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Trends in decision-making process for pharmaceuticals in Western European countries

A focus on emerging hurdles for obtaining reimbursement and a price

Abstract

Health care financing has become a topic on the political agenda in Western Europe in recent decades. For every government it has become a subject of continuous concern because the costs of health services and health care are an increasing important part of the collective burden of the economy. Most cost containment measures have relied on budgeting or price controls. Because those traditional central cost containment measures were only partially successful, due to lack of incentives, the health authorities in Europe started to establish incentives for efficient health care delivery by means of decentralisation of the health care decision-making process and the implementation of market mechanisms. Both traditional and recent containment measures focus especially on the pharmaceutical drugs sector in many countries. Recently there have been three parallel trends showing increasing data requirements at a central level, more decentralisation of the responsibilities and decision-making process and prescription restrictions. We address especially the increasing central data requirements and decentralisation of the pricing and/or reimbursement decision-making process. At a central level the demand is increasing for cost-effectiveness and budgetary impact data, which has already resulted in formal reporting requirements in some countries. The findings are based on the literature and expert opinion of local health policy experts in the various European Union countries, who co-authored this manuscript

Keywords

Health care costs · Cost containment · Reimbursement

Introduction

Health care financing has been a topic on the political agenda in Western Europe in recent decades. For every government it has become a subject of continuous concern because the costs of health services and health care are an increasing important part of the collective burden of the economy. There are a number of reasons, which may explain the increase in health care costs. The ageing of the population may be associated with an increase in morbidity and associated health care costs, although a recent study shows that population ageing may contribute much less to future growth of the health care sector than claimed by most observers. This study showed that costs may especially depend on remaining life time [1]. In addition to that health technology is also contributing to increases in health expenditures. In contrast to other economic sectors, new health technology scarcely reduces costs (e.g. personnel, energy), at least in the short term. Another reason is that the patient has become more knowledgeable. The asymmetry of information between physician and patient has become much less pronounced, because the patient has become more knowledgeable than in the past by means of better education and media. In addition the patient has become aware more demanding and is claiming maximum quality of life regardless of the costs. Because insurance is generally compulsory in the European Union, the patient is usually insured, and because third party payers pay the majority of the costs there is generally no direct demand control for a patient.

Every government is eager to control the increase in expenses by the implementation of central cost containment policies, which in particular relate to pharmaceuticals. For the most part these measures have relied on budgeting or price controls, including negotiated prospective budgets for hospitals, centralised negotiated budgets for ambulatory physicians including drug prescriptions, and limitations on payments

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for particular medications. Because traditional central cost containment measures were only partially successful, due to lack of incentives, the health authorities in Europe started to establish incentives for efficient health care delivery by means of decentralisation of the health care decision-making process and the implementation of market mechanisms.

Decentralisation

Most European health care systems, except that of Germany, have been based on the so-called Beveridge model, a central system of care consisting of public institutions financed by state budget. Local authorities councils have recently obtained increasing authority to implement policies and freedom to structure local health care organisation (e.g. Italy, Sweden) [2] (in Italy: Decreto Legislativo, 19 June 1999, no. 229). In France in 1996 a reform created the Agence Régionale d'Hospitalisation (ARH) and the Union Régionale des Caisses d'Assurances Maladies (URCAM). Their main rules are to organise the hospital supply according to a fixed budget and regional health care needs. They must also implement locally health care priorities that are fixed at a national level and monitor the quality of health care delivery [3]. While local health authorities in most countries usually receive funding from the central health authorities based on a per capita basis, in Italy and Sweden they can supplement this funding with local taxes and health service charges, which may vary locally depending on local budgetary needs (Decreto Legislativo, 19 June 1999, no. 229).

In Germany the principle of statutory social insurance is called the "Bismarck system". Main features of the system are the financing via contributions by employees and employers and a mix of service supply by private and public services. Although in Germany there are no formal layers below the state level (*Bundesländer*), statutory sickness funds are trying to implement local healthcare organisations, such as practice networks including hospitals.

