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Principles and methods

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HOW TO APPLY PHARMACOECONOMICS IN THE HOSPITAL PHARMACY



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Hospital pharmacists increasingly use pharmacoeconomics, for example, to assist with the profiling of medicines for inclusion in hospital formularies. Factors are discussed which influence the application of pharmacoeconomics from the perspective of the hospital pharmacist.

In recent years the opportunities for hospital pharmacists to be involved in pharmacoeconomics have grown, however, these new opportunities have been paralleled by an increasing heterogeneity in defining pharmacoeconomics. On one hand, the ‘core’ of pharmacoeconomics is generally agreed among healthcare professionals and essentially includes combined analyses of costs and outcomes for drugs and medical devices, decision-making in the area of reimbursements and cost-effectiveness profiling before inclusion in hospital formularies. On the other hand, there are differing views on the ‘contents’ of pharmacoeconomics. These are mainly concentrated on ancillary activities such as pharmacoepidemiologic studies with little or no emphasis on costs, economic studies with no assessment of outcomes, production of standardised in-hospital reports aimed at consumption monitoring and the generalisability of studies beyond their particular setting or country.

The focus here is mainly on the ‘core’ activities in pharmacoeconomics from the perspective of the hospital pharmacist. Since numerous factors can strongly influence the degree to which pharmacoeconomics can be applied by hospital pharmacists and the strategies of its application, five of the main aspects are discussed in detail.

VALUE-BASED PRINCIPLES

In relation to drugs and medical devices, the terms ‘cost-effectiveness’, ‘pharmacoeconomics’, ‘health-technology assessment’, ‘value-based strategies’, and ‘value for money’ have essentially the same meaning. Although subtle differences do exist between these terms, they have a more formal impact than a practical one. The number of countries where regulatory agencies

systematically use pharmacoeconomics is rapidly increasing, e.g. Australia, Canada, Finland, The Netherlands, New Zealand, Sweden and UK. However, many Western countries do not use any such approach [1]. The strategy employed by agencies which do not use ‘value for money’ generally relies on national agreements of a purely commercial nature made between the national health system and pharmaceutical manufacturers. Of course, historical data are the driving force in setting these types of agreements, generally on a yearly basis, e.g. the old Pharmaceutical Pricing Regulation Scheme in England [2] or the recent *Patto per la Farmaceutica* in Italy [3]. On the other hand, these countries and particularly Italy have tried to place the emphasis on appropriateness and information, rather than on cost-effectiveness, to better regulate pharmaceuticals.

IN-HOSPITAL CONSUMPTIONS OF INDIVIDUAL PATIENTS

Hospitals are typically where innovative drugs or devices are first used. Therefore, patients who receive these treatments in the hospital setting are the usual source of information from which to determine the benefits of the innovation. Unfortunately, in the hospitals of most European countries the resource use is not systematically traced at the level of individual patients mainly because, at best, the hospital electronic systems can only register data at ward-level. The absence of information technology to track and trace the in-hospital consumption of individual patients dramatically hampers the conduct of economic studies, e.g. naturalistic economic studies, based on the collection of individual data on resources use. Of course, this drawback applies to a lesser extent in countries where hospital unit-dose dis-

The principle of value for money can take different forms in different countries.

tribution systems are employed and electronic patient charts are widespread.

VALUE-BASED TOOLS

Over the past years, differentiating between value-based tools and the threshold adopted for their use has often been neglected by the technical literature. In fact, the advantages and disadvantages of the value-based tool have been frequently confused with those resulting from the threshold of pharmacoeconomic acceptance chosen to apply the value-based tool.

One such example comes from the UK, where reimbursement of some innovative anticancer agents, e.g. bevacizumab and cetuximab, has been restricted more than in other European countries. Bevacizumab has been assessed by the National Institute for Clinical Excellence through a standard cost-effectiveness analysis. The assessment was based on data from two different bevacizumab studies. The first investigated the effect of irinotecan, 5-FU and leucovorin (IFL) with and without the addition of bevacizumab. The cost per quality-adjusted life year (QALY) was calculated as GBP 88,364 (Euros 111,264) for bevacizumab combined with IFL compared with IFL alone. The second study investigated the effect of 5-FU and leucovorin (5-FU/LV) with and without bevacizumab. The cost per QALY gained for bevacizumab combined with 5-FU/LV was GBP 56,628 (Euros 71,321) compared with 5-FU/LV alone. Both results exceeded the threshold set by NICE (GBP 30,000 (Euros 37,790) per QALY gained) and consequently this drug was not approved for reimbursement by the National Health System [4].

Detractors of the value for money approach have claimed that this system has therefore been responsible for denying bevacizumab to patients. On the contrary, the value-based approach had actually little or no responsibility for this decision, which was instead the direct result of the threshold of pharmacoeconomic acceptance set at the conservative level of GBP 30,000 (Euros 37,790) per QALY gained [5].

