (especially drug containing similar chemical ingredients) (Level II).
3. Drugs with a comparable pharmacological profile (especially fixed combinations).

Level I drugs were grouped easily, but decisions on level II and III were more complex and only a selection of these drugs were clustered within the reference price system.

Spain has introduced very restrictive reference pricing, limited to level I drug classes in the German definition, involving 50 drugs with identical ingredients [9].

British Columbia (Canada), under its Pharmacare programme, introduced reference pricing in five drug classes only, chosen primarily because of the level of expenditure which they represent in the drug budget: NSAIDs, histamine-2 receptor antagonists, oral nitrate, ACE inhibitors and dihydropyridine calcium-channel blockers (BC Pharmacy Association).

The Netherlands uses for its reference price system (known as the GVS), the principle of therapeutic substitution [3,7]. The government identifies drug classes having the same therapeutic indication, mainly by using the ATC classification. This classification adopted by the Nordic Council and used by the World Health Organization, has been described earlier in this volume. It is considered an adequate basis for therapeutic classification for the purpose of reimbursement. The Dutch government also introduced some modifications to take into account therapeutically relevant side-effects which are not reflected in the ATC classification, but which in some cases provide a reason for classifying certain drugs into separate clusters.

2.3. Calculation of an acceptable reimbursement level

Techniques used to set the level of reimbursement prices also vary considerably from country to country. As a rule, countries calculate their reimbursement price for a particular drug class by using a (weighted) average of the prices of drugs in the group as sold on the domestic market. However, in countries where generic competition is substantial and leads to large price differences among products, the health funds or governmental agencies/commissions taking the decisions give a greater importance to the cheapest generic prices. With the growth of economic evaluation studies and investigations into cost effectiveness, some policy makers also introduced other criteria to calculate an acceptable reimbursement level based on the most cost effective therapy available (e.g., *British Columbia*).

The following are examples of the manner in which different countries have calculated an acceptable reimbursement level:

In *Germany*, the reference price is fixed in such a way that within each drug group a sufficient number of drugs remains reimbursable, thus ensuring that there is a degree of choice and sufficient availability of drugs falling within the selected reference price level, to supply the national market [1,8]. Within a comparable group, the reference price usually tends to be close to some of the lowest pharmacy prices. A model of the structure of the pharmaceutical market for each drug class is then constructed to take into account prices, pack sizes and dosages, and to estimate – through a regression technique – the prices for different dosages and pack sizes. However, there is not necessarily any justification for a linear relationship between various prices and dosage levels [8].

In *British Columbia*, the authorities have sought to take as a standard the reference drug that is most cost-effective within its class[2], based their choice on the scientific evidence as accepted by the national regulatory body. The figures for cost-effectiveness take into account the cost structure of the Canadian health system, but not necessarily the health care structures specific to the *British Columbia* province.

In *The Netherlands*, for each drug group recognized within the GVS, a reimbursement price is set per defined daily dose (DDD), in order to be able to compare drug prices within a reimbursement group. Instead of the treatment cost per day, the cost of an entire course of treatment is considered [7].

2.4. Use of international comparisons

Usually the price information used to set the reimbursement level reflects the price structure within the country that is implementing the system. It is therefore influenced by the results of the various tradeoffs in domestic price negotiations that have led to the prevailing national price structure within each drug class. Some countries may however, as noted above, opt to rely in part on international sources of price information in setting their reimbursement reference price levels. The Netherlands for instance, uses price comparisons with other European countries, such as France, Germany, the UK and Belgium, to determine maximum prices which then in turn affect the reimbursement price. The selection of countries in such a case is based on the criterion of similar identical close purchasing power.

2.5. The decision making process

The definition of drug classes and the setting of an acceptable reimbursement level is a highly political process, in particular since it may have major economic implications for industry. Most government agencies have set up committees drawn only from the Sick Funds or with participation of the Sick Funds, the medical professions or academic experts. In Germany for instance, the Federal Commission of Physicians and the health insurance funds specify the pharmaceuticals for which reference prices are to be determined [1]. The Board of the Health Insurance Funds sets the reference prices. In British Columbia, an independent advisory committee is in charge of thorough reviews of the published scientific evidence on cost-effective therapies.

2.6. Exception mechanisms

As pointed out already, physicians may not be willing to switch all their patients from the drugs which they have come to prefer to drugs falling within the reference price; they may have various reasons for objecting, one being a belief that another drug is better suited to a particular patient's needs. Some countries have therefore introduced into the design of their national reference price systems mechanisms to allow for exceptions to be made where these are justified. For instance, in British Columbia physicians can choose not to switch medications for particular patients if side effects or other adverse consequences are expected to result. A physician may present the case to the sick fund, arguing that the patient should be fully refunded, but the patient may ultimately have to pay the difference in order to receive a more expensive drug.

3. The effects of reference price systems

Since the first reference price system was implemented ten years ago, some studies have been performed to evaluate the effects of such a system. However, the assessment is still incomplete. Despite several years of implementation, there are still very few health outcome data related to drug utilization [10] nor is there as yet much research providing scientific evidence to evaluate the impact of such a system on various health outcomes [5]. A major initiative in this field has been undertaken by British Columbia province, in response to strong opposition to the system from the pharmaceutical industry,

British Columbia physicians and some other health care providers. An independent project for the Scientific Evaluation of the Reference Drug program has mandated studies from some leading US and Canadian research academic centers (Harvard University, MacMaster University, University of Washington).

One can however distill some conclusions from readily available facts, since the evolution of drug prices over given periods of time is well-documented. As a rule, pharmaceutical prices in the drug classes affected have adjusted to reference reimbursement price levels in European systems. Very rarely, companies have tried to maintain higher prices, but where they have done so, it has usually only been for a limited period. The scope of reference pricing is however generally limited to particular market segments (notably those with multiple similar products) and it is usually possible to observe that prices have gone up on other market segments. In Germany for example, drug prices in prescribing areas covered by the reference price system were over a given period reduced by 1.5%, while drug prices not covered by the system increased by 4.1% [9].

Some recent contributions to the field have assessed the impact of reference price systems on patient drug use and the use of other services. One series of epidemiological studies based on quasi-experimental designs, performed by the teams previously referred to, has begun to provide scientific evidence on the health outcomes of reference pricing. For instance, the Schneeweiss, Mclure and Soumerai study on ACE inhibitors [12] shows a 29% decline in the use of high-priced cost-sharing ACE inhibitors immediately after the policy implementation. After a transition period, the overall post-policy utilization rate of all ACE inhibitors was 11% lower than the projected pre-policy. Some discontinuation of such therapy was observed among low-income groups; however, according to the authors this did not appear to lead to a discontinuation of anti-hypertensive therapy as such. Switching patients to other anti-hypertensive drugs, under the influence of the reference price system, also led to a slight increase in use of physician services. One of the reasons why no study of the impact of the system on drug exposure or health care utilization by patients has so far been carried out lies, especially in Europe, in legal constraints concerning privacy and the protection of individuals. There are for instance no cross-institutional links of administrative databases on drug utilization at the individual level [10]. In the British Columbia program, privacy is secured by encryption of data.

Even if the Canadian initiative and its collaborative work with US centres provide scientific evidence on health outcomes, there will still be little research and few assessments of the actual or potential impact of reference pricing (and consequent drug switching) on the appropriateness of the drug treatment which patients receive. The Thomas and Mann study [13] on the prescribing of statins in New Zealand may provide some evidence on the adverse effects of certain uses of products within this drug class.

In terms of the impact on health care expenditures, budgetary savings on drugs are generally attained within the classes covered by a reference pricing system (Germany, The Netherlands). As the impact on other services is not usually measured provided, it is not simple to estimate the effect on global health care budgets. In the case of ACE inhibitors in British Columbia, the saving on the drug budget far outweighed the increase in the cost of physician services. Drug budget savings amounted to Can\$ 6.7 million and the policy led to a net saving of Can \$6 million over 12 months. However, the budget savings achieved with reference pricing are considered to be relatively [4,6].

Reference pricing approaches have become increasingly popular among European countries, but the principle remains controversial. The main points of controversy are the objections to the system raised from an industry or clinical perspective, the definition of drug classes, the breadth of application of the system and the reimbursement level which will be sufficient to ensure continued availability of drugs (for instance in CCEE countries). In the first drug benefit programs that aimed to use generic competition in order to provide drug coverage at the best available price (e.g., Medicaid MAC program in the USA), the

concept of interchangeability between original brands and generic drugs having similar bioequivalence was applied. Reference pricing, however, may use concepts of interchangeability that go beyond generic substitution and may be more questionable from the point of view of industry, the physician or the patient. Issues of heterogeneity within drug classes and limitations on interchangeability have already been extensively discussed in the literature (see [14]). When applying reference pricing, decision makers have usually addressed such issues by increasing the number of drug classes (smaller groups) or by considering “safeguard mechanisms” or providing for exceptions. However, incremental approaches or experiments pursued by countries such as Spain or Canada aim to search for solutions in particular to the dilemma of balancing the need for innovation with the need to contain health care budgets.

Industry usually opposes reference pricing on the basis that it does not take into account the characteristics of incremental innovation in the drug discovery process as it relates to a drug class. Companies market their recently developed drugs with claims of unique advantages in order to justify a higher price and reimbursement level than the other products with which the authorities have sought to group them. A reference price system may cause R&D resources to be diverted to therapeutic areas not covered by reference systems, as price setting in those categories is basically free.

Clinicians or *patients* may also question the grouping on drugs: physiological responses from individual patients to “similar” drugs may be different, in term of quality, absorption, indications, secondary effects, mode of preparation, application forms, the frequency of undesirable effects and contraindications. Adequate information for health professionals and for patients can deal with this problem. Payers and health care organizations may also reconsider drug classes and the switching of drugs, since the use of one drug may require greater involvement of other health care resources (e.g., more physician visits) than the use of another; it may also affect the duration and extent of treatment, with direct and indirect consequences for the overall health care cost [3].

Views on reference pricing within governmental agencies, industry, the medical profession and patient groups are very diverse. Efforts to refine methods of grouping and product classification so as to render them as realistic as possible will therefore continue. Reference pricing is here to stay, and is extensively in use in many major drug markets; as it continues to evolve, its influence will certainly further expand.

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Chapter 9

Experiences with patient charges

Flora M. Haaijer-Ruskamp

1. Alternative co-payment systems

Pharmaceutical policies generally provide for patients to pay a part of the costs of the drugs which they receive. A variety of co-payment systems exist. As noted in Chapter 3, they can take the form of (1) a fixed sum per prescription; (2) a percentage of the overall cost of the prescription; (3) a combination of fixed sums and percentages; and (4) deductibles. In OECD countries the system of fixed sums is used less than the proportional system, i.e. a percentage of the prescription price. Fixed sums are payable in Australia, Austria, Germany, Japan, New Zealand and the UK, while percentage charges apply in Belgium, Canada, Denmark, France, Greece, Hungary, Ireland, Korea, Luxembourg, Norway, Portugal, Spain, Sweden, Switzerland, Turkey and under private insurance schemes in the USA. Belgium and Italy employ mixed systems. The proportion of co-payment required varies in some countries with the therapeutic value of the drug. In many low and middle-income countries co-payment has been introduced since the 1980's as an element in cost recovery schemes or revolving funds in which patients are asked user fees (see Chapter 15).

2. Effects on prescription volume

The effects of co-payments on the volume of prescribing depend on the process by which patients weigh up the costs involved against the risk or inconvenience of doing without the drug. Many studies have therefore looked at this so-called question of "price elasticity" of drugs. Most of the studies carried out in the 'eighties agreed that the demand for prescription drugs and even, to a lesser degree, the demand for over-the-counter (OTC) products is reduced as the direct contribution to costs required from the patient rises, though they may disagree about the extent of this influence [2,4]. Much less agreement exists on whatever differences there may be between short-term and long-term effects.

The level of the co-payment is, as one would expect, relevant for its impact. If it is low it will have no effect. In The Netherlands, a co-payment of 20% with a ceiling of f200/(€91) per year was too low to affect prescription levels, and any possible savings were offset by the high administrative costs involved [3]. Excessively high co-payment levels, on the other hand, may lead to undesirable effects, such as a decrease in the use of essential drugs. In the USA it was shown that a cap on the number of prescriptions reimbursed clearly resulted in lowered drug use. However, if the patient had to pay too much, the use of essential drugs decreased, together with that of non-essential drugs, resulting in an increase in other health related costs [8]. In the Australian system such effects did not occur after the introduction of a

flat fee (with exemptions for the needy); the reduction appeared to be primarily related to 'discretionary drugs', and not to essential drugs [6].

The impact of co-payments differs between different groups of patients; health status and ability to pay are particularly relevant. For example, with the implementation of full coverage a greater increase in drug use was seen in patients with a lower health status, suggesting that the co-payments had acted as a deterrent [1]. The low-income elderly are less likely to use medication for a given health problem than are elderly patients in the top income groups [10]. These studies show how important it is for public schemes involving co-payments to provide protection for the vulnerable groups (elderly, chronically ill and low-income groups), a consideration which means that in many countries such groups enjoy exemption from payment. In fact, this indicates the inherent tension between the objectives of co-payment schemes as a cost containment policy and social policies regarding access to pharmaceuticals. In any scheme capable of having a reasonable impact on pharmaceutical expenditure, the less privileged groups of the population can be adversely affected. It is precisely these groups that society will want to protect from the (undesirable) effects of co-payments on moral grounds.

Doctors and patients will try to minimize the cost burden. The lessons learned in the eighties were that as a result of co-payment systems prescribing may shift from cheaper drugs with a high co-payment to more expensive drugs with a lower co-payment (for example, from paracetamol to diclofenac). In addition, shifts to larger amounts per prescription were observed, as a means of reducing the effect of flat fee co-payments [9]. Both mechanisms thus led to higher public expenditure instead of producing the intended savings.

3. Effect of particular co-payment systems on the cost burden

Given the variety of schemes it is not possible to provide any generally applicable conclusions as regards the impact of different forms on the burden of costs borne by the patient. In a study assessing the cost burden in a sample of European countries using typical prescription scenarios, the delicate interplay between drug price, co-payment system and exemptions is illustrated [7].

The economic burden on patients proves to be consistently lower in some countries than in others. France, Italy and Germany had lower costs to the patient, while in Austria, UK, Denmark and Finland they were generally higher. However, the underlying reasons differ. In a system using proportional co-payments, low drug prices translate into low costs to the patient, as for example in France and Italy. In Germany, the only country with a fixed fee system and relatively low costs to the patient, the reason was the generally lower level of the fee on individual items. The Netherlands goes a step further in using a reference price system and not requiring co-payments at all. Patient costs incurred in alternative drug treatment regimens are likely to be similar or identical in fixed charge systems whereas in proportional systems the cost burden for the patient can differ from one regimen to another since the contribution varies with the drug price. Beyond this, any link between cost burden and therapeutic need is tenuous, and is not recognized by patients in comparable clinical circumstances

4. Exemptions and reinsurance

Countries in the industrialized world have implemented specific safety nets to counter the negative effects of co-payments. As a result, in the UK almost 50% of the population is exempt from co-payments.

Table 1
Reinsurance in OECD countries

Country	Reinsurance allowed?	Does reinsurance offset co-payment?
Australia	Private, mainly for hospital	Not usually
Belgium	In hospital only by non-profit insurance, profit insurance is allowed	N/a
Canada	Yes	N/a
Czech rep	Yes	N/a
Denmark	Yes	In some cases
Finland	Yes	Yes
France	Yes	Yes
Greece	Yes	No
Hungary	Yes	N/a
Luxembourg	Yes	N/a
Mexico	Yes	Yes
Netherlands	Yes	N/a
New Zealand	Yes	No
Norway	Yes	N/a
Sweden	Yes	Yes
US	Yes	N/a
Austria	No	Nr
Germany	No	Nr
Japan	No	Nr
Spain	No	Nr
Switzerland	No	Nr
Ireland	N/a	N/a
Italy	N/a	N/a
Turkey	Unknown	Nr
United Kingdom	Unknown	N/a

N/a: not available; nr: not relevant. Source: [5].