Market mechanisms

A growing number of countries have recently adopted some form of purchaser-provider split, although the others have retained the more conventional budget setting structure. The basic idea is to create a demand side (purchasing agency) that is separate from the supply side (providers). The reforms split the system into purchasers and providers. For example, in the United Kingdom health authorities and general practitioner fundholders became purchasers, while the Trust hospitals and directly managed units became the providers. General practitioner fundholders are now grouped into primary care groups, which will become trusts (PCTs). Primary care trusts will control the whole budget (except for some specialist services); they will provide primary care and purchase hospital care and other services including drugs. Also in Sweden and Italy there are signals at local level of establishing purchaser-provider split by local health care councils. As stated, for example, in the two Italian laws on the "reordering of the National healthcare system" (Decreto Legislativo 30 December 1992, no. 502; Decreto Legislativo 7 December 1993, no. 517). In other countries, with the more conventional budget setting structure, market mechanisms may be limited to drugs only and especially hospital drugs. In France private (and also public) hospitals buy drugs through tenders. Private hospitals negotiate with the local sick fund payer according to their activities and receive a fixed budget per patients for drugs.

Other related strategies

The decentralisation of the health care decision-making process and the implementation of market mechanisms resulted in various other related strategies.

Shift to primary care

Throughout the 1980s and 1990s the trend has been away from hospital-based consultations and towards primary care. The function of the general practitioner has switched from a physician treating patients to a gatekeeper of the health care system, whose main responsibility is avoiding inappropriate optimal referring of patients to secondary care in order to save costs. For example, in Germany the so-called *Hausartzmodelle*, meaning that the family physician should navigate the patient through the system, emerged and to avoid hospitalisation out-patient surgery was encouraged through special contracts by sickfunds together with statutory health insurance physicians associations to induce a shift from inpatient to out-patient care. Further, health authorities have encouraged the development of practice networks and integrated care models integrating inpatient and out-patient care. The respective legal requirements have been implemented into social security laws in recent years (http://www.bmgesundheit.de/engl/healthcare.htm; German social security law, SGB 140a-h). Due to the legal framework of the German healthcare system these measures had only limited success up to date. On the other hand, a country such as France is still a pure fee-for-service country, and there is almost no barrier to any health goods. French citizens can access either specialist or hospital directly without any inputs from the general practitioner. In Denmark, for instance, in the past decade it was considered an improvement in quality of health services that the patient was allowed to choose the type of care, primary or specialised. However, a co-payment was introduced for those patients using directly specialised care. After some years of follow-up the results show that the majority of patients keep attending the primary care services and only a lower than 10% uses specialised care. This might be considered a compromise between freedom to choose by the patient and respecting the principles of cost containment.

Co-payment

The health systems of the Western European economies have generally offered universal coverage with a comprehensive benefits package. Recent financial pressures have prompted most countries to look for ways to limit public sector financial liability by limiting benefits and influencing the demand side of the health care market, which resulted in an increase of co-payment by the patient. The bulk of co-payment is limited to the ambulatory health care setting, especially pharmaceuticals, although in Germany and France there exists also co-payments for in-patient care (German social security law, SGB 31:39 V). The objective of co-payment is to establish financial incentives for patient's demand control, which in many countries fail be-

cause of complementary insurance for co-payments. In France most French citizens have complementary private insurance, which is paid both by the employee and the employer, at least in large companies. This complementary insurance covers a significant part of the patient co-payment left by the Sécurité Sociale [4].

Clinical guidelines/disease management

Clinical guidelines outline the proper care of medical conditions and performance of clinical procedures. The intended goal of guidelines is to reduce inappropriate care and to improve patient outcomes. In addition, these guidelines are potential tools for reducing the costs of health care and for improving medical education [5].

Pharmaceuticals

Pharmaceuticals expenditures have risen in Europe and the United States during the 1990s. In most countries pharmaceutical spending has reached 10–15% of the total health care budget (in some countries, such as Greece, Portugal and Spain, this proportion is higher than 20%; OCDE health data 2000). Both traditional central containment measures and the cost containment measures resulting from the above strategies (decentralisation/free market regulation) focus especially on the pharmaceutical drugs sector in many countries, as these constitute a health technology that is relatively easy to introduce and implement compared to other forms of care. Recently there have been three parallel trends showing increasing data requirements at a central level, more decentralisation of the responsibilities and decision-making process and prescription restrictions.