CONVERSION TO QUALITY-ADJUSTED SURVIVAL GAINS

One critical factor in the application of pharmacoeconomics is that, in the great majority of cases, this discipline requires that all clinical benefits are expressed as either a survival gain (units of measurement: months or years of life) or a quality-adjusted survival gain (units of measurement: quality-adjusted life years or QALYs). Handling benefits this way is the prerequisite for the subsequent calculation of the cost per QALY gained. Since standard clinical studies do not generally express the clinical benefits as QALYs gained, pharmacoeconomic analyses require that benefits are converted from their original measurements into QALYs. This conversion raises a large number of questions in the application of pharmacoeconomics, which, at the same time, is also the main challenge that both physicians and pharmacists must face to appropriately employ value-based principles.



It is often worthwhile to describe an example of the conversion of the clinical benefit into an economic countervalue. Left ventricular assistance devices prolong survival in end-stage heart failure. One trial published several years ago [6] showed that median survival was 14 months in the experimental group versus five months in the control group (survival gain = nine months). Since, according to the most widely used threshold for European countries, every year of life gained can be valued at Euros 50,000 and every month at Euros 4,200, a gain of nine months per patient translates into an economic countervalue of Euros 4,200 x 9 = Euros 37,800. Thus, it can be concluded that this artificial heart can be 'good' value for money and the device may therefore be introduced into the hospital formulary, provided that its cost remains less than approximately Euros 40,000.

NEW PERSPECTIVES

It is increasingly apparent that the principle of value for money can take different forms in different countries, particularly when it is used for handling the complex issue of drug reimbursement. The 'traditional' cost-effectiveness approach (Case A), wherein decisions proceed according to the scheme described previously, is the one most frequently used in the practical application of value-based reimbursements. Under

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these circumstances, the effectiveness data for the innovative treatment are first analysed to determine a reliable estimate of the incremental benefit in comparison with the previous treatment, e.g. mean survival gain = six months per patient. It should be noted that the average is therefore drawn on the side of effectiveness, e.g. an average gain of six months per patient can result from 50 non-responders who gain nothing in terms of survival plus 50 responders who gain 12 months each. Then, the average magnitude of the (incremental) benefit is converted into an economic (incremental) countervalue. For example, if each month gained is valued at Euros 4,000 according to the accepted threshold, the (mean) survival gain of six months per patient translates into the decision that this benefit can be valued at Euros 24,000 per treatment (irrespective of whether the individual patient who receives this innovative treatment is a responder or a non-responder).

The principle of value for money can, however, find a second and different type of application, which is generally referred to as 'risk sharing' or 'payment by results', or Case B in this context. This second approach [7] has been employed less frequently, but recently some regulatory agencies, e.g. AIFA in Italy, have been using it to a greater extent. Under these circumstances, no average is drawn on the side of effectiveness. Instead, all patients are assessed individually using an all-or-none classification, e.g. responder versus non-responder where, for example, each responder gains 12 months while each non-responder gains none.

The outcomes are then individually converted into an economic countervalue, e.g. Euros 48,000 for responders versus Euros zero for non-responders. The risk-sharing policy agrees to pay Euros 48,000 for each responder and nothing for non-responders (alternatively, according to some modifications of the risk-sharing approach, non-responders are initially paid at Euros 48,000 each, but then this amount of money is requested from the manufacturer as a pay-back for each non-responder). Therefore, if there are 50 responders and 50 non-responders, drawing the average of the 100 individual economic countervalues (50 cases valued at Euros 48,000 plus 50 cases valued at Euros zero) gives the same result as in Case A (maximum 'acceptable' expenditure = Euros 24,000 per patient).

The approach according to Case A is particularly suitable for circumstances where the clinical evidence is clear, therefore, the national health system and the manufacturer are willing to share the same expectation about the treatment outcome. The application of the economic agreement can thus be prospective. In contrast, the approach according to Case B is

suitable for circumstances where the clinical evidence is not complete, and so the national health system and the manufacturer tend to have different expectations about the treatment outcome. The controversy can therefore be solved by adopting this 'payment by results' system wherein the value for money principle is applied retrospectively.

In Italy, the national regulatory agency (AIFA) has recently been favouring the 'payment by results' system, at least for certain innovative antineoplastic agents. The first practical implementation of this has assigned a key role to hospital pharmacists. In fact, a national website to handle these drugs has been constructed by AIFA where individual patients are introduced in real time by oncologists and where hospital pharmacists introduce, in real time, the data of the treatments administered to the patients. Therefore, Case B could be seen as an excellent approach for handling the cost of expensive but poorly documented medical devices.

CONCLUSION

Pharmacoeconomic principles and policies play an important role in the selection of drugs or medical devices for use in hospitals or inclusion in the hospital formulary. As such a number of topics which have recently been a matter of lively debate, particularly in the setting of hospital pharmacies.

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