In France, despite co-payment for drugs, prescription drugs are virtually free for the 80% of the population who enjoyed supplemental insurance in 1990. The supplemental private companies or co-operatives reimburse most or all of the co-payments. The recent law on universal health insurance coverage will extend this supplemental insurance to 100% of the population [5]. Such exemptions, and reinsurance options for the population, offset the effect of co-payment in reducing the use of drugs that are not needed, or too expensive. Of OECD countries only Austria, Germany, Japan, Spain and Switzerland have officially excluded such a cost shifting by reinsurance in second-tier payment systems (Table 1).

5. Conclusions

Co-payments can be effective as a cost containment measure. There is no evidence that one method is more effective in reducing public pharmaceutical expenditure than another. The advantage of the proportional system is that the costs to the patient are directly related to the duration of treatment; this prevents individuals from partly evading charges by arranging to receive prescriptions for a large quantity of a drug at once. When a system involving a fixed fee per prescription is employed, evasion is much easier, and special measures are called for to counter it.

The disadvantage of *any* co-payment system is that it may act as a deterrent for essential care and run counter to the social objectives of a health care system. This is the advantage of a reference price system in which the emphasis is on the use of low-priced drugs and in which co-payments can therefore be avoided.

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Chapter 10

Switching to non-prescription status

Peter R. Noyce

After a new drug has been in use as a prescription-only medicine (POM) for an agreed period after licensing – usually five years – and has proved to be safe and effective during that time, regulatory authorities are prepared to consider submissions for re-designating the product where appropriate so that it becomes available for non-prescription “over the counter” (OTC) use.

A re-designated OTC product may be licensed for the same indications, in the same strength and in the same form and packaging size as the original POM product, or the OTC license for the drug may vary in one or more of these respects. In many countries, for example, H₂-antagonists have been licensed as OTC products at lower strengths and with more limited indications than the corresponding prescription products. In the United Kingdom, the pack sizes of the newer antihistamines are limited by regulation to 10 tablets when they are destined for OTC use.

The basic purpose of re-designation of a drug as an OTC product is frankly commercial; the manufacturer requests the change in the hope that, without the need for a prescription, the sale of the drug will increase. However, the change also has a secondary effect in that the drug will no longer – at least in its OTC form – be primarily funded by a national health system or insurance fund; if he has obtained the drug by private purchase, the patient will pay for it in cash, and this will therefore result in cost saving to the health system.

Whether it is still possible to prescribe an OTC drug and therefore have it paid for by the health system is a matter on which the rules differ by country. In many European countries, national health insurance schemes will reimburse OTC items in the same way as prescription-only medicines, provided they have in fact been prescribed. In the UK, for instance, deregulating a drug from prescription-only to OTC status does not affect the availability or cost to the patient under the NHS. In some other EU countries, the co-payment rating is adjusted so that the cost to the patient is the same irrespective of whether it is purchased direct from the pharmacy or obtained on a doctor’s prescription under the health insurance scheme. In yet other countries, OTC drugs have – with some exceptions – been entirely de-listed by health funds since the 1990’s as one of the measures for reducing pharmaceutical expenditure, as for example in The Netherlands, Sweden and the US. What this means is that, in these countries, once a medicine has been accorded OTC status, a patient will have to pay for it, whether it has been prescribed or not, unlike a prescription-only medicine which can be reimbursed. The reasoning behind this latter policy is that OTC drugs are regarded as being in principle safe medicines for minor ailments, used in conditions in which a physician might not prescribe a drug at all. Exceptions are sometimes made (Sweden, Netherlands), in cases where such a drug is needed for the chronically ill.

Because the OTC product can differ in its strength, packaging form and indications from its prescription-only equivalent, there will obviously be plenty of situations where the one is primarily a medical tool meriting insurance coverage and the other is a consumer item.

There is no simple relation between the reclassification of a medicine as an OTC and the level of subsequent prescribing [4]; external factors may play the dominant role. When aciclovir cream was de-listed for the treatment of cold sores the event coincided with heavy advertising for its use. The publicity may have affected the extent of OTC use, but there was little change in the volume of prescribing. When on the other hand clotrimazole products for the treatment of vaginal candidiasis (thrush) were released for over the counter sale, the increase in overall use was accompanied by a decline in the prescribing of these products.

The fact that consumers often prefer to purchase a recently deregulated product directly over the counter, rather than obtaining it on a doctor's prescription, is related to the individual's confidence in self-treatment and his or her ability to pay. Thus there is a tendency for younger and wealthier consumers to purchase deregulated products of their own volition from pharmacies [3] whilst older and poorer patients continue to rely on the doctor's choice of product on prescription. Within the UK, a study was undertaken to predict the impact of deregulating of a product on its prescribing under the NHS [2]. The four key factors influencing consumer decisions to purchase directly were, in decreasing order of importance: a stated preference for OTC purchase; an awareness of OTC availability; liability for prescription charges; and the fact that one was not taking other prescription medicines simultaneously.

If the cost of deregulated medicines is to shift away from National Health Insurance Schemes consumers must be made aware, either through health professionals or advertising, of the availability of these products without prescription. If the cost is a factor – for example if the retail price is considered high while the prescription item will be obtainable for a small charge or none at all – or if the over-the-counter product is available only in an inconveniently small package – there will be an incentive to continue to obtain a product on prescription under the National Health Insurance System. In short, various factors determine what the impact of de-listing of a medicine will be on its continued cost to the public budget. Cost and convenience to patients of deregulated medicines are key factors.

In those countries where the switch to OTC does imply elimination from reimbursement, savings are to be expected unless physicians as a consequence shift their prescribing to more expensive but reimbursable alternatives. Such shifts have been described in the past, but there is only limited evidence for them [1,5]; more recent publications indicate that a switching to OTC status can be successful in reducing public or insurance expenditure.

Switching products from POM to OTC status may also result in secondary savings, depending on the health care system. When doctors are paid per consultation (as in France), the reduction of physician visits implies additional savings. When doctors are paid a capitation fee, no direct savings will occur, but their workload might diminish, as has been described for Sweden [1].

In conclusion, there is now fair evidence that where a drug is widely used and has proven safe over a sufficient period, it can be entrusted to patients for "over-the-counter" use and that by removing it in whole or in part from the preserve of professional medicine savings will result. It would however be very wrong if products were to be shifted to OTC use primarily as a means of saving public money; drugs (and especially new drugs) are placed on prescription for sound medical reasons, and if a shift to OTC status is to be considered those reasons must be considered before the decision is taken. In some parts of the world it is fair to say that too many drugs have traditionally been available without prescription or other forms of control, and that as health services develop there may need to be a trend to less rather than more OTC sale.

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Chapter 11

Experiences with generics

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1. Background and definition

A “generic drug” contains the same active ingredient as the original brand name product on which it is based. Provided it is well made, it is to all intents and purposes identical to (and hence interchangeable with) the branded product. Quality requirements for generics need to be the same as for the corresponding original branded products. Generics are usually manufactured without a licence from the innovator company and are only marketed after expiry of the latter’s patent or other exclusivity rights. A generic drug may be marketed either under the approved international nonproprietary name of the active substance or under a new proprietary (“brand”) name chosen by its manufacturer [23].

Good generic medicines are affordable alternatives to more costly, patented brand name products; by providing precisely the same medical benefit at a lower price, generics reduce the cost of pharmaceutical care.

2. The concept and effects of generic competition

Generic competition is usually used in deregulated markets to encourage price competition. It is considered as one of the major forms of leverage which can be exercised in a relatively liberal environment to contain market prices on multiple source products. In Europe, conclusions reached by the European Council of Ministers in May 1998 concerning the single market in pharmaceuticals declared that the development of a more competitive generic European market is one priority in European drug policy in respect of patent-expired medicines [5]. Nevertheless the situation still varies considerably among the national markets in the EU (see Table 1), and it is not possible to analyse the situation for the large European market as a whole [4].

The American market has a much longer experience of large-scale generic price competition; several important studies, started in the late 80’s and early 90’s, have analysed the effects of generic competition in that country [1,2,7,8,15,16,21]. The experience from the USA seems to show that the global trend is a decrease in the average market price for most products which exist in both branded and generic form. However, the prices of branded products, viewed individually, have generally increased over the years despite the launching of generics at much lower prices. It appears that the main reason for the increase of originator drug prices is usually the segmentation of demand for drugs and the existence of different price elasticities at a micro-level; in other words, there is a part of the market which will continue to demand the high-priced branded drug even if it becomes increasingly expensive, while a separate segment of the market will look for the cheapest product available. In the US it was found that the price differential

Table 1
Comparison of generic medicine markets

Country	Drug market size (US\$ million) in 1997	Market share held by generics in 1997	Pricing policies for generic medicines	Average price differential generic/originator
Canada	670 (1997)	40% of prescriptions 15% of value	Provincial formularies pricing; In Ontario prices are deregulated; Reference pricing exists in British Columbia	40–50%
United States	9,600 (1997)	42% of prescriptions 11% of value	Free (market) pricing	25–60% ¹
France	789–969 (1998)	3–4% of value – pharmacy sales 20% of value – hospital sales	Regulated pricing	30% ²
Germany	2,600 (1997)	40% of prescriptions 17% of value	Free (market) pricing	27% ³ , 80–90% ⁴
The Netherlands	276 (1996)	22% of prescriptions 12% of value	Reference pricing and price equalisation (comparative scheme with prices from Belgium, France, Germany, UK)	20%
Spain	50.8 (1998)	1% of value	Regulated pricing	10–50% ⁵
Sweden	1,156 (1996)	70% of prescriptions ⁶ 39% of value ⁶	Prices set by National Insurance Board	10% ⁷
UK	1,100	49% of prescriptions 21.7% of value ⁸	Prices set by monthly Drug Tariff	80%
Hungary	338 – 405	50–60% ⁹	Regulated prices and price comparisons with UK, France, Spain, Greece, Czech Republic	n.a.
Poland	360 (1996) ¹⁰	70% of prescriptions ¹⁰ 30% of value ¹⁰	Prices set by Ministry of Finance based on cost recovery and profit, and price comparisons with UK, France, Greece, Italy, Spain	n.a.
India	450 (1996)	15% of value	Regulated pricing	n.a.
Philippines	104	15% of prescriptions 8% of value	Free (market) pricing	30%
Brazil ¹¹	1,977 (1998)	30% of value	Free (market) pricing	

¹ Discounted prices on popular generic medicines can be as much as 80% below the brand price.

² Through administrative act.

³ Based on sick-fund estimates for all ‘second applicant’ products.

⁴ For “blockbuster” drugs.

⁵ Based on reference prices which are set in comparison to the most expensive product in each reference price group.

⁶ Estimates are based on all multisource products (i.e. including the original patented drug).

⁷ For reimbursement purposes only.

⁸ Based on net ingredient costs of UK NHS spending at community pharmacy level in England.

⁹ Includes low-priced copy drugs.

¹⁰ Includes domestic companies only.

¹¹ Primarily copy drugs.

Data: WHO and London School of Economics.

between branded and generic products was usually not passed on in its entirety to the consumer but was in part absorbed by an increase in the margins of the wholesalers and the retailers [17].

In those European countries with a comparable experience, though on a smaller scale than in the USA, trends as regards prices and margins have not been homogeneous and events have been influenced by national controls on pricing which do not have their equivalent in America [10]. For instance in the UK an increase in the prices of both branded and generic drugs was observed on a sample of products similar to that used in the Grabowski and Vernon's American study [7], in which a price decrease was observed on several pioneering products when they faced generic competition. The difference is probably linked to the negotiation on product portfolios in which firms engage with the British government. Certainly the existence of generic products is of itself no guarantee for low prices. Where there is no competition in the off-patent market, because only one or two generic versions of a product are available, prices have been reported to go up as in other monopolistic situations [11]. Even where there is a fair amount of competition between generics, one is not likely to see them obtain a substantial share of the market unless deliberate measures are taken to catalyse the process. Those measures range from the provision of information and encouragement to "generic substitution" – an arrangement by which the pharmacist is entitled or even obliged to dispense the generic version of a drug even where the physician has prescribed the original product (see 4.4. below).

Effective competition between generic products and the original brands on which the patents have expired is today of key importance in containing the costs of pharmaceutical care. There is now a clear recognition of the importance of using generics in a country's health care system as a means of freeing funds for other purposes, including the financing of truly innovative new products; it has been argued that, in this way, generics create "headroom" for innovation [20].

3. The situation of generic prescribing and dispensing in various countries

The strength of the national market for generic drugs in any given country is largely a function of three characteristics:

- (1) the national pharmaceutical pricing policy;
- (2) the system of patent protection; and
- (3) cultural aspects of pharmaceutical use, in particular the attitudes of both doctors and patients and the information available to them.

The extent to which generic drugs, rather than the more expensive branded originals, are prescribed and dispensed varies widely among countries throughout the world (Table 1). Market shares can be expressed either in terms of units prescribed or as expenditure, and both modes of calculation are presented here wherever possible.

The countries with the highest penetration of generic medicines into the pharmaceutical market are the United States, United Kingdom, Denmark, Germany, The Netherlands and Canada. In many developing countries generic penetration is high as well, but as various of these countries have not until recently maintained strict laws on the protection of intellectual property, the "generics" on sale here have in part been copies of drugs still widely patented; they are regarded by the manufacturers of the latter as illegal and they do not circulate in other parts of the world. Of the items on the WHO Essential Drugs list, however, more than 90% are off-patent and available as generic drugs.

The policies put in place to promote generic medicines are quite varied, as is the degree of interest in implementing such policies. In the industrialized world penetration by generic medicines is most

marked in countries where the prices of innovative medicines are unregulated and high. By contrast, those countries – like France, Spain and Italy – that generally have used regulation to lower the prices for patented drugs, were until recent years less strongly motivated to encourage low-cost generics to enter the market, as the price differentials were less. More recently these countries too have initiated national programmes to increase the use of generic products [12,14].

In Denmark the use of generics is stimulated through generic substitution, official publicity campaigns to promote the use of generic medicines and non-financial incentives for physicians and pharmacists. Substitution is mandatory if a substitutable product is available and meets certain criteria regarding the savings which will be achieved by prescribing it. The non-financial incentive for generic prescribing is through the use of databases which reference only the cheapest available product.

The success of national policies in this respect is also explained by different factors. In the USA the high level of private expenditure on medicines plus the increasing coverage of the population through managed care with its strong cost-containment incentives have been the big driver for high generic penetration. The strict regulatory control exercised by the FDA has been critical in generating confidence in generic drugs. In the UK the market for generics has been successfully developed through financial incentives to physicians (fundholding practices) and pharmacists, and the promotion of generic prescribing in medical education. Generic substitution is not permitted, but more than 65% of prescriptions are in fact now written generically, thus allowing for dispensing of the cheapest product. In Germany generic penetration is driven largely by generic substitution, the reference price system and the setting of prescribing budgets for general practitioners, making doctors and consumers price-conscious.

In Canada the provinces use a wide range of policies to encourage the use of generic medicines including generic substitution (which is mandatory in most provinces) and incentives to pharmacists and physicians. In addition a reference price system is in place. Finally, The Netherlands has implemented a variety of measures including reference pricing, non-financial incentives for health professionals, generic substitution, teaching generic prescribing at universities, and financial incentives for the pharmacists: when a generic product is dispensed instead of a branded drug, the pharmacist is allowed to retain 33% of the price differential.