The objective of this manuscript is to give an overview of the current pricing and reimbursement environment for pharmaceuticals in Western European countries. We address especially the increasing central data requirements and decentralisation of the pricing and/or reimbursement decision-making process. The information was obtained from published literature, local published or available policy documents. A survey was conducted with local health policy experts in the key countries to validate the findings from the literature, add missing information and update the information, if necessary. The local health policy experts co-authored this manuscript and are involved in pricing and reimbursement issues in their domestic markets. We focussed on the key countries (United Kingdom, Germany, France, Italy and Spain), but also included relevant information from other countries (e.g. The Netherlands, Sweden and Denmark).

Traditional central managed policies

Pricing and reimbursement

Registration and pricing/reimbursement decisions are currently distinct processes: registration of a new drug is based on quality of manufacturing and efficacy/safety data from randomised clinical (phase III) trials and a product has market approval after registration. The drug is available on the market but does not have reimbursement status, and consequently the patient must pay for the drug alone. Therefore registration is only the first entry barrier for a new drug, which is followed by hurdles due to pricing and reimbursement procedures. Although it is difficult to disentangle pricing and reimbursement decisions, a recent overview by our group for Europe clearly indicated that reimbursement and pricing may be considered as two separate procedures: decisions are made by different bodies, different laws apply, different reporting data are required, and reimbursement and pricing are sequential decisions [6, 7, 8, 9]. For example, in France the Transparency Commission decides on reimbursement, while the price is negotiated with the Comité Economique des Produits de Santé (CEPS). An exception is Italy, where pricing and reimbursement are strictly related to, the Commissione Unica del Farmaco (CUF), which is the Italian drug regulatory agency, in collaboration with the Comitato Interministeriale per la Programmazione Economica (CIPE; a body of the Ministry of the Treasury [10].

Cost containment measures

Although there does not seem to be any systematic approach in selecting policies to curb the costs of pharmaceuticals, governments in general more and more have resorted to central demand and supply-oriented policies to limit drugs expenditures. An example of a supply-oriented policy constitutes direct price control, whereas a demand-oriented policy would imply the introduction of a limited list of reimbursable drugs (i.e. a formulary). Hence governments have opted for limiting demand as well as supply of pharmaceuticals available under public reimbursement schemes.

Drug pricing

Pricing of drugs is often limited by either price negotiation or price laws, which define an upper limit based on a reference price basket consisting of prices in neighbouring countries or a European average price, except for the United Kingdom, Germany and France. In the United Kingdom and Germany pharmaceutical companies are free to price their drugs that have received marketing authorisation. The only limitation is that medicines may only be sold at one price sold throughout the country. However, in the United Kingdom, pricing is constrained by pharmaceutical company's total profit in the domestic market, which can vary between 17% and 21% according to United Kingdom based research and development activity and exporting. France is a price state regulated country: unit price is negotiated with the Comité Economique des Produits de Santé on the basis of Amélioration du Service Médical Rendu (ASMR) and the drug budget impact (Décret du CEPS, 2000). In Italy both pricing procedures apply, which depend on registration: (a) price negotiation, which applies to any innovative drug approved by European Agency for the Evaluation of Medicinal Products (EMEA) or introduced by a mutual recognition procedure and (b) directly calculated price, by means of the so-called "European average", which applies when market drug authorisation is allowed directly from national government (Ministry of Health) instead of the European Agency for the Evaluation of Medicinal Products [10]. Pricing of inpatient drugs is less centrally regulated and corresponds more with a market model. Pharmaceutical companies are free to set drug prices, and drugs can be sold at different prices to various hospi-

tals based on a negotiation process. The governments do not intervene in regards to the price that is negotiated, although the results of the tender are deeply influenced by an out-patient price. Discounts can widely vary and better discounts are obtained for widely used drugs. Competition between manufacturers has the strongest influence on drug price negotiations, followed by the volume of sales and package deals. Because in most countries in-patient drugs are within the hospital budget, hospitals may not always be able to finance premium priced drugs. Central authorities or local health insurers have recently taken over financing of those drugs. Drugs are excluded from the traditional hospital budget and prescriptions are often limited to selected centres in order to control the number of prescriptions. An example is Remicade, an expensive drug for the treatment of severe rheumatoid arthritis, which requires day-care because of the intravenous route of administration. The use of this drug results in an average annual costs of 30,000 euros per treatment, which exceeds the budget of most hospitals. Dutch health authorities took over financial responsibility for this drug to guarantee it is available for the patients, especially because of shortage of Enbrel, an out-patient drug for the same indication.

Reference price system and co-payment

Drugs are usually grouped according to chemical structure and the reimbursement level depends on necessity of a treatment. Essential drugs may be fully reimbursed, while complementary drugs may be partly reimbursed, and non-essential drugs may be fully paid by the patient. Often usually a number of categories, including chronically ill, and pensioners do not have to pay co-payment for drugs. This system is called the reference price system, which is applied usually only to drugs when there are several brands with the same compound available [11, 12]. This system does not set drug prices; rather, it sets the reimbursement levels at which the sickness funds pay for each out-patient prescription drug (consumers pay the amount by which the product prices exceed the reimbursement levels). Drugs in each group are all reimbursed on a fixed amount. Reimbursement decisions regarding new innovative drugs will be based on judgement of a clinical benefit compared with standard therapy in the target patient population (indication). The judgement of the clinical benefit is based on traditional clinical outcomes derived from phase III clinical trials used for registration: efficacy, safety and quality. In addition other clinical criteria are taken into consideration: route of administration, or other relevant clinical information. When the evaluation of a drug is positive from a clinical point of view, the drug price has been the critical factor for final decisions on reimbursement until recently. The reference price system has two primary functions: first, to lower the prices of drugs by inducing price competition, and, second, to encourage greater use of generic drugs by making consumers pay a greater share of the cost of higher-price brand-name drugs. Patients usually can have co-payment for drugs refunded through additional private insurance. Therefore this demand-oriented policy is usually not an effective cost containment measure, because patients remain relatively insensitive to the co-payment system, when co-insurance is possible. There is usually no or limited co-payment for drugs supplied during hospitalisation. It is important to note that while we describe general mechanisms, that there is a wide variation across EU.

Positive and negative lists

There is an increasing trend to the development of positive and negative lists, which aim at reducing the number of reimbursement drugs as well as total spending on pharmaceuticals. The selection of drugs for a list is mainly on the basis of efficacy/safety parameters. At central level a positive list contains drugs which will be reimbursed, while drugs on a negative list (e.g. Black List in the United Kingdom and the former List 1B in The Netherlands) must be paid fully by the patient. The Black List contains drugs, which are not reimbursed, although licensed. These are mainly old and ineffective products for which better and cheaper alternatives are available. In the United Kingdom there is also a grey list of drugs for use in limited circumstances, for example, Viagra. In Germany there is an established negative list [social security law, SGB 34(3) V] which is technically updated by a federal committee (Bundesausschuss Ärzte/Krankenkassen). Further, the first draft of a positive list is due for submission on 30 June 2001, which is set up by a special committee (German social security law, SGB 33a V).

The increase in pharmaceuticals expenditures in Europe up to 10–15% of the total health care budget [4], shows that the traditional central cost containment measures were not sufficient to control the drug costs leading to drug policy reform, which is described below.

Current restructuring of drug policies

Recently there have been three parallel trends showing increasing data requirements at a central level, more decentralisation of the responsibilities and decision-making process and prescription restrictions.

Data requirements

Pricing and reimbursement have been based until recently on the traditional clinical trial outcomes (efficacy, safety and quality parameters) used for registration. We can distinguish various data requirements which all relate to the use of the drug in real daily practice, while the traditional clinical trial outcomes are only derived from randomised clinical trials.

Effectiveness

There is an increasing demand for effectiveness data. Efficacy and effectiveness are two different concepts. Both, however, have an impact on the effect of a drug. In the case of efficacy, the effect is examined under ideal conditions in a homogeneous group of patients, and usually with the assistance of intermediate (surrogate) end-points. Effectiveness data, on the other hand, offer a clearer picture of the actual value of a drug because the effect is examined under more realistic conditions using a more heterogeneous group of patients. This information about use in common practice also provides more insight into whether the aim of the treatment will ultimately be achieved. Effectiveness re-

search is therefore oriented towards definitive outcomes such as a reduction in morbidity and mortality. A recent Italian law allows phase III clinical experimentation (both randomized controlled trials and uncontrolled, observational studies) at present conducted only in hospitals and/or specialty clinics, to be conducted also in an out-patient setting. This kind of experimentation provides data from a large sample of population in a "naturalistic setting", therefore providing good insight into the "effectiveness" of the pharmaceutical technologies (SOLE 24 Ore Sanità, no. 3, 23–29 January 2001). In France the Transparency Commission considers the public health value of the drug, which is called an Amélioration du Service Médicale Rendu (ASMR), which may be considered as a comprehensive effectiveness measure.