4. Measures to implement generic drug policies

As implied by the few examples above, generic drug policies can be effectively implemented through a mix of measures influencing both supply and demand. On the supply side this may involve introducing and implementing:

- legislation and regulations that guarantee the quality of generic medicines (and which need to be explicitly made known to prescribers and the patients, in order to secure their trust in the products);
- regulations to facilitate market entry for generics, such as fast-track and simplified registration procedures (omitting the need for presenting a full dossier with clinical data, but basically concentrating on quality and information issues);
- differential registration and licensing fees;
- “Bolar” or “experimental use” provisions (that allow for generic product development while the innovator product is still under patent, so that the generic equivalent can enter the market as soon as the innovator’s product patent expires).

On the demand side, these policies largely focus on encouraging generic prescription, both with financial as well as non-financial incentives, on stimulating generic dispensing by the pharmacies through financial incentives and price regulations like reference pricing and degressive margins, as well as through professional incentives, and on encouraging the patient to use generic medicines (financial savings where it concerns out-of-pocket payment, as well as awareness campaigns, and differential co-payments).

Some of these approaches are reviewed below.

4.1. Marketing authorization and registration

The European Union has provided a definition of what can be considered to comprise an “essentially similar product” for purposes of marketing authorization. This is necessary since, where a particular product has already been registered on the basis of a complete file, an “essentially similar” product can be registered through a simpler “abridged application”, in which the results of pharmacological and toxicological tests and clinical trials do not need to be submitted [18]. The agency that is reviewing an abridged application will naturally have to be aware of the various problems which can arise with bioequivalence; in some cases two versions of a product which are very closely similar in formulation can nevertheless show significant difference in bioavailability, and in the clinical documentation accompanying an application for marketing authorisation, reports on the assessment of bioequivalence will sometimes be needed. Some countries require stronger assurances of therapeutic equivalence than do others. Certain regulatory agencies, such as the United States FDA, also publish lists of drugs that can present bioequivalence problems – for example, certain drugs where the margin between the therapeutic and the toxic dose is very narrow – and some formularies restrict the list of therapeutically equivalent products to exclude any products which could present a problem with bioequivalence or any other aspect of quality. In those industrialized countries with strong regulatory systems, there have few if any well-documented cases of therapeutic failure due to bioequivalence problems [13].

4.2. Patent protection issues

The other important issue here is the timing of the application. In those countries with legislation that allows for “experimental use” (or with the “Bolar” exemption), like the USA through the Waxman Hatch bill, generic manufacturers can develop their products while the innovator product is still under patent, and can submit their application to the regulatory authority and get it approved during the patent period. This allows generic competition to start basically on the day after patent expiry, and normally results in a strong price drop with several generic companies competing. This is especially likely to be achieved where the market for a particular product is very large. One should add however that innovator companies have been building their defences against this rapid erosion of their market. In the case of the USA they have obtained compensation in the form of additional years of patent protection. In recent years there have also been a number of cases of innovator companies seeking to delay generic competition through legal challenges to generic firms based on alleged defects in applications and or unlawful use of data that are claimed to belong exclusively to the innovator’s files [22].

In those countries where such “experimental use” clauses are not in force, as is the case in much of Europe, there is normally no such rapid onset of competition when patents expire, and often the innovator product enjoys another 2 to 3 years monopoly, until generics products make it to the market. This also allows the innovator company to start marketing its own generic product, and thus benefit from the first-entry advantage in order to achieve generic market share, before competitors reach the market [19].

The other area that has come under scrutiny is the period of data exclusivity (i.e. the period during which it is not permitted to use data contained in the dossiers of the innovator companies for preparing new submissions by generic companies). Data exclusivity clauses were introduced at a time when certain types of products (such as biotechnology products) could not obtain a patent, and it was considered important to provide an incentive for innovation. Though patents have now also been introduced for biotechnology products and for therapeutic indications, the principle of data exclusivity has continued to exist. Periods of data exclusivity vary from 5 years (the current standard in the USA) to an optional 6 or 10 years in EU countries. Current proposals by the EU Commission aim at extending the data exclusivity to 10 years, while at the same time introducing a “Bolar” clause in the European legislation [6].

Concern has been expressed that excessive data protection is more an impediment to innovation than a stimulus, as it may cause funding to be diverted from innovation to marketing, in order to maximize the benefits of an extended monopoly situation in the market.

4.3. Encouraging generic prescribing

Much can be done to encourage doctors to prescribe generic drugs where there is no specific therapeutic reason to prefer the more expensive branded products. Generic products can be listed in therapeutic guidelines and in (printed or electronic) formularies; training and education programmes can focus on generic prescribing both at medical school as well as in continuing education. Prescribing by physicians is strongly influenced by drug promotion and this is often a major barrier to generic prescribing. In many medical schools throughout the world, physicians learn of drugs using their generic or scientific names, but drugs are introduced into the marketplace under the generally simpler and intensely promoted brand names, and it is the latter that most physicians soon grow accustomed to, when prescribing a product. Unless the very strong influence of brand name promotion is adequately counterbalanced by a reasoned and ongoing campaign to generate medical belief and trust in generic prescribing there will continue to be excessive medical reliance on expensive brands.

In addition financial incentives to generic prescribing can be provided, especially by allocating each physician a total prescribing budget as an encouragement to keep the cost of individual prescriptions low. Several countries have used variants on this method (fund holding practices in the UK, budgets and systems for remuneration for doctors in France and Germany); the physician may simply be obliged to stay within the limits of the budget, or savings on prescribing costs may be made available for use in the physician's practice. In Ireland, if physicians can create savings by generic prescribing, they can keep 50% of the savings. Overall goals may also be set: in France the health insurance system agreed in 1999 with the country's physicians that 7% of prescription volume in the year 2000 would be in the form of generic products.

4.4. Encouraging generic dispensing

The fact that a doctor has prescribed an expensive brand name drug does not always mean that the pharmacist will dispense it. A public policy on generics often relies on a clear rule regarding substitution, i.e. the dispensing of an equivalent drug which is less expensive than that which has been prescribed. In different countries and at different times pharmacists have variously been forbidden to substitute, allowed to do so on certain conditions, or even encouraged or obliged to do so. There are also differing rules on consultation: a pharmacist may be free to substitute on his own initiative or obliged to seek the agreement of the prescriber, the patient or both before doing so. Rights of substitution for pharmacists exist in

America and several European countries such as Germany, Denmark, The Netherlands, Luxembourg and more recently France. Substitution is mandatory in some of the States of the USA and some European countries such as Denmark for particular categories of drugs. In other countries, it remains optional. Usually, when the physician writes on the prescription pad that he or she will allow substitution, the pharmacist is free to replace the prescribed speciality by a generic product. In Denmark, since the “G” agreement of 1991, the physician can write a G (for “generic”) on the prescription, and the pharmacist must then dispense the least expensive drug in groups of essentially similar products.

In those countries where the pharmacist’s income is in the form of a percentage earned on each product dispensed, substitution by a cheaper drug will adversely affect the pharmacist’s earnings and comprise an important disincentive unless special measures are taken. Various countries (Belgium, Estonia and more recently France) have introduced parallel measures – such as degressive margins – to avoid a reduction in the pharmacists’ remuneration as a result of generic substitution. Pharmacists can also be motivated to collaborate by a provision entitling them to retain a proportion of the savings made by dispensing a generic instead of the brand name equivalent. The problem of decreased earnings does not arise where the pharmacist has a fixed income or receives a standard dispensing fee on each drug which he supplies, whatever its price.

Whatever the approach adopted, pharmacists are clearly key players in a successful generic policy and all the various factors which can motivate or influence them must be borne in mind.

4.5. Influencing the patient

The patient can influence the doctor’s prescribing as well as the pharmacist’s dispensing. The public can be told and taught that generic products are as effective and safe as their branded equivalents. All branded products should be required to display the generic name prominently alongside the brand name, in labels, literature and advertising, thus repeatedly stressing the fact that the branded and generic product are identical. In this respect public campaigns to promote the use of generic drugs over branded ones may usefully put the question “Why pay the premium price if you can get the same medical benefit against a much lower cost?” However, there is no documented proof of the effectiveness of such campaigns, and on occasion they have been counterbalanced by promotion from the innovative industry playing on the belief of some members of the public that cheap drugs are likely to provide only second-rate treatment. Obviously in a system where patients pay a large part of drug costs themselves, it will be simpler to create public acceptance of generics than in an environment where drugs are publicly financed, and the patient contribution is limited. In the situation where the patient bears part of the cost, a reference price system will ensure that it is to the patient’s financial advantage to request (or accept) a generic product.

Both for the physician and the patient it is important that lists of drugs eligible for insurance payment or reimbursement indicate the prices of the various branded and generic versions of a drug so that the financial choices and consequences are clear.

4.6. The need for a multi-faceted approach

Generic drug policies can only be effective if the regulatory policy is appropriate, if doctors, pharmacists and patients fully understand, endorse and embrace the concept, and if positive incentives and rewards are provided. The simple fact that in many countries pharmacists are, as noted above, now permitted to substitute the prescribed brand product by the generic has substantially increased the use of the latter. Overall measures aimed at increasing information and transparency in the market should provide

for regular publication of a current list of interchangeable products available to physicians, pharmacists and consumers. The regulatory authority should publish a list with drug products that can be substituted and those that cannot because of problems with bioequivalence, e.g. "the Orange Book" published by the Food and Drug Administration (FDA). Generic prescribing by doctors can be stimulated by the introduction of all the various methods outlined before.

The success of any of these policies is also dependent on the nature of the relationship between physicians and their patients. Other competing factors are the cost sensitivity of the physician and the degree of trust that the physician himself has in the safety and efficacy of generic medicines. While it is clear that physicians can be persuaded in one way or another to change their prescribing habits, there is little or no evidence that physicians have changed their as a result of legislation on generic substitution in the pharmacy.

5. Manufacturing and trading in generic products

There is generally little need for a government or health service to encourage directly the growth of manufacturing and trading in generics since it develops spontaneously as soon as a market environment comes into being in which the trade can grow, obstacles to the use of low-cost drugs are removed and competition between generic and branded drugs is encouraged, in the manner reviewed above.

A somewhat different situation can exist in some countries where there is a weak manufacturing tradition. The European Community's Development Council has expressed support for the institution of local generic drug production and quality control in developing countries [3], but it is not at all clear what can be achieved in countries where there is no existing tradition of pharmaceutical manufacturing at all. It could prove more profitable to encourage the existing manufacturers of high-quality generic drugs, especially those in low-cost countries such as India, to expand their business by providing them with ready access to both western and developing markets.

6. The generic situation in developing and transitional countries

In low income countries with a high incidence of frank poverty in the population there is an especially strong reason to promote the prescription and use of generics [9]. Particularly in developing countries a high proportion of drugs in the public sector are donor-funded and these are almost exclusively generic; however alongside the public sector there is usually a thriving private sector, especially in the towns and cities, funded almost entirely by out-of-pocket payments. Unfortunately in practice, various factors tend to result in a greater use of these expensive specialities than is therapeutically justified, in particular the widespread belief among the public that the branded product is better or safer than the generic; even more unfortunately, the weakness of some regulatory systems allows the marketing of some poor quality generics which further foster this belief. Other problems arise from the lack of transparency on prices and the widespread existence of corruption which can hinder the production, prescribing and availability of quality generics at affordable prices. These matters are referred to at greater length in Chapters 14 and 15 of this book.

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Chapter 12

Experiences with pharmacy benefit management programmes in the USA

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1. Introduction

As an increasing proportion of health care services in the US move from fee-for-service to managed care arrangements, drug prescribing is also moving toward more centralized, proactive management. Pharmacy benefits management (PBM) activities are being developed and implemented by payers such as self-funded employers and managed care organizations (MCOs) as well as provider organizations such as large medical groups and integrated delivery systems. These activities are aimed at controlling drug costs and improving the quality of health care, although critics charge that cost control goals play the dominant role.

While pharmacy benefits management activities can and are performed within MCOs and integrated health care delivery systems such as Kaiser Foundation Health Plan, the main and growing locus of these activities is in dedicated companies, themselves generally known simply as PBMs. PBMs design, implement, and administer outpatient drug benefit programs for employers, MCOs, and other third-party payers. Currently, there are about 100 PBMs in the US [8], and they provide drug services for more than 100 million Americans [4]. As elsewhere in the world, the pressures to contain drug costs flow from the increases in those costs for both public and private MCOs [7,12,16,21,22]. Despite the dramatic increase in costs, very little is known about the nature and consequences of the strategies used by PBMs and their contractual partners to manage drug benefits.

2. The role of PBMs

The main functions that PBMs perform for their clients in today's US health care system are to provide drug-related administrative services and to manage pharmacy costs. This latter function is increasingly important as pharmacy costs increase while MCOs and employers feel continuing pressure to keep the costs of premiums down [8,10]. The cost containment functions are accomplished through a wide variety of drug payment and utilization management strategies, including but not limited to:

- the processing of drug claims,
- the management of pharmacy networks,
- the negotiation of rebates with pharmaceutical manufacturers,
- the implementation of restrictive positive lists,

- promoting the use of generic drugs [8].

Each of these functions is described in turn below.

2.1. Processing of drug claims

Most PBMs undertake the processing of drug claims as a service and in fact nearly all of their clients rely on them for this function. These claims processing services comprise the automated assessment of drug claims, typically conducted at the pharmacy and meant to detect potential drug payment problems that should be addressed before drugs are dispensed to patients (e.g., checking patients' eligibility for drug coverage, or checking if the prescription has already been filled at another pharmacy).

2.2. Management of pharmacy networks

Another pharmacy benefits management service is the creation and management of pharmacy networks. These networks consist of outpatient pharmacies under contract to MCOs and/or their contractual PBM partners to provide drug services, typically at a negotiated, discounted fee. PBMs have reported that drug cost savings for their clients have been achieved, in part, by use of discounted fees for pharmacies in their networks [3,8].

2.3. Negotiation of rebates

Negotiating contracts with pharmaceutical manufacturers, and particularly negotiating rebates, has been a major component of PBM activities during the past decade [5]. Rebates are among the most sensitive and controversial of PBM activities, potentially posing issues of discriminatory pricing for pharmacists. Use of rebates has also generated suspicion on the part of government regulators, physician organizations and consumer groups that where PBMs are owned by manufacturers they may engage in anti-competitive behaviour. One study using data from 1995 information estimated that typical rebates were about \$1.25 per prescription claim, with reported amounts ranging from \$0.80 to \$2.50 (an exceptional case) [8]. Other estimates come to a total of \$113 million in rebates in 1995, accounting in various health plans for 2–21% of total cost savings attained by the use of PBMs [3].

It is considered that where the clients served by PBMs have aggressive drug use management programs, involving for example managed or closed positive lists, therapeutic interchange programs, and drug-risk sharing arrangements with physician organizations, they can achieve higher rebates since rebate levels are often linked to market share changes, i.e. shifts in market share from the products of one manufacturer to those of another. In practice, however, even a PBM using aggressive drug management interventions may not be able drive market share to the extent anticipated because there may well be multiple stakeholders trying to influence physician prescribing, such as competing PBMs, drug manufacturers, and multiple MCOs contracting with individual physicians or physician groups.

Although there is hardly any published research available on the nature and effects of PBM rebates, available information indicates that a PBM which has negotiated a rebate with the drug manufacturer may then turn over to the client that negotiated amount after retaining an "administrative" portion. The data indicate however that the extent to which this occurs is highly variable, with anything from zero to 100% of the manufacturers' rebate actually being passed on to the client by the PBM [5,8]. Some reports indicate that PBMs also earn income by taking their data on patients' drug use and expenditure, stripping it of identifying information, and selling it to pharmaceutical manufacturers and other interested parties. Such income may sometimes exceed the revenues that PBMs receive from rebates [8,14].

2.4. Therapeutic interchange

Therapeutic interchange programmes encourage the substitution of a non-formulary drug with a lower-priced, therapeutically drug of similar efficacy (e.g., within the class of nonsteroidal anti-inflammatory drugs or the group of H₂ antagonists). The interchange typically occurs when a computer indicates to a community pharmacist that a prescribed drug is not on the positive list (= formulary) applicable to that patient's coverage. The pharmacist will then call the physician to obtain consent for the interchange. Available evidence suggests that most PBMs offer therapeutic interchange programs, including reimbursement of pharmacists for contacting the physician to obtain approval for an interchange. This pharmacist-physician contact is a central feature of therapeutic interchange programs [8]. Some evidence indicates that PBMs believe that physician calling is an effective approach to influencing prescribing behaviour, and that mail-service pharmacies have an advantage over retail pharmacies in this respect because mail-service pharmacists face fewer time pressures in contacting the prescribing physician, are trained in communications skills, and are educated about targeted diseases and drug therapeutic classes [8,10].

Evidence suggests that pharmacies are reimbursed for therapeutic interchange activities at levels ranging from \$7 to \$15 for each time that the pharmacist contacts the physician about switching a patient's prescription and/or successfully obtains approval for the switch from the physician. It is difficult to assess how well these programmes achieve their goal of reducing clients' drug costs because there are no publicly available data on cost savings attributable to therapeutic interchange programs. Opponents of these programmes argue that they intrude on the physician-patient relationship and lead to increased overall health expenditure because the health of patients may suffer when they have restricted access to medically necessary drug therapies. On the other hand, supporters maintain that these strategies hold the greatest potential to slow the rate of growth of pharmacy expenditure.

2.5. Generic substitution

Another type of drug interchange programme used extensively by most PBMs is generic substitution. Whereas with therapeutic interchange the pharmacist can replace a prescribed therapeutic agent by another having similar effects, with generic substitution he or she can only replace it by another (generic) version of the same drug. All PBMs offer their clients mechanisms to increase the use of generic drugs. Programmes of this type are more common and less controversial than therapeutic interchange programs because, in most instances, there are fewer disputes over the therapeutic equivalence of generic substitutes for brand name drugs.

Like therapeutic exchange programs, generic substitution programs can include a mix of physician and pharmacy education activities as well as financial incentives and penalties. For example, some PBMs send letters to pharmacies reminding them of their contractual obligations to meet certain generic drug dispensing standards, and the associated penalties that include possible removal from the pharmacy network. These forms of pressure may be combined with economic incentives such as dispensing fees or patient co-payments that differ for generic and brand name drugs. "Maximum Allowable Cost" programs can provide still another economic incentive to dispense generic drugs. Here, the PBM or its client distributes to the pharmacies a list of prescription drugs for which MCO reimbursement will be provided only at a generic price level, regardless of which drug is actually dispensed. This principle is comparable to the reference price system, used in several European countries.

2.6. Formularies /positive lists

One of the major ongoing activities of PBMs is development and maintenance of drug formularies or positive lists. The term formulary can be confusing. In this book the term is used for a volume containing summary drug information about individual drugs including at least the generic name, indication(s) for use, contraindication(s), dosage schedules, and warnings (see Chapter 4, Section 5). Though PBMs in the US usually use the term 'formulary' merely to refer to a list of drugs approved for use by a health care organization, the term 'positive list' is preferred in this book to distinguish it from the information-type formulary. If a physician or other health care professional wants to prescribe a drug that is not on the positive list, the procedures involved and the out-of-pocket cost to the patient will vary, depending on how restrictive the positive list is.

The most restrictive positive list is a *closed formulary*, which allows patients access to drugs outside the list only if they provide a higher co-payment or even pay the entire cost of the desired drug, or if their physician can successfully override the positive list. A *managed formulary/positive list* uses a more comprehensive approach by combining incentives and financial penalties in order to encourage the use of 'preferred' drug products. For physicians, one favourable aspect of positive lists can be consultations from PBM or MCO pharmacists intended to educate them about cost-effective drug prescribing. This educational approach can, however, be combined with sanctions in the form of economic penalties which can be imposed on physicians. For pharmacists, the economic rewards may take the form of higher dispensing fees payable to pharmacies if targeted rates of adherence to positive lists are met. For patients, higher co-payments may be required for 'non-preferred' drugs. An *open positive list* is the least restrictive type of list and allows full reimbursement for non-formulary drugs. Typically, it lists all drugs and drug products, but provides rankings that indicate preferred products.

However strong the pressure may be from a PBM to encourage the use of preferred drugs, managed and even closed positive lists always include some provisions to allow prescribing outside the list. The override mechanism can range from allowing prior authorization requests (which may or may not be granted), to allowing override if the physician concurrently provides information showing that particular drug is medically necessary for the patient involved. Some PBMs allow override without imposing particular requirements; in such a case, the physician may receive periodic reports from the PBM that list all instances of his or her having prescribed outside the list over a specified time period and remind him or her of the preferred drugs.

As MCOs continue to search for drug cost savings, they are increasingly moving from open to managed or closed positive lists. A survey of pharmacy benefit management trends and forecasts found that in 1996, 25% of surveyed MCOs described their positive lists as closed; one year later, the figure was 32%. Interestingly, the percentage reported by employers held constant at 12.5% for both years. Looking toward the future in 1998, MCOs predicted that almost 40% of them would have closed positive lists in 1999, whereas less than 20% of employers expect to offer closed positive lists in that same year [12].

Given these trends, increasing attention is being paid to the criteria set for including a drug on a positive list. Although those criteria have traditionally included safety and efficacy, one study found that seven of eight large PBMs stated that the cost of the drug product was an important criterion in decisions [18]. As discussed above, one way to decrease the cost of a particular drug is for the PBM to negotiate rebates or discounts with the manufacturer, then place that drug on the formulary but omit all (or certain) other therapeutically equivalent drugs produced by other manufacturers.

3. Controlling drug costs or overall health costs?

Although most pharmacy benefit management strategies employed in the US today are focused on containing the costs and utilization of drugs, some health care organizations are adopting innovative approaches to integrating pharmacy and medical services in an attempt to achieve savings in overall health care costs. This strategy recognizes that although drug costs might increase if case management of chronically ill patients leads to improved medication compliance, overall costs might decrease if there are reduced rates of hospitalization and/or visits to emergency departments. Asthma, depression, gastrointestinal conditions and diabetes lead the list of PBM-sponsored disease management initiatives, largely because it is believed that improved compliance with self-management practices, prescriber adherence to best practices, and appropriate use of medications used to treat these conditions can result in overall cost savings [11,12].

All major PBMs and many MCOs have developed and are implementing disease management programs designed to integrate pharmacy and medical services. Such programs assume a comprehensive, integrated view of disease, focusing on chronic, high-cost medical conditions in which drugs play a critically important treatment role. Disease management treats a disease across the continuum of care: from wellness to critical condition, from prevention to tertiary care, from home to hospital. Designed to prevent acute episodes of illness, disease management works proactively to educate patients and assure compliance with drug regimens and to educate physicians to improve prescribing decisions and other clinical practices. Proponents maintain that disease management fulfills the promise of managed care by managing the quality and processes of care, not just by containing costs [2].

MCOs and some PBMs have identified several barriers to successful large-scale implementation of disease management programs [8]. Many PBMs do not have access to diagnostic data and must therefore rely on patient self-report or drug use information to develop assumptions about patients' diagnoses. Another challenge is the need to integrate medical and pharmacy databases, a necessary step for successful disease management, but difficult and costly to achieve. Finally, there is the problem of timeliness of data on medical claims, which are often available only after delays in claims processing. Although numerous reports suggest that disease management programs can have promising results, no studies have yet been published in peer-reviewed journals to document the results of disease management programs sponsored by PBMs.

4. Countervailing forces

At the same time that MCOs and self-funded employers attempt to control increasing drug costs through use of internal pharmacy benefits management activities and PBMs, they must contend with a range of countervailing forces. Some of the most important of these forces are negative reactions to positive lists on the part of the public or elected officials; concerns about patient confidentiality; and increased use of direct-to-consumer (DTC) drug advertising by pharmaceutical manufacturers.

4.1. Public reaction to positive lists

As MCOs increase their efforts to control the rising costs of drug therapies, there is growing public awareness of and sometimes criticism of these efforts, which are sometimes regarded as an example of putting cost concerns ahead of health care quality. Even as elected officials at the national level grapple with concerns about managed care by putting forth competing visions of a comprehensive "Patients'

Bill of Rights”, state lawmakers are enacting laws in response to more specific concerns about managed care cost containment efforts. These new state laws cover such topics as requiring health plans to allow women specified minimum hospital stays after childbirth or mastectomy, or requiring physicians to inform certain male patients of specified diagnostic procedures for prostate cancer detection.

In this political environment, it should not be surprising that California, a large state considered to be at the forefront of managed care health system changes, enacted laws pertaining to positive lists and, more generally, pharmacy benefits management. One of these laws requires that MCOs maintain an ‘expeditious process’ by which prescribing providers may obtain authorization for a drug outside the list. The MCO must notify the patient of its reasons for any disapprovals [17]. Another California law prevents an MCO from limiting or disapproving payment for a patient’s drug if that patient had previously been taking that drug, had been covered for it by the MCO, and if the patient’s physician continues to prescribe it. This law also requires all MCOs to disclose publicly “in language that is easily understood and in a format that is easy to understand” whether they use a positive list, what a positive list is, how that MCO determines which prescription drugs are included or excluded, and how often the MCO reviews the content of the positive list [1].

These laws illustrate the lack of understanding and support among part of the public for many of the pharmacy benefit management strategies now taking place. Such restrictions and disclosure requirements can be expected to continue and to become more widespread if the public perceives PBM and payer activities as being motivated more by cost containment than by health care quality considerations.

4.2. Patient privacy concerns

Analysts have raised issues about ethical and legal conflicts created by disease management programs sponsored by PBMs. PBMs have access to drug use and sometimes diagnostic data about enrollees and these data are used to target patients in attempts to enroll them in disease management programs. Identifying employees for voluntary participation in PBM-sponsored disease management programs through medical and/or pharmacy claims data is permissible under current law. Some analysts have however questioned whether such efforts might not constitute an invasion of patient privacy [14]. The Joint Commission on Accreditation of Healthcare Organizations and the National Committee of Quality Assurance, two powerful groups that inspect and accredit hospitals and MCOs, have announced that although they already have standards to safeguard medical privacy, they are considering several additional requirements to protect patient confidentiality while still allowing quality improvement, care management, and other important oversight activities to go forward. More generally, health officials, private sector accreditation bodies, and consumer advocates have been holding patient confidentiality conferences to discuss the need to enact general privacy safeguards before the US federal government establishes a national health care database. Mandated under the 1996 Health Insurance Portability and Accountability Act, commonly known as the Kassebaum-Kennedy Act, the federal government will require the health care system – including physicians, pharmacists, and MCOs – to maintain a uniform computerized record-keeping system. In view of this imminent centralization of information (the US Secretary of Health and Human Services was required to issue privacy regulations by February 2000 if Congress fails to act), public figures are concerned that there are no federal rules to protect the confidentiality of medical records, and want to respond to reports of damaging consequences such as employees being fired when their employers learned they were taking medication for depression or had other potentially stigmatizing health problems. It remains to be seen whether medical privacy concerns will present new obstacles to improved pharmacy benefits management interventions, including the movement toward more comprehensive disease management programs.

4.3. Direct-to-consumer advertising

Although direct-to-consumer prescription drug advertising (DTC) first appeared in the US in the early 1980's, these activities have increased sharply. DTC advertising expenditures for pharmaceuticals in the first half of 1998 were \$631 million, a 16% increase over this spending in the same period the previous year [6] and it has continued to rise since. There may be several reasons for the widespread and growing use of DTC. Perhaps one motivation underlying this development is manufacturers' attempts to circumvent PBMs cost containment efforts by trying to inform patients about specific drug products and by encouraging them to ask their physicians to prescribe them. There is some evidence that physicians fear that consumers will obtain misinformation from DTC advertisements [9]. Specific physician criticisms were that these advertisements raise unrealistic expectations among consumers, minimize potential side effects [9] and fail to identify equally efficacious and less expensive alternatives [20].

There is some evidence that prospective drug consumers believe differently, suggesting DTC is effective in reaching the consumers' mind. One survey reports that 59% of consumers think DTC advertisements help them "make their own decisions" about different drugs [15], and another survey indicates that 28% of consumers would change physicians in order to obtain an advertised medication that they desired [19]. Some large MCOs report that these new channels of drug manufacturers' product promotion are driving up drug costs by creating unprecedented patient pressures to increase pharmaceutical use and to use the advertised and perhaps more expensive drugs [10].

5. Conclusion

Pharmacy benefit management strategies are evolving and are characterized by experimentation and innovation. Insurers feel ongoing pressure from public and private health care purchasers to contain drug costs, and can be expected to continue using pharmacy benefit management activities as an important part of their cost control efforts. However, insurers and the PBMs which they employ must move carefully to avoid appearing too restrictive to lawmakers, patients, and potential drug consumers. The US public generally supports the effort to keep health care costs down, but the public is also becoming more informed and less tolerant of some of the specific restrictions and economic incentives currently in use to control drug expenditure. Disease management may be a key part of future efforts by PBMs to address both cost and health care quality concerns, but there are significant practical, legal, and economic issues to address before these programs can be effectively implemented on a large scale.

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Chapter 13

Experiences with professional education

Stephen Chapman

1. Why do we need to influence demand?

Health care systems, regardless of how they are funded, are cost constrained. Therefore, to maintain equity it is important that physicians extract the maximum health gain possible for their responsible population from the resources available to them. It can be argued that this is as much an ethical responsibility as a means of obeying Hippocrates' injunction to "do no harm" [30]. A prerequisite to achieving such cost effectiveness for drugs is that physicians should understand and act upon the published evidence base for the medicines they prescribe. The first stage of Continuing Medical Education (CME) is critical appraisal of the literature to establish the evidence base for the teaching which is to be offered, after which the relevant information will have to be made available, regardless of how it is delivered (see Chapter 3). It is possible to obtain relevant evidence, even in countries with limited capacity, since initiatives such as the Cochrane Collaboration conduct systematic reviews to establish the evidence base around specific medical issues: their findings are available internationally. In this chapter different approaches are described to implementing in practice the principles emerging from such evidence.

2. Implementing proven principles

Having established the evidence, the role of CME is to persuade prescribers to change their practice; although change is always happening, its deliberate inducement is usually slow and labourious [18]. Doctors are like any other group of people when responding to new ideas [11,24]; the idea is initially taken up by a few innovators and then spreads slowly to include early adopters who are respected by their peers. The rate of uptake then increases as the majority take up the idea, only to slow again as the process reaches the final group, the laggards, who are slow to change and cling to traditional values [18]. Several approaches have been tried, as described in general in Chapter 3. In this chapter the key features, strengths and weaknesses of the various initiatives are discussed.

3. Postgraduate lectures and conferences

Lectures provided through post graduate centres or universities are voluntary; they therefore attract only those who are motivated and interested: if we look again at the model proposed by Horder [18], these doctors would tend to be the "innovators" or "early adopters" who form the minority of primary care doctors. As primary care doctors work in geographically distant locations, the opportunities for the

innovators and early adopters to network and share ideas are limited, and any diffusion of new practice is limited. It is not surprising then, that lectures or short conferences generally produce no change; in the six studies reviewed by Davis, all the teaching provided was found to have inconclusive or even negative effects [14].

4. Educational outreach and academic detailing

Since doctors do not all regularly attend postgraduate training centres to keep up to date with advances in medicine, it makes sense to take the education out to them in their own practices. Mailings of written information have been shown to be ineffective [4], so direct communication is the only alternative. This is the principle underlying educational outreach – put simply, it uses the same techniques that the pharmaceutical industry has used for so many years in employing medical representatives to visit doctors and persuade them to use their company’s products. Avorn and Soumerai undertook the seminal randomised control trial of educational outreach by using clinical pharmacists to undertake “academic detailing” of Medicaid physicians across four states in America [4]. The pharmacists were trained in communication and influencing skills as well as being given the necessary clinical knowledge, and then made two brief visits to the physicians to discuss inappropriate prescribing of cerebral vasodilators, cephalexin and propoxyphene. They supplemented their discussions with specifically designed support materials summarising the key points in an eye catching and memorable style, with key references provided to underline the messages regarding prescribing change. The visits reduced inappropriate prescribing by 14% and were a significant improvement on merely mailing the support materials to physicians without making a visit. A formal economic analysis of the results indicated that an operational scale programme would produce savings two to three times greater than the costs of mounting such a programme, and this excluded the extra benefit of reduced health care costs from improvements in the quality of care [26]. A follow up study showed that physician characteristics such as age and speciality did not affect their response to the educational intervention; a second reinforcement visit substantially increased compliance with prescribing recommendations [27]. The most important techniques and principles for academic detailing were described in a later review [28]. These are summarised in Table 1.