Cost-effectiveness data by a health economic analysis

The fourth hurdle in drug development is the growing burden on manufacturers to demonstrate the cost-effectiveness of their products before acceptance for reimbursement or, less relevant, pricing, may have considerable consequences for all players involved. Health economic data should permit reliable, reproducible and verifiable insight into the effectiveness of a drug, the costs that will result from its use, and the possible savings that will be made compared with other drugs and/or treatments. Health economic studies are already being used for the reimbursement of new drugs in Australia and Canada. Those countries have official requirements for submission of health economic data since the early 1990s [13, 14]. There is currently a trend towards an increasing demand for health economic data in the decision-making process information in Europe and in several countries to formal reporting requirements now (the United Kingdom, Finland and Portugal) or in the near future (The Netherlands and Norway) [6,14]. This is also true in Italy. In fact, a recent provision (February 20001) by the Comitato Interministeriale per la Programmazione Economica (CIPE; the Ministry's Board of Economic Planning) claims that a new drug is admitted to reimbursement when its cost-effectiveness ratio is favourable in comparison to other drugs already admitted for the same indication, or it is useful to prevent and treat symptoms and pathologies not already treatable by others drugs (Delibera CIPE 1 February 2001, no. 3/2001). In France health economic data help at supporting premium price, as part of the negotiation process.

Budgetary impact data by a financial analysis

In addition to the cost-effectiveness of a new drug, reimbursement decisions will also be based on the budgetary impact of a new drug on the annual national health care budget, especially the impact of a new drug on the drug budget. Therefore the authorities are requiring an assessment of the impact of a new drug on the annual drug budget. For the financial analysis, data on the following subjects will be required: descriptive epidemiology (data on incidence and prevalence). The patient group that is indicated for the drug and the anticipated substitution effects (i.e. the extent to which the existing treatment will be replaced); the use of the drug (e.g., posology, length of the treatment), the price of the drug; the expected market share plus the variables that would facilitate or slow down the drug sales and the total treatment costs. On the basis of the cost-effectiveness analysis and financial analysis an advice can then be drawn up as to whether the drug should be reimbursed; examples include The Netherlands, United Kingdom and Italy (in Italy: Delibera CIPE 1 February 2001). For example, in Italy the recent Comitato Interministeriale per la Programmazione Economica (CIPE) provision (see above) specifies that the drug price is negotiated also on the basis of appropriate economic evaluations of the drug in its market and competition context. However, the budgetary impact analysis is not clearly defined and no formal guidelines exist, for example, it is not clear yet what is taken into account, drugs costs only or also other medical costs. In France the price is negotiated with the Comité Economique des Produits de Santé (CEPS) on the basis of the Amélioration du Service Médical Rendu (ASMR), but also incidence/prevalence of the disease, public health concern and drug budget in order to assess the budgetary impact (Décret du CEPS, 2000). In Spain the budget impact is also considered during the price and reimbursing negotiation. The royal decree 271/1990, which regulates these processes, requires a forecast of the sales as an element for the final decision.

Decentralisation and/or prescription guidelines

Financing prescription medicines in ambulatory care has been a central responsibility. The central authorities have recently begun often to shift the responsibility for development of prescription lists to the local authorities.

Decentralisation

The responsibility for financing prescription medicines in ambulatory care is moving from the central to local level (e.g. Sweden, The Netherlands, United Kingdom). For example, the Dutch government considers giving the local health insurers the responsibility for the purchasing process for drugs, which means that they will directly bargain and negotiate with pharmaceutical companies. In the United Kingdom drug financing is no longer a central funding mechanism. Primary care trusts now have "devolved" budgets and can set their own drug budgets. In Sweden from the beginning of 1998, the responsibility for financing prescription medicines in ambulatory care was transferred from the National Social Insurance Board (RFV) to the county councils over a 3-year period. Under the new structures local consumption patterns and total cost of medicines are more transparent to regional administrators and prescribers. As a result, treatment should be more responsive to local needs and cost containment measures should become more effective. Although the local authorities are becoming more involved in influencing the prescribers to reduce volumes and switch to cheaper drugs (supply side), decisions on a reimbursement status level and reimbursement price in general is still the responsibility of the central authorities.