As the majority of prescribing is in the community, educational outreach programmes tend to be in primary care, although academic detailing has been successfully used in a teaching hospital setting to reduce the incorrect use of antibiotics [5], and in nursing homes to reduce the use of psychoactive drugs

Table 1
Key principles of academic detailing

– Conduct interviews to investigate baseline knowledge and motivations for current prescribing patterns
– Focus programmes on specific categories of physicians as well as on their opinion leaders
– Define clear educational and behavioural objectives
– Establish credibility by having a respected independent organisational identity, referencing authoritative and unbiased sources of information, and presenting both sides of controversial issues
– Stimulate active physician participation in educational interactions
– Use concise graphic educational materials highlighting and repeating the essential messages
– Provide positive reinforcement of improved practices in follow-up visits

[6]. Since the original American trial, academic detailing has been piloted in many countries with widely varying health care systems; in some countries it has been institutionalised and become part of the routine health service, though in others some of the basic principles have been lost in the process.

The first UK trial employed a single academic detailer to make a single visit in order to advise general practitioners on the choice of non-steroidal anti-inflammatory drugs [21]. Like the Avorn trial, the “detailer” was a clinical pharmacist who received training in special communication skills, and who used specifically designed support materials to support the message: in order to give the project an independent identity, it was identified by the acronym “PRIDE”. The message and the evaluation were very much cost focussed.

Not long after the PRIDE trial was completed, the UK health service set up a network of prescribing advisers; initially the majority were doctors, but within a couple of years pharmacists had become the dominant prescribing advisers. There is usually at least one full time prescribing adviser per health economy, covering on average 20 primary care general practices. Resource constraints have mitigated against these advisers fully exploiting the principles of academic detailing; few of the advisers have for example received formal training in communication and influencing skills; clinical updates are provided by the National Prescribing Centre, but the key messages are not standardised and there are no specially designed materials to support advisers during their visits. Given the number of practices they have to visit, as well as other tasks within the health authority, advisers rarely visit doctors more than once a year, and often less frequently. Since previous studies have shown that repeat visits are most effective to produce a change, advisers need further support if they are to fulfil their objectives of encouraging appropriate cost effective prescribing by the general practitioners in the area they cover.

Several different models have been tried. That which is most rooted in the principles of academic detailing is the IMPACT project [10]. The model is based on the one proposed by Avorn and Soumerai, but is modified to make it more easily replicated. Teams of community pharmacists are employed on a sessional basis, covering about twenty practices each rather than using a full time clinical pharmacist to cover all practices. This has several advantages; the community pharmacists are familiar with general practitioner prescribing patterns and see the same community of patients and so are more empathetic with family doctors attitudes to prescribing. As they are paid per visit made, they are focussed on the task and there is less possibility of the “job drift” that can happen with full time advisers. Data is used to generate “target matrices and prioritise visits, and the pharmacists are supported by a mentoring system and regular update programmes to hone both clinical and influencing skills.

The pharmacists receive an initial three-day training programme focussed on influencing skills and using role-plays to reinforce the clinical messages. Once trained, they receive a two-day update course when a new programme starts – on average every four months. Support materials to help structure the interview and reinforce the messages support each programme. A page from a typical brochure is shown in Fig. 1. All materials also have the key references attributed.

5. Practice based audit and feedback

If access to patient records is possible, and there is a sufficient pool of suitably trained auditors, practice based audit and feedback can produce a lasting change [29,31,32]. The success and effectiveness of audit and feedback are variable, and initiatives may falter when it comes to implementing the change suggested by the audit [7]. Like academic detailing, the first stage is to establish the potential for change from baseline prescribing habits; again, it is important to place the emphasis on the quality of prescribing

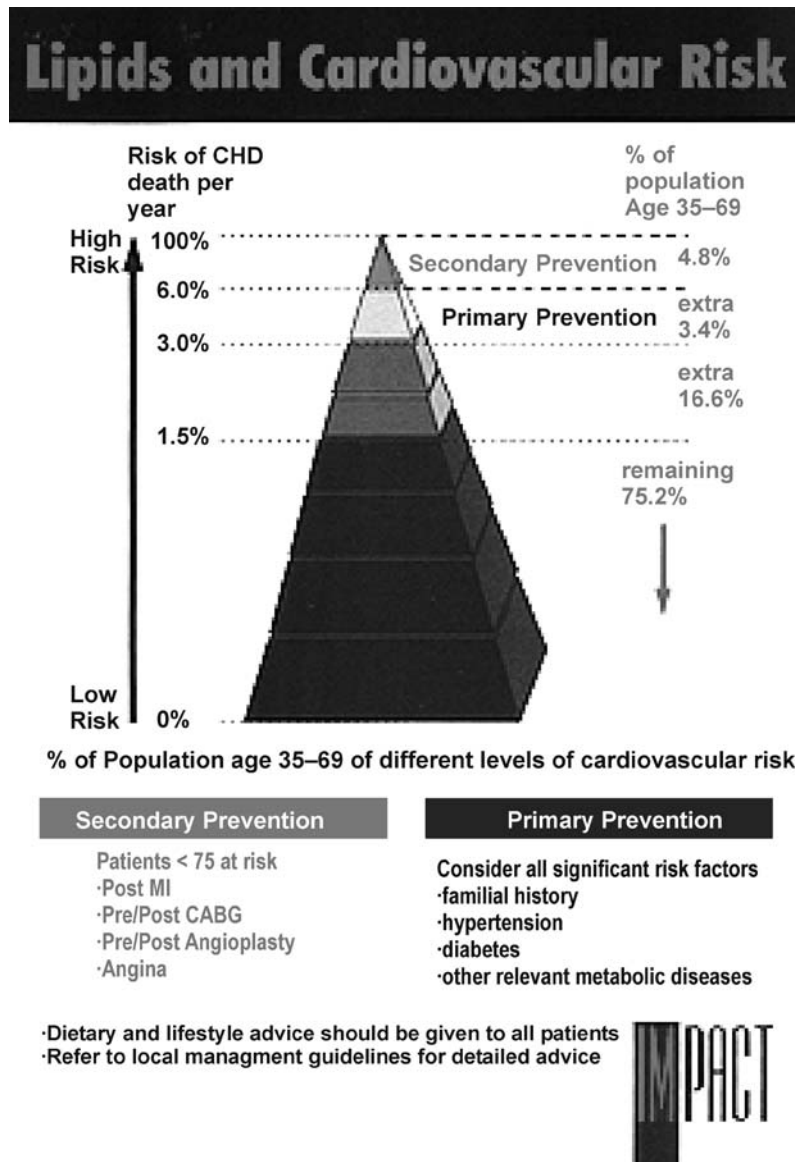


Fig. 1. An example of an Impact detail aid.

and allow cost reductions to follow. Considerable changes and substantive savings can be realized from revising and refining practice repeat prescribing systems – it has been estimated that 80% of drug costs are from repeat prescriptions. Doctors initially had reservations about community pharmacists being involved with repeat prescribing but over time they have come to agree with the concept.

Medication reviews can be conducted by either community or clinical pharmacists or clinical pharmacologist depending on local circumstances, but both need further training. Community pharmacists need their clinical knowledge updating and must learn how to read case notes, whereas clinical pharmacists and pharmacologists need to become familiar with the structure and processes of primary care general practice.

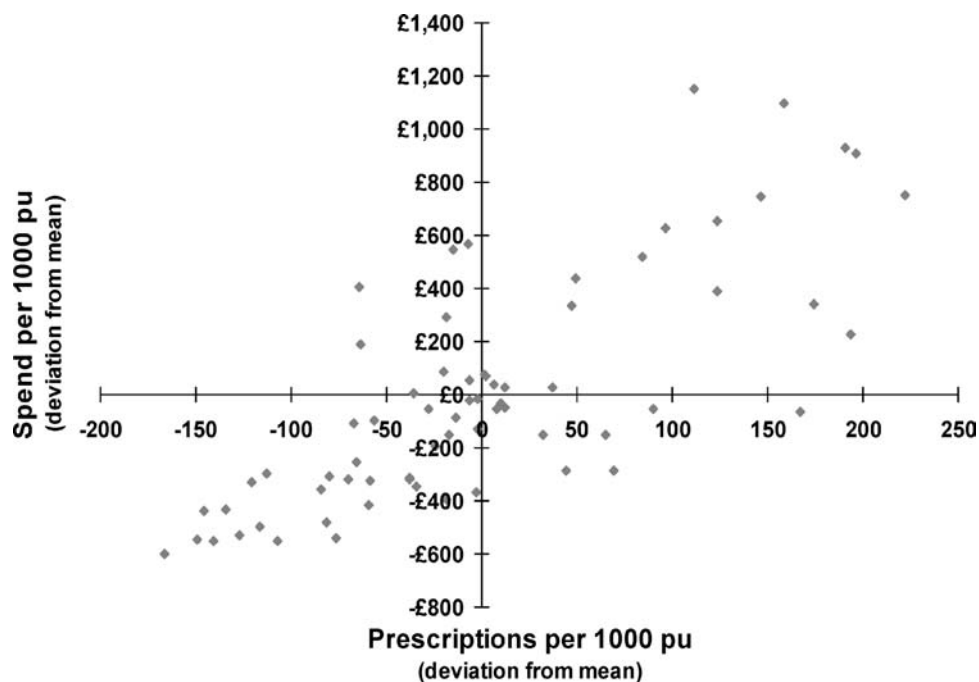


Fig. 2.

Having identified patients with the potential for change, the pharmacist produces an action list for the prescriber. At this point either the doctor follows up the patients concerned and writes to them inviting them for a medication review, or the pharmacist facilitates this on behalf of the prescriber. Occasionally, such a pharmacist has also held advisory clinics to explain the medication change to the patient. One model used a clinical pharmacologist to support the pharmacist, but this was not possible to replicate in the UK due to the high costs and the limited number of clinical pharmacologists available to undertake this work. In The Netherlands, small groups of GPs discuss their individual prescription profiles together with the local community pharmacist and agree on first-choice treatment options. Once patients have had the medication change explained to them, the majority prove to be comfortable with the change, trusting the doctor's opinion. Thus changes can be brought about, facilitated by practice-based pharmacists, with which both the prescribers and their patients are comfortable. Practice based work is resource intensive, so it is best targeted at those practices with greatest potential for change; it can achieve remarkable synergy if used in conjunction with educational outreach.

6. Conclusion

In summary, while traditional methods of continuing medical education do not produce change in prescriber behaviour, well designed methods specifically designed to influence prescribing in a favourable manner have been proven to do so. Such a form of continuing education is critical if prescribing practices are to be kept up to date and evidence based. The first stage of implementing change is to evaluate all evidence. Thereafter one should make use of practice based pharmacist facilitators; given specialised training they can be effective agents for change. Subsequent training of medical and pharmacy undergraduates

should include critical appraisal skills. The most successful change strategies use several approaches to achieve their aim.

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Chapter 14

Providing affordable medicines in transitional countries

Kees de Joncheere and Tamas Paal

1. Introduction

The term “transitional”, as currently applied to national economies and countries, refers to those former communist systems which are still engaged in the long process of transformation; a centrally planned economy is progressively being replaced by market orientation, and communist ideology and totalitarian rule have gradually given way to democratic political structures. That process has come into motion in many parts of the world, but nowhere more conspicuously than in the Countries of Central and Eastern Europe (CCEE) and the Newly Independent States (NIS) which emerged from the former Soviet Union.

Because of this ongoing process of change, the question of drug pricing and cost containment in these countries unavoidably has to be approached in a broad perspective, involving various other aspects of health and drug policy; well-intended measures on one front could all too readily disrupt a fragile situation on another. In fact most aspects of the health care system in these countries, largely shaped in the past according to the Semashko model, have been undergoing major reform. Whereas previously the system was totally state-run and controlled, and pharmaceuticals were produced in state factories, distributed by state wholesalers and supplied and reimbursed through state pharmacies, the health care market has in most of these countries now rapidly and even suddenly opened up; systems have generally been restructured around health insurance schemes [3], and drug production and supply have largely been privatized, with subsequent changes in reimbursement schemes [1]. Many countries in the CCEE have already made great progress in their transition towards a democratic society and a market economy. Most of these countries have embarked on health care reform, separating financing and health services from the State, and in parallel separating health financing from health services delivery (the purchaser-provider split). At the same time, macroeconomic pressures have generally forced governments into implementing a large degree of deregulation, including measures in the health care and pharmaceuticals market. In carrying out that process of deregulation, the authorities have unfortunately often failed to take into account the special risks of market failure which exist in the field of medicines and which render strong government involvement essential; as long experience in the West has shown, regulation in matters ranging from advertising and drug safety studies to pricing is essential if society is to be protected. Particular caution is called for in view of the marginal health situation: the state of health of populations varies widely across this part of Europe, and in many of the transitional countries it has declined. Particular concerns relate to the spread of tuberculosis and HIV-AIDS. There are also considerable differences within countries in terms of health status as well as access to health services [2].

However far reform has proceeded, it has much further to go before a stable and acceptable situation is reached.

Processes other than internal reform have also affected the situation. Ten CEE countries have applied for membership to the EU and are hoping to join in the period 2004–2007. In that connection, further upgrading of their drug regulatory systems and legislation, in order to conform with EU Directives, is underway. Membership of the EU will also have implications for the drug industry in the CCEE as regards issues of intellectual property protection, potential export markets (particularly to existing EU countries but also in their traditional export areas including the Newly Independent States), and the need and opportunities for foreign investment. In Albania, Bosnia and Herzegovina and the Federal Republic of Yugoslavia, on the other hand, the transition process has, unhappily, been severely hampered by prolonged armed conflict and social unrest; only more recently has it regained momentum [4].

Despite the progress which has been made, the increasing health needs and expectations of patients and society generally, as well as those of health professionals, have not yet been matched in this part of Europe by an increase in resources within the health sector. For the supply and reimbursement of medicines this has meant that part of the costs of medicines (often a substantial part) are having to be borne by the patient, either through co-payment for reimbursed drugs or through direct purchases of OTC medicines or non-reimbursable items.

In the NIS the immense transition from the former unitary Soviet system and the creation of a group of new countries has had far-reaching implications for people's daily life and values, and has dramatically changed the social fabric, not always for the better. Growing inequalities, unfair salary systems, unemployment, corruption and lack of perspectives have affected large groups of the population. The emerging market economy requires a different concept of public services and management structures, and new attitudes and skills at all government levels. The changes also impact on the health and the pharmaceutical sector and as noted above they have brought about a real deterioration in the health status of populations. Major health indicators have shown a worsening trend over a period of years, and only now are they in some countries improving again. The very necessary process of ongoing health care reform unavoidably brings with it disruption. Many citizens of the NIS are currently find that even elementary health care services and essential drugs are out of their reach, and this has led to a decrease in life expectancy, increased morbidity in cardiovascular and infectious diseases, emerging epidemics of poverty-associated disorders and increased antibiotic resistance due to irrational drug treatment (over-prescribing or prescription-free sale) [5].

2. The drug market in Central and Eastern Europe

Before 1989, drug needs in the CCEE were supplied largely by domestic state-owned companies. These companies also exported their goods to the former Soviet Union. The consumption of medicines was high in volume terms due to inappropriate prescribing habits, a highly specialized and hospital-based health care system, and strong patient pressures.

With the transition, the distribution of drugs through wholesalers and pharmacies was largely privatized. Manufacturing companies in several countries are still (at least partially) state-owned, often through public property investments. Multinational companies have gradually increased their market share (attaining up to 50% in value terms in most markets). Drug expenditures have been rising fast, both in absolute terms and as a percentage of health expenditure (Table 1, Fig. 1). Generic drugs have been losing market share to imported brand name products, due to the perception that the latter are superior,

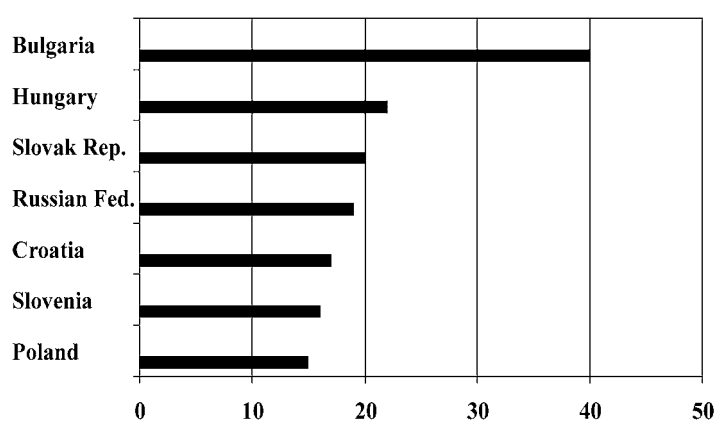
Table 1
Drug market CCEE, estimated figures 1999 (or latest available)

Country	Total drug expenditures, million \$	Per capita, \$	% Total drug expenditures reimbursed	Drug costs as % of health expenditures	Drug costs as % of GDP
Albania	23	7	30	23	1
Bosnia : Fed (1)	Na	Na	Na	Na	Na
Bosnia : RS (1)	6	Na	Na	20	Na
Bulgaria	70	25	70	25	2.1
Croatia	432	90	Na	17	2.2
Czech Republic	1040	101	80	25	1.9
Estonia	13	47	50	23	1.8
Hungary	990	104	55	26	2
Latvia	65	46	40	16	1.3
Lithuania	190	51	54	18	1.8
FYR Macedonia	42	20	73	17	1.4
Poland	2350	61	45	10	1.7
Romania	320	14	42	20	1.4
Slovak Republic	490	70	86	25	2
Slovenia	235	114	84	18	1.5
Average CCEE		54		20	
EU figures		275 (average)		7 to 11%	

Sources: Ministries of Health CCEE, WHO/EURO, World Health Report, European Observatory.

Note: Bosnia Herzegovina: Federation of Bosnia and Herzegovina, and Republika Srpska. FYR Macedonia = Former Yugoslav Republic of Macedonia.

% rise in drug expenditures 2001 in Eastern Europe



Data from Scrip 2000

Fig. 1. Percentage rise in drug expenditure in one year.

a belief often fostered by marketing practices. And while the level of expenditure per capita, expressed in dollars, is low as compared with figures from the countries of the European Union, it is substantial as compared with the levels of earnings.

This rise in drug expenditures continues and has reached unsustainable levels; it is largely due to the introduction of new imported drugs, shifting prescribing patterns, intense marketing efforts and the rapid autonomous growth of health needs.

Investments in the CCEE drug industry have come from multinational companies as well as from companies in the CCEE themselves, particularly Hungary, Slovenia, Croatia, Poland and the Federal Republic of Yugoslavia. Domestic manufacturers produce basically generics, which mostly comprise off-patent drugs. Their traditional export market to the Newly Independent States has been in decline. Productivity, compliance with GMP standards and the implementation of patent protection will be key issues for the CCEE industry over the coming years.

3. The drug sector in the NIS

The biggest changes in the delivery of pharmaceuticals in almost all of the Newly Independent States have been the introduction of a market oriented drug distribution system and diminishing budget allocations for health care. Pharmaceuticals are often the first item to fall victim to health care budget cuts, which means for the patient limiting access to drugs and limited access to health care.

There are large differences between the twelve NIS countries in size, demography, economic and level of human development. In the pharmaceutical sector these countries originally inherited a common system of supply and financing (free drugs, subsidized supply) and similarities in medical practice, pharmacy education, social background. Now differences between them are emerging as regards the structure of the sector (production, privatization, etc.) and in payment, pricing and reimbursement systems.

Clearly (see Table 2) [5], there are large variations in health expenditure and drug expenditure, even when taking into account the ability to pay. In addition, the numbers of registered drugs and the numbers of establishments (production units, wholesalers and pharmacies) vary enormously. The growth in the number of wholesalers and pharmacies since 1990 has been caused by the (mostly uncontrolled) privatization wave in the sector.

4. Provision of medicines, containment of costs, and the quest for rational use

As already noted, rising drug expenditures throughout the CCEE and in the NIS have led to increased private spending and greater co-payments for reimbursable drugs, thus also leading to problems with equity of access to needed medicines. Cost-containment policies, affordability and access to drugs for the population are therefore matters at the top of government agendas.

Most reimbursement systems still use a structure inherited from the former system, limiting eligibility for reimbursement to certain drugs or to vulnerable population groups and patients with chronic diseases. Reimbursement has also been restricted by using positive lists and other instruments, such as the limitation of prescribing of listed drugs to particular specialists or the hospital level. Increasingly CCEE countries are using elements of economic evaluation for reimbursement decisions [7,8]. Varying degrees of patient co-payment have been introduced in a number of countries, and some drugs have been

Table 2
Economic indicators, drug expenditure and pharmaceutical sector structure NIS (1996–1997)

Country	Popul- ation (Million)	GDP per capita (US\$)	Health expend. in % of GDP		Drug expenditure per capita (US\$)	Average monthly wage ('97) (US\$)	Number of regis- tered drugs ('97)	Production		Establishments in the sector (1_1_97)		Inhab- itants per pharmacy
			1996	1997				plants	Full assorted wholesalers	Phar- macies	Kiosks	
Armenia	3.5	450	4.2	19	16	80	1200	10	6	600	120	5800
Azerbaijan	7.6	451	2.8	13	7	20	6000	3	2	1000	200	7600
Belarus	10.3	1308	5.1	67	16	145	3000	5	10	1250	4000	8200
Georgia	5.4	841	4.5	38	12	90	1500	20	7	850	600	6400
Kazakhstan	16.4	1278	2.0	26	12	100	2000	22	130	1700	1220	9700
Kyrgyzstan	4.6	379	3.4	13	8	Na	830	9	20	260	500	17700
Moldova	4.4	443	3.9	17	10	40	3500	5	10	680	0	6500
Russian Fed.	147.5	2985	2.8	84	40	155	11000	370	10	16000	25000	9200
Tajikistan	6.0	177	8.0	14	2	90	Na	1	1	507	Na	11800
Turkmenistan	4.6	461	5.0	23	5	Na	665	1	2	390	120	11800
Ukraine	50.9	864	3.3	29	10	Na	5000	22	10	Na	Na	Na
Uzbekistan	22.7	391	3.4	13	3	60	1920	16	20	5200	0	4400
Average		836	4.0	30	12	87	3051	484	228	28437	31760	9000
Total	283.9											

Sources: Economic data: EBRD, EIU, BCE, IMF; health care expenditure: WHO Health for All database; sector data and drug expenditure: Ministries of health and Drug Agencies of NIS countries.

Table 3
Drug price regulation in CCEE, 1996–1997

Item	ALB	BIH	BUL	CRO	CZR	EST	HUN	LVA	LTU	MAC	POL	ROM	SVK	SLO
	Yes	No Fed.	Yes RSr	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Price regulation?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Price regulation applied to:														
Prescription drugs	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes		Yes	Yes	Yes	Yes
OTC drugs			Yes		Yes	Yes	Yes	Yes	Yes			Yes	Yes	Yes
Other products			Yes		Yes		Yes		Yes		Yes		Yes	Yes
Manufacturers	Yes			Yes		Yes					Yes	Yes	Yes	
Importers				Yes		Yes					Yes	Yes	Yes	
Wholesalers	Yes		Yes	Yes	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pharmacies	Yes		Yes	Yes	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	

Source: Ministries of Health CCEE.

accorded over-the-counter status. As financing remains one of the major difficulties for health care systems, especially in NIS – where most countries spend only some 4–5% of their GDP on health – the need for such out-of-pocket payments for medicines has become substantial [6].

Prices of medicines are mostly controlled, either through policies designed to limit production and import costs, various measures regarding distribution margins or introduction of either international reference pricing, or national reference pricing criteria for reimbursement (Table 3).

Whereas many western countries have succeeded in increasing the market share held by generic products, the trend in CCEE runs counter to this with generics losing market share to expensive imported specialties. These may in some cases offer new and necessary therapeutic possibilities, but at the same time they lead to overall affordability problems. CCEE will have to strike a balance and ensure that as great a part as possible of the market is covered by low-cost generic items [12].

Armed conflicts in Albania, Bosnia and Herzegovina and the Federal Republic of Yugoslavia have disrupted not only the reform process but also the pharmaceutical supply system. Humanitarian organisations have helped to ensure the maintenance of basic health services and the supply of medicines. Donations of drugs have proved of vital importance in such exceptional conditions, with an estimated 80 to 100% of medicines at times being provided through humanitarian assistance. Donated drugs have however often been inappropriate and of poor quality, due to lack of coordination and experience among the charities involved [13], and it is clear that they do nothing in the longer run to ensure a sustainable flow of affordable drugs. In some situations they have even been found to lead to an unhealthy distortion of prescribing practices [15].

Several CCEE countries were among the pioneers of drug utilisation studies in the seventies and some developed extensive systems to monitor drug use. Most of these systems later collapsed, and complete and reliable data on drug consumption and use are currently difficult to obtain. Such studies as have been performed in recent years point to marked differences between countries in prescribing patterns, attributed largely to differing therapeutic practices and the changing reimbursement environment [14].

Health professionals in these countries still have little access to objective and independent drug information, yet marketing practices by the pharmaceutical industry have greatly intensified over recent years. Some countries have developed policies seeking to improve the use of drugs through the establishment of drug information centres, the promotion of independent drug information services and the adoption of essential drugs lists and formularies.

5. The regulation of medicines

Some of the radical developments have taken place in the area of drug regulation, particularly because this is a requirement of the EU accession process. As early as 1997 regulatory authorities in ten CEE countries organized themselves under the CADREAC arrangement [9,10], and this has now developed into an intensive collaborative programme with the EU Commission. CCEE experts now participate regularly in the expert committees of the EU regulatory system, and many of the CCEE have updated their drug legislation since the early nineties and brought their legislation in line with EU Directives and Regulations [11]. The enforcement of regulations will however need to be strengthened. At the same time it is clear that the harmonisation with EU criteria may create a series of problems around the availability of medicines, as some of manufacturers may find it difficult to fully comply with GMP in time, and as it may prove difficult to complete the full review of old registration dossiers before the day of accession. This will lead to a welcome cleaning up of the eastern European drug scene, but at the same time may also lead to disappearance of many cheap generic products from the market.

Most CCEE and NIS have established national medicines agencies – through a transformation of what was earlier a quality control institute – and made them responsible for drug regulation as a whole. In some of these countries procedures for obtaining marketing authorizations nevertheless remain cumbersome and lengthy; most agencies face a significant backlog in marketing applications. This too can have economic repercussions, where generic products fail to reach the market in good time.

6. Current challenges

Several major challenges for the coming years in Central and Eastern European and the Newly Independent States can be identified:

- The available funds for drug reimbursement will not be sufficient to meet the rising demand from patients and professionals; effective cost containment measures will be necessary, while at the same time access to needed medicines will have to be guaranteed and quality of treatment improved. The policies to meet these conflicting needs will have to be developed and implemented through a participatory process that can ensure public and professional confidence.
- Drug regulation is rapidly brought into line with EU regulations, as negotiations for the enlargement of the Union proceed; however it will at the same time be necessary to prove better systems for the enforcement of regulations and policies than those currently existing, and it is vital to ensure that this harmonization will not lead to decreased access of needed drugs.
- In each country the domestic pharmaceutical industry will face the need for an ongoing improvement in quality and efficiency if it is to compete effectively in a rapidly changing market. Patent legislation will change product portfolios. Export markets, particularly those offered by the Newly Independent States, will remain of major importance to successful developments for CCEE companies. These industries will therefore need to be commercially astute and enterprising, and in that they will no doubt be supported by the governments; that however must not prejudice the implementation of critical policies on drug pricing and use.
- In the Newly Independent States the pharmaceutical sector is now entering a new stage of development. Modest economic growth and decentralization in principle offer opportunities for new development; health care reform may gradually deliver results. However, despite the positive economic development in several of these countries, it is clear that all will remain in a transitional stage for

several years at least, and that the environment for change and innovation will not always be positive and stable. Recent economic turmoil only underlines the need for ongoing reform and adaptation of the sector if one is to achieve sustainable systems and structures.

- In all CCEE and NIS countries, continuing improvements in sector management should strengthen recently established structures and create sustainability. National drug policies will continue to play a stimulating strategic role. The quality of the drugs on the market and of domestic production in general needs further development. However important price is, one will have to be wary of the temptation to let economy prevail over quality.
- Rational selection and prescribing of drugs is critical because of the often low standard of inherited prescribing practices and the current lack of money. A comprehensive approach, with initiatives at regional and hospital level, is needed to achieve tangible results. Fundamental changes in the educational system should make health professionals more patient focussed and health outcome oriented, with special emphasis on drug selection and prescribing.

7. Conclusion

The situation of the countries of Central and Eastern Europe and the Newly Independent States is immensely variable, as is their rate of progress, both economically and in the development of health systems. Viewed globally they occupy a situation intermediate between that of the industrialized west and the developing world. Some, particularly the countries approaching the point of accession to the European Union, have the potential to attain western standards within a decade. For others it will take much longer and they may for a generation or more continue to struggle with large populations which will not be capable of affording drugs at the price levels customary in the west. For these countries it would seem essential to contemplate the application of strongly differentiated pricing for drugs available internationally, as discussed in Chapter 15 with respect to the developing world.

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Chapter 15

Access to medicines in low-income countries

Marthe Everard

1. Introduction

The World Bank classifies countries by *per capita* Gross National Product (GNP). “Low-income” countries are regarded as those with a national income *per capita* of US\$ 755 or less and “middle-income” countries as those with *per capita* income lying between US\$ 756 and US\$ 9265 [12]. Both these groups are generally referred to as “developing” countries. “High-income” countries or “developed” or “industrialized” countries are classified as those with *per capita* income of US\$ 9266 or above [12]. The distinction between these three classes of countries thus reflects differences in the levels of income and standards of living of their populations. In low and middle-income countries a large proportion of the population live in poverty and their condition is characterized by high rates of mortality, morbidity and disability, as well as limited access or none to health care and services. The bulk of the population in high-income countries, on the other hand, have better standards of living and health and enjoy extensive access to health services, while their countries also have the ability to develop health technologies [5].

Notwithstanding these differences, the governments of developing and industrialized countries share an interest in health and health care. Irrespective of their level of development or national income, people desire better health status and greater access to health care including appropriate pharmaceutical services. It is clearly in the national interest that health budgets be allocated effectively so as to maximize the contribution made to attaining national health objectives and advancing social welfare [1].

A global analysis shows that world consumption of pharmaceutical products increased dramatically from US\$ 70 billion to US\$ 317 billion in the period between 1975 and 2000 [10]. During this period the world's *per capita* consumption of medicines increased from US\$ 17 to US\$ 53. Yet more than 80% of all pharmaceutical products are consumed by the 15% of the world population living in industrialized countries, a figure which reflects a grossly uneven distribution of pharmaceutical consumption across the world [3,13,16].