Drug formularies

There is a tendency to shift the development of lists to local authorities leading to local lists. Formularies have been used

already by hospitals for in-patient drugs, but key actors in local health care (e.g. specialists, general practitioners, pharmacists and insurers) are now developing formularies for ambulatory drugs. In general drugs are added to the formulary when there are no similar drugs available. Drugs are substituted mainly when major clinical improvements and/or drug cost savings are expected. The use of expensive drugs is usually rationed by means of prescription guidelines or delivery restriction.

Prescription restrictions

While traditionally reimbursement decisions applied to the officially registered indication, which was usually a broad indication, authorities have recently been imposing restrictions on the claim made for the drug. These restrictions usually relate to follow a treatment protocol, to limit the prescribers or to limit the range of indications (United Kingdom, Germany and France). In Germany prescriptions are more and more restricted by the prescribing guidelines given by the federal committee of physicians and sickness funds (*Arzneimittelrichtlinien*). For example, these prescribing guidelines restrict drug therapy to the approved indications from clinical trials. The Bundesinstitut für Arzneimittel und Medizinprodukte (Federal Institute for Drugs and Medical Devices) tends to approve drugs only for indications which were part of the clinical trials. Specific to Italy is the issue of the so-called "Note CUF". This set of criteria for reimbursement of some selected active principles are specifically meant at reducing drug availability by identifying specific drug indications for which the drug is reimbursed. For example, ondansetron, granisetron and all 5-hydroxytryptamine type 3 antagonists are limited by Nota 57 to "prevention and treatment of nausea and vomiting in patients undergoing emetogenic chemotherapy", thus excluding all other potentially emetogenic indications (Decreto Ministero della Sanità, 22, December 2000). The narrowing of the indication especially depends on the efficacy, but also the results of the above health economic analysis and financial analysis may be taken into consideration, which may suggest that within the registered range of indications a further limitation of the field of application must be made from the point of view of cost-effectiveness and budgetary impact. In the United Kingdom the National Institute for Clinical Excellence (NICE) is producing clinical guidelines incorporating technology and economic results, which include specific advice on targeting drugs, although it is not legally binding.

Financial liability

Prescription guidelines may be also used to audit physicians in terms of quality assurance to determine whether these guidelines are being correctly followed. Financial sanctions may be imposed if the recommendations are not followed. Prescription behaviour (or prescriptions patterns) of physicians may be also be directly linked with financial liability. We may distinguish between budget and envelop responsibility, budget being individual and envelop being collective responsibility. In Germany physicians have a target budget for pharmaceutical expenditure and exceeding the budget may result in financial sanctions. This target budget is calculated by applying the so-called *Richtgrößen* per member or *Richtgrößen* per retiree multiplied by the number of treated members or retirees per quarter. The sum per quarter times four results in the yearly target budget. The *Richtgrößen* take criteria such as physician specialty and status (member, retiree) into account. In addition, some products and some indications are considered as 'essential' and exempted from these guidelines (*Praxisbesonderheiten*, *Wirkstoffausnahmen*), which means that they are not included in the total prescribing bill of the physician. In Germany the Kassenärztliche Bundesvereinigung (National Association of Statutory Health Physicians) and the leading *Krankenkassen* associations form a federal framework, the Bundesausschuss Ärzte/Krankenkassen, which is responsible for setting up and updating prescribing guidelines (*Arzneimittelrichtlinien*) which should guide the physicians prescribing behaviour with regard to economic viability. The introduction of these guidelines means that the physicians are individually liable for mal-compliance with these guidelines, and that this mal-compliance may result in financial sanctions. Through the creation of these guidelines for certain drugs, the Bundesausschuss can exercise control over physicians prescribing. In general, there seems to be a mix between prescribing guidelines (*Arzneimittelrichtlinien*) and physicians individual budgets based on *Richtgrößen*. In the United Kingdom the individual prescriber is monitored by hospitals and primary care trusts. "Overprescribing" is a problem only if budget constraints are broken. "Underprescribing" can become a political issue, for example, not following the National Institute for Clinical Excellence (NICE) guideline. Each trust must decide on prescribing policy: peer pressure is used to make individuals conform. In France groups of health care provider have their own envelop. In case they exceed the value of the "key-letter" might be reduced or its increase may be lower than inflation. In Spain during the past decade the position of primary care pharmacist has been created in several regions. This person is committed to develop recommended lists of save, effective and cheap drugs that are mailed to physicians, and also to advice prescribers. The pharmacist is also performing an ex post control of the type and budget impact of prescriptions and interviewing physicians to keep the expenditure in the established limits.