Despite the increased world consumption, problems remain in ensuring the availability and affordability of medicines, including those which are essential for treating the majority of common diseases prevailing in low and middle-income countries. The reasons for this are complex. They are not only related to financial constraints, but also to the attitudes of key actors in the health sector – a sector which comprises a network of relationships between the government, public and private providers in the health and pharmaceutical sectors, an important volume of industrial activity and the consumer.

This chapter will provide a general overview of the situation in developing countries regarding access to essential medicines, and especially their problems in ensuring affordability and possible strategies to overcome them.

In this overview traditional medicines will not be considered, although their role should not be underestimated.

2. Access to essential medicines: Four components

After immunization for common childhood diseases, appropriate use of medicines is one of the most cost-effective components of modern health care but that is not to say that all are equally necessary across the board; where means are limited, priorities can and must be set. Decisions on the range of medicines which one must strive to make available throughout a nation have to be taken in the face of challenging political, social, ethical, economic, and medical difficulties and developments. Governments, non-governmental organizations, and households in many low-income countries struggle continuously to ensure and secure access to even the most basic life-saving medicines, especially in rural areas. In low-income countries therefore, the most urgent concerns relate to the need to attain affordability and equity of access with respect to these vital pharmaceuticals, and beyond that to attain the same for a somewhat wider range of “essential medicines”, a concept developed by the World Health Organization in 1977.

The description of essential medicines is as follows: *Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility*” [25].

The term “essential medicines” is usually applied to those medicines that are listed on the World Health Organization (WHO) Model List of Essential Medicines, most of which are off-patent; many countries have developed their own lists.

WHO has developed a global framework for “Access to Essential Medicines” which has been adopted by United Nations’ agencies and consists of four components:

(1) rational selection and use; (2) affordable prices; (3) sustainable financing; and (4) reliable health and supply systems [19]. Different stakeholders have differing roles to play in developing these components positively and seeking both to remove old obstacles and create new opportunities.

2.1. Rational selection and use

Medicines are one of the important elements in the provision of health care. While advanced methods of treatment for major infectious diseases and related conditions tend to become ever more complex and costly, many highly effective medicines are – or can be – made available at very low cost. Commonly, therefore, fully acceptable and affordable treatments can be found if one chooses well. Rational selection of medicines includes defining which medicines are most needed, identifying the most cost-effective treatments for particular conditions while taking full account of quality and safety as well, and then ensuring that they are used effectively.

Appropriate use of medicines by health professionals and mid-level health workers is being pursued by introducing evidence-based national treatment guidelines and protocols. Based on these treatment guidelines a national list of essential medicines and key pharmaceuticals can be prepared and disseminated.

In-service training programmes and availability of unbiased drug information are needed to update the knowledge and skills of clinicians, pharmacists and nurses in effective drug use. Encouraging rational drug use by patients is of equal importance.

2.2. Affordable prices

Affordability of medicines by individual patients in low-income countries is an important factor influencing access to care and treatment. Seeking care is more commonly a question of buying medicines than of consulting a qualified health worker. Drug prices, which are sometimes actually higher than those in high-income countries, often have to be met entirely by sick persons or their households; it is estimated that some 50–90% or more of pharmaceutical expenses are out-of-pocket purchases [16]. The bulk of the out-of-pocket health expenses which have to be met by the individual or household commonly relate to medicines [15]. Various ways of reducing this burden on the family will be considered below, but an important one is clearly to ensure that prices are brought to the lowest attainable level. That can be ensured variously by promoting competition among quality generic medicines where off-patent items are concerned, negotiation of prices, and therapeutic competition for on-patent medicines, use of the provisions stipulated under the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) where necessary to increase affordability of medicines still under patent [24], reduction of duties and taxes, and reduced wholesale and retail margins. It is equally important to provide transparent price information for healthcare providers and consumers so that the community knows how to find the most affordable products when they are needed.

2.3. Sustainable financing

This third component of access must be viewed in the context of overall funding of health care, including financing for prevention and treatment of priority infectious diseases with a high public health impact.

For decades, the public health sector in developing countries was mainly financed by the government, and the public health sector commonly provided medicines free of charge. Over the years, diminishing budgets have increasingly led to drug shortages in the national health system, particularly in rural areas, and to a widespread collapse of free drug supply. This is the principal reason why, as already pointed out, health care in low-income countries is today predominantly financed privately. This is illustrated in Fig. 1, contrasting the sources of health financing in eleven low-income countries with those in nine high-income countries [20].

By far the most common form of private finance is out-of-pocket payment, made at the time when people seek care and treatment, rather than through a prepayment scheme. Figure 2 shows that out-of-pocket payment in the high-income areas of the world seldom exceeds 20% of the total while it exceeds 90% in some low-income countries. Out-of-pocket payment for health care tends to be both inequitable and inefficient when it plays a major role in health financing; there is clear evidence that the burden of payment for health care falls heavily on the poorest households at the time when a family member is sick; at these times, income may actually be reduced by illness and it is likely that the medicines which will be needed will be bought in insufficient quantities or not at all.

In this respect, change is underway, though it still has far to go. Thirty-three of the 37 Sub-Saharan African countries in which public health services were previously free-of-charge and funded by domestic tax revenues have introduced health financing strategies based largely on private financing in the form of fee schemes or co-payment [2].

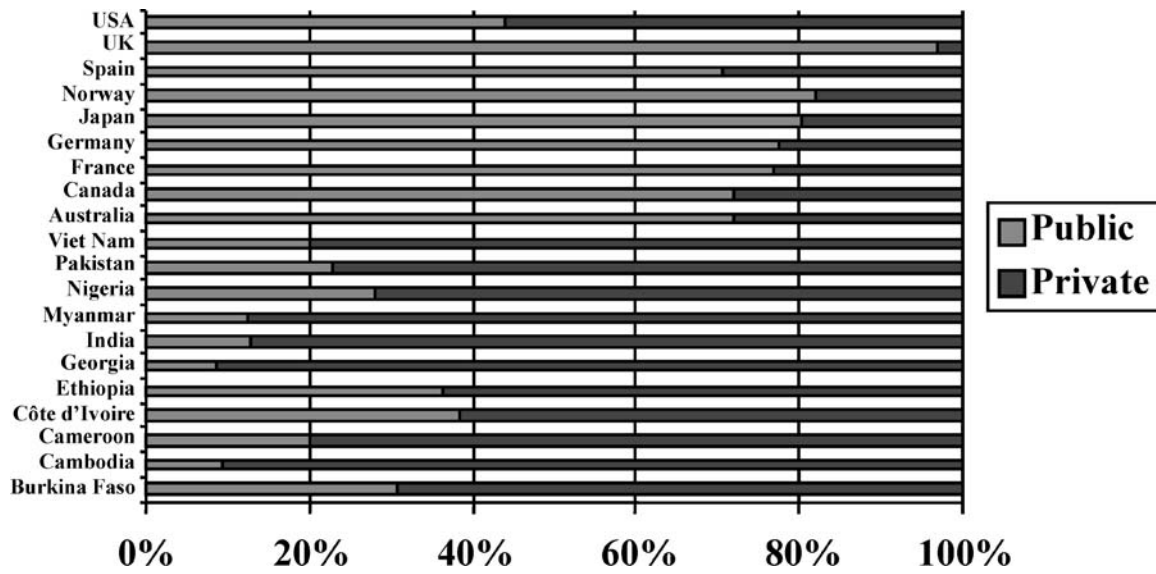


Fig. 1. Public and private shares in health financing differ in high- and low-income countries.

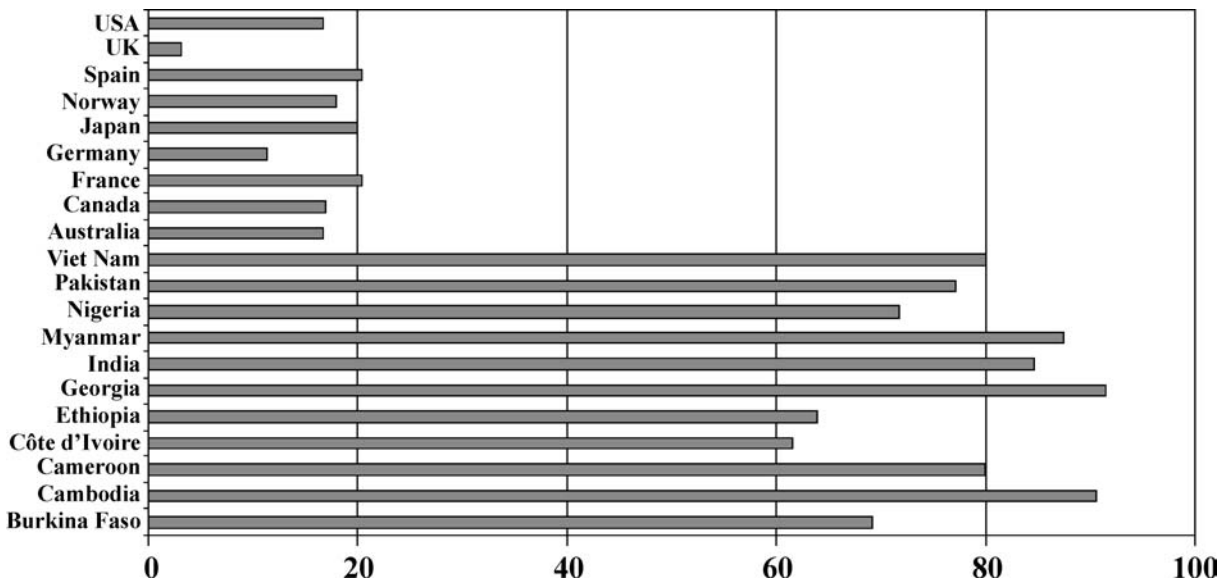


Fig. 2. Out-of-pocket payment as % total health expenditure is more important in low-income countries.

Health insurance schemes are another option, though it may be difficult to implement them in low-income countries. Whereas social insurance schemes are common in Europe and are on the increase in Latin America and Asia, one finds that in Sub-Saharan Africa, protection by social insurance coverage provides for less than 8% of the population [15,21].

Sustainable financing can also be achieved by a combination of several viable financing mechanisms, including, in addition to the above, reallocation of public funds, better use of out-of-pocket spending, and international financing through grants, donations, and loans under appropriate circumstances.

2.4. Reliable health and supply systems

Health systems should provide a certain minimal level of health care which has the capacity to treat major infectious diseases and related conditions effectively with essential medicines and when necessary with key pharmaceuticals. Improvements to existing drug supply systems are usually central to health sector development.

Tackling the overall cost of health care became high on the political agenda of governments from both developing and developed countries because of increasing health and pharmaceutical expenditures. Governments had to look for new ways of financing and delivering health services in a cost-effective way. Mechanisms for cost-containment introduced by industrialized countries and relating to medicines have been, among others, national drug formularies, non-reimbursable drug lists, restricted reimbursement schemes, price regulation, promotion of generic prescribing and substitution, and surveillance of prescribing costs [14].

In 1993, the World Bank published its report “Investing in Health” and encouraged governments from developing countries to set priorities in health services and to allocate resources efficiently by promoting an approach based on “the burden of disease” and the cost-effectiveness of interventions so to design an “essential national package” of health services. That would comprise a “minimum package” of public health (preventive care) and clinical (curative care) services, including the provision of essential medicines. Governments should ensure universal access to their national packages and allocate a certain amount of resources to satisfy the needs of the poor and other target groups [11].

Drug supply systems must serve to ensure continuous availability of essential medicines and medical supplies of assured quality. Supply should be well planned and dependable so that shortages and stock-outs are rare, and the total costs for a given level of service should be low. In order to meet increasing drug demands and the expectations which the public have of the public health services, and to improve on failing public drug supply systems, governments have looked for new – and cost-effective – ways of financing and managing drug supplies [11]. In many low-income countries, creative mechanisms and an efficient mix of public, private, and NGO sectors in national drug supply and distribution systems have evolved [15]. It is particularly important that effective national drug legislation and regulations, including drug quality assurance and control systems be in place for monitoring both imported and locally produced medicines circulating in the local market. In addition regulatory control is needed to determine which health professionals are authorized to prescribe and dispense medicines (an essential part of ensuring the quality of medical care), to assure the quality of drug supplies, to combat counterfeit products, and to contain drug resistance in both public and private sectors [15].

Despite all the efforts which have been made in developing countries in advancing both general health policy and the performance of the pharmaceutical sector, it is an unhappy fact that the access problem is far from being solved. Two thirds of all deaths of children under 15 are due to seven diseases for which effective prevention and therapies exist, as shown in Fig. 3 [17]. Vulnerable groups of society are still dying because of lack of access to these essential treatments. It is an unhappy fact that the world’s poorest people too often are served by the most inefficiently performing health systems [20]. Their health status is below what is attainable, and health and supply systems are unresponsive and unfairly financed.

3. Strategies to increase affordability of medicines and reduce expenditure

Throughout this volume, alternative methods of rendering medicines more affordable and containing overall expenditure have been presented, and experience with them reviewed. Some of those methods

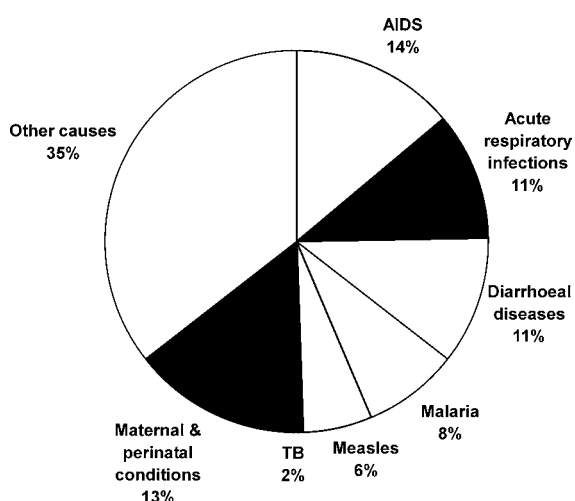


Fig. 3. Two out of three deaths among children and young adults in Africa and South East Asia are due to seven causes (age group: 0–44 yrs).

Table 1
Examples of measures for controlling drug expenditure

Examples	Explanation/comments
Bulk purchasing	E.g., by Government Medical Stores, generally with extensive use of tenders May include pooled procurement (by several institutions or even several countries)
Capping of expenditures	Ceiling of pharmaceutical expenses per insured patient <i>or</i> Limits on expenditure allowed per treatment episode
Drug selection	Positive lists, such as essential medicines lists, based on criteria for inclusion (public health needs, therapeutic value, cost) <i>or</i> Negative lists, excluding certain products
Restrictions on marketing and advertising expenditure	Advertising and promotion can make up a significant portion of ex-factory drug costs and are intended to raise consumption. Limitations are thus intended both to reduce price and help rationalize consumption
Prescribing controls or incentives	Intended to reduce consumption and/or shift prescriptions towards cheaper or generic medicines
Price control	Mainly on ex-factory or retail prices or on distribution margins
Promotion of rational use	Strategies include national drug formularies, post-graduate education, lists of non-reimbursable medicines, substitution, and surveillance of prescribing costs
Use of generic products	Substitute for brand name products, providing cheaper alternatives
User fees and co-payments	May discourage excessive consumption but can have negative consequences for affordability and equity of access

are simple to apply while others demand considerable resources and may not be feasible in developing countries where the input to policies is constrained in terms of staffing, finance and technical abilities. The best known of these methods are summarized in Table 1, and certain of these will be discussed further in this section.

3.1. Factors determining prices: The role of competition

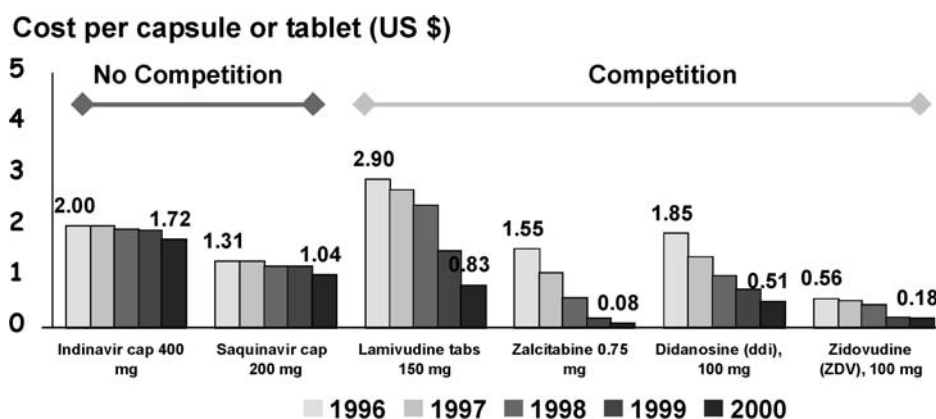
In order to design programmes which will render medicines more affordable, one needs to understand how the prices of medicines are normally determined. It is well known that in a competitive market for goods of any type, where there are no barriers to entry, and a large number of buyers and sellers are active, prevailing prices are close to producers' long run minimum average cost of production. The discipline of the competitive market prevents any individual producer from raising prices very far above production cost.

That general market rule does apply to a limited extent to pharmaceuticals, namely to generic products, where a particular medicine is available from various competing sources. Here, price determination responds to competitive pressure in the way the economic theory predicts. However, barriers to entry are common in the rest of the pharmaceutical market. Essentially these are economic barriers, in the form of the large initial investments which are required to develop a drug and maintain the activities of a multinational corporation.

Secondly, there are legal barriers. The originating firm will go to great lengths to secure and retain a monopoly of production and sale for a long period, making use of patent legislation to do so. Where patent rights exist, drug prices can be many times the marginal cost and manufacturers have a substantial amount of freedom to set prices for their patented medicines, varying these from country to country to secure the highest income which the market will bear. It is only as a patent nears the end of its term that competition begins to play a major role in price determination. The only element of price competition before that time comes will be competition across therapeutic groups, where two or more drug substances having similar therapeutic effects may battle with one another for the market. Although the research-based manufacturing industry claims that its often high prices are justified by its costs and the need to take risks, this claim is in fact impossible to assess in detail, since information on manufacturing costs is not publicly available. It is however certain that a large margin exists for many patented medicines between the costs of production and the manufacturers' price. Laing has used publicly available data to demonstrate how the very large sums earned from medicines may to a substantial extent be used to provide profit or finance advertising rather than to conduct innovative research [4,8]. It is also clear that where a firm finds it commercially attractive to reduce a price it can and will do so. The art of the policy maker often lies in creating a situation in which, particularly through increased competition but also through other means, a company can be induced to reduce prices of its own initiative.

One of the main options available to governments is, in short, to steer the market towards greater price competition [16]. Figure 4 illustrates the effects of price competition concerning medicines for HIV/AIDS in Brazil over a period of 5 years [9]. The prices of each of the six medicines listed declined over this period, but the decline was only slight for the two medicines which had no generic competition whereas it was dramatic for the four where such competition was introduced.

Many developing countries have to date not succeeded in following this course. Often poorly informed as to the possibilities which exist to obtain better prices, not endowed with an efficient national purchasing system and commonly not having large markets of interest to international manufacturers, such countries all too frequently find themselves obliged to pay whatever prices manufacturers ask. According to findings by Médecins Sans Frontières (MSF) and in other studies, many low-income countries pay generally higher prices than necessary, and as pointed out above the prices may even be higher than in the industrialized world [16].



Source: UNAIDS, B. Samb, 2000

Fig. 4. Effective price competition.

3.2. The role of reliable price information

National agencies in some drug-importing countries have discovered that reliable information on drug pricing across the world is an important tool in seeking to tackle the pricing issue in their own country. As explained in earlier chapters, well organized public purchasing agencies, e.g., in Canada, and New Zealand, or social insurance schemes in Europe acting on behalf of very large populations, are aware of prices paid by bulk purchasers elsewhere, and therefore negotiate directly with manufacturers to obtain prices which are at least as favourable. In some countries, as described in Chapter 8, prices are deliberately set with reference to prices in other countries (e.g., Bulgaria, The Netherlands, Canada). In such countries, a high proportion of patented drug are thus negotiated, rather than simply manufacturer-set [22].

Even developing countries have access to some important sources of data showing the prices at which reliable medicines can be obtained across the world. A vital tool is the "MSH International Drug Price Indicator Guide", published regularly by Management Sciences for Health in Boston, MA, in collaboration with WHO, and available both in printed form and through the Internet. This shows for most essential medicines a range of dependable sources and the prices which they charge [6]. A country can also determine the prices at which international agencies such as UNICEF have succeeded in purchasing certain types of medicines and can set out to attain comparable prices. A further alternative is to purchase medicines through international low-cost supply agencies which provide a guarantee of quality.

Once a drug has entered a national market, availability of pricing information remains equally important. Policy-makers, health professionals, wholesalers, retailers and distributors, and consumers all need complete, accurate and up-to-date information on drug prices. For example, in India, Pakistan and other parts of Asia, the requirement that the maximum retail price be printed on drug packages means that the system not only regulates retail prices, but also provides price information directly to the consumer [15]. Price information is increasingly being included in national drug formularies, in therapeutics manuals and clinical guidelines. Price information may be given as relative price levels (such as the relative price bands in the *British National Formulary* and the French *Dictionnaire Vidal*), as price comparison bar charts for selected therapeutic categories (such as the Kenyan or Zimbabwean *Clinical Guidelines* or the Dutch *Pharmacotheapeutic Compass*), or simply as the current price for each drug.

3.3. The question of differential pricing

It is clear that, viewed globally, the burden of drug costs should not be equally shared between rich and poor nations; the only fair approach is for a country to pay the prices which it can reasonably afford and no more. Drug firms have always to some extent adjusted their prices from one country to another, but generally only to a minor extent and primarily with the intention of setting for each country the highest prices which the market will bear [8]. This traditional concept of “tiered pricing”, as it is known, is not helpful in developing a constructive approach for developing countries, since it tends to shift prices upwards rather than downwards. WHO has called for a more systematic form of “differential pricing”, structured so as to ensure that much lower prices are charged in countries with a weak economy. There are some indications that the appeal for change is being heard by parts of the research-based pharmaceutical industry, though consumer critics have argued that the response is too meagre. A gesture by five international pharmaceutical manufacturers to cut prices of antiretrovirals for Sub-Saharan African countries at all events reflects industry recognition that current pricing of patented medicines is unfair for low-income countries and politically unsustainable [23]. In fact, the industry has made it clear on several occasions that differential pricing is an acceptable mechanism, provided there is no parallel importing back to the higher priced markets. Such mutually satisfactory arrangements have been achieved, for example, with vaccines (see below) and with oral contraceptives sold through international agencies at a tiny fraction of their normal prices [8].

One might add that the more general concept of “equity pricing”, which WHO has advocated [23], is not essentially different to that of “differential pricing”. To attain prices which are equitable for a given population and compatible with equity one will necessarily have to adjust them to the wide variations in income which exist between countries, and this will involve marked differentiation. The concept of differential pricing is illustrated in Fig. 5.

3.4. Exploiting the use of generic medicines

Means to ensure that low-cost generic (off-patent) medicines are used to the greatest extent possible have been reviewed in Chapter 11. Most of those methods can be used to a greater or lesser extent in developing countries. It is particularly crucial to ensure that the generic medicines on sale are of assured quality and that the population is emphatically made aware of this fact; too often people who cannot afford high prices have nevertheless paid them in order to secure a branded speciality in the belief that it is in some way superior to the generic equivalent.

3.5. Large-scale competitive procurement

For a large pharmaceutical firm, it is hardly rewarding to negotiate extensively with a mass of small procurement agencies, each requesting better prices yet each offering only a minuscule market. One important step is to bundle the procurement process into larger units. Within a country, for example all hospitals may do well to procure jointly. Public procurement for an entire public health service should as far as possible be centralized nationally; decentralization of government administration may be a laudable aim, but if it means that drug purchasing will henceforth be handled by twenty or more inexperienced and small provincial bodies the quality of procurement can hardly be expected to improve. A remarkable price reduction was experienced in Delhi State when the annual needs of approx. 300 medicines for hospitals and health centres, were pooled and procured in bulk. Even an entire nation may represent only a tiny market for a multinational corporation, and there can be very good reason for several small countries to

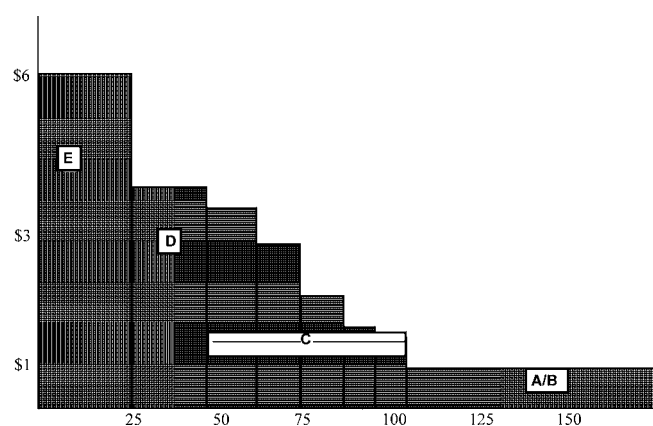


Fig. 5. Schematic example of differential pricing. Option 1: smaller amounts are sold in high priced markets (D and E), while Option 2: larger amounts are sold to low priced markets (A/B) and greater volumes can provide the same total revenues, though with lower profit margins, at a lower tiered price. The multiple bands for C reflect the fact that market forces will determine the price in these situations.

Table 2
Use of price controls in high and low-income countries

Countries	Sample size (# countries)	With price control		Without price control
		Limited	Substantial	
High-income	23	48%	52%	0%
Low-income	33	24%	55%	21%

act together in a pooled purchasing arrangement. Examples of pooled procurement are bulk purchasing mechanisms of the Maghreb countries; joint drug purchasing is also undertaken by the countries of the Eastern Caribbean and by the Gulf States [22].

While there is some place for price negotiations and closed tenders, by far the most successful means of obtaining fair prices is for a large purchasing agency to buy medicines through an open tendering system.

3.6. Price controls

Price controls are another important option for government intervention to adjust price levels with the intention of maximizing affordability or minimizing overall drug expenditures. Table 2 shows that this is a very commonly used option throughout the world [16].

Price controls involve not only the setting of the initial or current price of a drug, but also the regulation of price increases and sometimes also the power to reduce existing prices which have been found to be excessive. Controls may relate primarily to the prices paid to producers or importers, insofar as these are not kept in hand by a tendering system, or they may relate to the ultimate purchase price. In the latter case it will be necessary to obtain a grip on the margins earned throughout the drug supply system; distribution margins are important, not only because they often account for 50% of the consumer price of a drug, but also because the structure of distribution margins provides economic incentives for dispensing. Reduction and control of distribution and retail margins often needs to be better regulated than is currently the case [15].

The various forms of price control are further discussed in Chapter 3.

3.7. Prices of new essential medicines and vaccines

While the problem of prices needs to be tackled for all essential and useful drug items, there are two class of products for which a special effort is needed. The one comprises “new” essential medicines as defined as – important new medicines which represent a substantial advance in the treatment of major diseases yet which are still under patent and therefore expensive. The other class comprises vaccines, especially those used in national vaccination programmes.

For *new essential medicines* it is not acceptable for low-income countries and poor populations to pay the same price as the industrialized countries. The poor simply cannot be expected to contribute equally to research, marketing, and shareholder returns, especially as it is unlikely that the return will be used for drug research and development for neglected diseases; the prices will in any case render these vital items largely inaccessible. During 2000, the endeavour known as “Accelerating Access to Care and Treatment”, in which UNAIDS and other partners are involved, has stimulated discussions with five pharmaceutical companies to achieve “equity” or “differential” pricing of new essential medicines for low-income countries [20].

As the *vaccine* industry is a largely fixed cost business, increases in production scale and increased experience in production of a specific vaccine (the “learning curve”) can drive costs down. Thus, additional production volume has a value when sold at lower prices, even if the revenues per dose resulting from this marginal volume are low. Revenue per dose is, however, a more important driver of profitability. When new vaccines are produced, production costs have to be spread over a smaller volume, and thus prices are higher. Increasing volume can lower production costs and increase profits. New high-priced products have a limited market: if markets of low-income countries can be accessed as well, economies of scale can be increased [7].

3.8. Elimination of tariffs, duties and taxes

WHO, the World Trade Organization and other partners advocate the elimination of import duties (still over 30% in some countries) for essential medicines including HIV-related medicines, and the abolition of value-added and other national and local taxes (still over 20% of the final consumer price) for essential medicines [20].

3.9. The role of domestic production

WHO and other partners support local production of essential medicines, manufactured in accordance to good manufacturing practices (GMP), where this results in lower prices. This can be facilitated by voluntary licensing, transfer of technology by the originator companies, and other suitable mechanisms [15]. It must be recognized however that local production will not always result in lower prices and it may run into considerable problems where technical experience is lacking; establishment of a new production plant in a country where none existed before is a step to be undertaken only after careful consideration.

3.10. Application of TRIPS safeguards

Essential medicines are a public good and not simply just another commodity. Patents for pharmaceuticals should be managed in a balanced manner, protecting the interest of the patent holder yet safeguarding public health principles. Measures consistent with the TRIPS agreement which may be used under specific circumstances to reduce drug prices and increase access include prompt availability of

generic medicines through “early workings” (“Bolar provision”), compulsory licensing, and parallel importing [24]. These are specialized issues which cannot be dealt with in detail in this chapter, particularly since developments in the interpretation and application of TRIPS are still under way.

4. Conclusions

The challenge for governments of developing countries is to find a balance between the need to attain national health objectives, the effort to respond to the health needs of the population, the political climate, the capacities existing in the public and private health and pharmaceutical sectors, and the economic realities of these countries.

As the governments of developing countries seek to achieve their public health goals they will find it necessary to ensure equitable access to “old” and “new” essential medicines, probably using innovative approaches with which successful experience has been gained elsewhere. It is to be hoped that governments of developed countries will provide ongoing technical and financial assistance to the developing world in its effort to implement this facet of health policy. At the global level, too, suitable strategies in support of these efforts can be developed and endorsed so as to ensure a significant increase of access of essential medicines among the world’s poorest and most vulnerable populations.

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During recent decades, society has attached great importance to improved health, and has witnessed a fast rising demand for health care. The very rapid growth of expenditure on medicines is of particular concern and it has attracted considerable political attention, in part no doubt because it is a concrete issue which at first sight appears readily amenable to economic control.

Many member states have over the years approached the World Health Organization for advice or information on the feasibility of measures to control the growth of expenditure on medicines. Such calls for help led the Organization as early as 1983 to undertake a study under the title "Drugs and Money"; it culminated in a deliberately concise report, providing a critical overview of the effectiveness of older cost-containment schemes while also paying attention to innovative ventures. The report was widely used and repeatedly updated, and this is now its seventh edition.

This latest edition aims to provide policy makers and regulators with a compact and practical review of the various approaches that have been developed and tested to date in an effort to contain the overall costs of pharmaceutical services and drug treatment. The true art of good housekeeping in this field is clearly to ensure that drugs continue to benefit society wherever they can, while eliminating every form of waste of public funds. Although the title "Drugs and Money" may to some suggest otherwise, this book also addresses issues of the organization, standards and delivery of health care. Many regulations concerning the intrinsic quality of pharmaceuticals, the quality of prescribing and the proper use of medicines have been introduced over the last four decades, and their influence is complementary to that of measures designed primarily to have economic effects in this field.

Unlike earlier editions of "Drugs and Money", this volume devotes considerable attention to the special problems of developing countries and those where the economy is currently in transition.

ISBN 1 58603 334 4 (IOS Press)
ISBN 4 274 90582 9 C3047 (Ohmsha)
ISSN 0924-6479