Clinical guidelines/disease management

There is a trend to development and implementation of clinical guidelines, which usually are only prescription guidelines for physicians. These guidelines usually contain a recommendation for prescribing generic drugs and encourage the optimal use of drugs. Through the creation of guidelines for certain conditions, the health care authorities can exercise control over physicians' prescribing. These recommendations are seen as an extension of the non-reimbursement list. However, as described above, most of the prescribing guidelines enforce the use of drugs in the approved indication instead of the optimal use of drugs. These prescribing guidelines should strictly be distinguished from clinical guidelines or treatment recommendations from specialty associations or opinion leader. In France the Agence Nationale d' Accréditation et Evaluation en Santé (ANAES) issues clinical guidelines. The Réference

Médical Opposable (RMO) is the official prescription guidelines for physicians (http://www.anaes.fr). The French guidelines are determined by a scientific committee who consider general themes (prescription, diagnostic tests, biology, surgery) and/or different pathologies. Included in these guidelines are regulations indicating what the physicians should or should not prescribe following a certain diagnosis. All drugs were revisited by the Transparency Commission to check again their public health value. The development of guidelines is usually a decentralised local process with involvement of representatives of physicians and local insurers. Another example is the United Kingdom; one of the objectives of the National Health Service is to promote rational prescribing amongst general practitioners. The Department of Health pays for general practitioners' subscription to the Drug and Therapeutic Bulletin, an independent publication from the Consumers' Association, which contains evaluations of treatments and pharmaceutical products. However, this is not always in line with the official guideline, for example Relenza.

In summary, we have three recent parallel trends showing additional data requirements at a central level, more decentralisation of the responsibilities and decision-making process and prescription restrictions.

Discussion

The objective of this contribution was to present an overview of the current pricing and reimbursement environment for pharmaceuticals. Financing prescription medicines in ambulatory care has been a central responsibility, which was based on the traditional clinical trial outcomes (efficacy/safety parameters) used for registration. Although there is large variety between the various countries, there are three related trends: decentralisation of the health care decision-making process, prescription restrictions, and additional data requirements. Decentralisation and prescription limitations are not independent processes: Central authorities often shift the responsibility for development of prescription lists to the local authorities. At a central level the demand for cost-effectiveness and budgetary impact data is increasing, which has already resulted in formal reporting requirements in some countries (e.g. The Netherlands). Although the most evident impact of health economic studies is expected for central reimbursement audiences, evidence for the use of health economic studies by other audiences is expected to increase (e.g. patients, hospitals, insurers, formulary committees) [16]. We already notice that this recent decentralisation process is adopting some of the economic criterion to better inform medical decisions on prescription. For instance, in Spain that probably is the most decentralised EU country, a new type of staff has been incorporated, in some regions, for primary care: the primary care pharmacists. These are committed to report on safety, efficacy and effectiveness of drugs as well as on the prices and rough cost-effectiveness values. Their recommendations are published and handed out to primary care physicians. A close follow-up of the prescriptions is carried out and an evaluation of the outcomes after the pharmacists reports are implemented. This approach to prescription has contained costs where applied, and it is observed by other Spanish regions with interest.

Below we address first general potential limitations of decentralisation and market mechanisms in the health care market and then focus on drug-specific issues.

We distinguish two potential limitations of decentralisation and market mechanisms in the health care market limitation. Firstly, in the current free market developments health care remains free at the point of delivery or is paid for indirectly through insurance premiums. Although there is an increase in co-payment, private health insurance is taken out for those services that are not provided free of charge. Hence customers will not shop around for the lowest price, and consequently there is still little pressure on producers to keep prices down. Instead, they may compete with one another by providing more attractive services, which may in fact lead to price increases rather than reductions; this is referred to as non-price competition. Secondly, the decentralisation of the health care decision-making process by broadening the role of health insurers from financial controllers to purchasers increased competition by increasing the number of buyers from one central body to more potential buyers. There are two recent developments which may inhibit the favourable consequences of this competition. Firstly, the increasing opportunities of administrative databases may lead to mergers between purchasers: The use of databases allows management at a larger scale (e.g. larger number of patients) and may be beneficial only when benefitting from economies of scales. As a consequence mergers may lead to an oligopoly inhibiting the intended efficiency of purchaser-provider split.

On the other hand, the use of clinical guidelines outlining proper care will increase the homogeneity of the health care services, and therefore the products can compete on price and be comparable with one another. The increasing information technology (e.g. decision support tools for physicians) may facilitate implementation of more standardised treatment from prescription guidelines to more comprehensive disease management. The use of evidence based medicine will increase the consensus in clinical decision, increase the homogeneity of health care and improve the assessment of appropriateness and quality of care. The increasing information technology (e.g. databases) may contribute to data collection of evidence-based data associated with different treatments.

In addition to the above general trends, there are other drug-specific developments, which need to be considered. While registration procedures for Europe are becoming centralised with central European decision-making by the European Agency for the Evaluation of Medicinal Products (EMEA), pricing and reimbursement decisions are still national affairs. Although opponents argue that drug registration and reimbursement must be kept strictly separate, there are signs that economic evaluation may become part of the registration dossier in the near future. Secondly, harmonisation of guidelines and further moves towards Europe-wide decisions on drug pricing and reimbursement are likely, given the increasing interdependency of European markets and regulatory authorities. A consequence is that the role of the central authorities will further decrease. On the one hand, centralisation of pricing/reimbursement decisions shifts to the

European level, and, on the other hand, decentralisation of the other health care decisions (e.g. prescription restrictions, local formularies, clinical guidelines) shifts to the local level. However, the second part of this conclusion needs to be considered with prudence because the local sickness funds are financed differently in the various European countries, which will affect the option of the decentralised decision process in each country.

Another consideration is how cost-effectiveness data could be used at a central European level for pricing and reimbursement decisions. A key principle in health economics is that cost-effectiveness is based on the country-specific health care setting: local treatments patterns and local financing system determine the clinical and economic outcomes. Consequently a European cost-effectiveness ratio (e.g. 10,000 EURO per quality-adjusted life year) cannot be determined or is meaningless. Hence the use of health economic data at a central European level needs an in-depth examination. Some other important difficulties for European pricing and reimbursement are drug price differences between countries and parallel import. Furthermore, cost-effectiveness needs to be a particularised not only at the country level but also at the regional level. The reason is that once there are decentralised budgets, regions have political power to adopt decisions that consider more efficient given their health policy, costs (for instance, salaries are not equal across Spanish regions), patient management and epidemiological conditions. Trying to foresee the future, due to international trade and patent agreements, similar pricing will become a more and more common policy throughout EU countries, but reimbursement policies – and hence adaptation of cost-effectiveness studies to inform on reimbursement and prescription practices –will have to be tailored more specifically to a difficult range of medical decisions.

Finally, we address the option of temporary reimbursement, which is being considered by Dutch and French authorities. Health economic evaluations consider efficacy and especially effectiveness. However, effectiveness data are usually not available at time of reimbursement procedures. Therefore temporary acceptance of an innovative drug to the reimbursement package might be considered. A conditional acceptance would permit initial decision-making on reimbursement based on the cost-effectiveness of the new drug derived from modelling data, followed by validation through subsequent prospective data collection. This would minimise the logistical and methodological concerns related to current policy. It would also reduce the concern of industry that health economic evaluation guidelines would delay product launch, shorten the period of useful patent life and the return on research and development investment. New drugs would be made available more quickly if prospectively data collection were not required prior to reimbursement. On the other hand, removal of a drug from a reimbursement package after additional prospective data were evaluated might have ethical concerns and lead to some social unrest. Regardless of the issue of temporary reimbursement there will surely be a need for collection of real-life data after the introduction of a new expensive drug, which accords perfectly with the concept of evidence-based medicine. The principle of evidence-based medicine is that clinical encounters should be supported by scientific conclusions based on data as much as possible.

Although the objective of this manuscript is to address the increasing central data requirements in the pricing and/or reimbursement decision-making process, the decision will be at least partially political. First, guidelines prescribe proper execution of health economic evaluations but not cut-off points for approving reimbursement. The decision about how much society will pay for increased effectiveness is political. Second, the weight of all data (e.g. data of the health economic evaluation and the financial impact analysis) in the decision-making process is currently not defined. Therefore we may conclude that the decision-making must become more transparent for a successful implementation of the new drug policies.

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