PHARMACOECONOMICS SHORT OVERVIEW AND PERSPECTIVES IN BOSNIA AND HERZEGOVINA

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ABSTRACT

Pharmacoeconomics is a sub-discipline of health economics, which itself is a relatively new science, formerly appearing in the scientific literature since the 1960s. Pharmacoeconomic studies weigh the cost of alternative drugs and drug regimens against the outcomes they achieve to guide decisions and policies about which drugs should be used in general or which drugs should be paid for by the government or other payers. The importance of pharmacoeconomic information to healthcare decision makers will depend upon the viewpoint from which the analysis is conducted. Pharmacoeconomics is needful in pharmaceutical industry, government, and in the private sector for comparing various cost consequences. In order to perform, apply in practice and understand pharmacoeconomic studies it is crucial to have solid education in this field, which could be provided through pharmacy faculties’ curricula.

Key words: pharmacoeconomics, health economics, pharmacoepidemiology, pharmacist education, social pharmacy

SAŽETAK

Farmakoekonomika je poddisciplina zdravstvene ekonomike, i predstavlja relativno novu naučnu disciplinu koja se u literaturi pojavljuje od 1960. godine. Farmakoekonomskie studije mjese troškove alternativnih terapija i sihode koji se dobivaju, a u cilju donošenja odluka i politika o finansiranju lijekova od strane vlada ili drugih platioca. Važnost farmakoekonomskih informacija za donosioce odluka u zdravstvu ovisi o perspektivi iz koje je analiza rađena. Potreba za farmakoekonomikom ima farmaceutska industrija, vladin i privatni sektor, prilikom poređenja različitih troškova i posljedica. U cilju provođenja, praktične primjene i razumijevanja farmakoekonomskih studija od ključnog značaja je edukacija na ovom polju, a koja može biti provedena kroz programe farmaceutskih fakulteta.

Ključne riječi: farmakoekonomika, zdravstvena ekonomika, farmakoepidemiologija, edukacija farmaceuta, socijalna farmacija

INTRODUCTION

Health care funders (governments, social security funds, insurance companies) are struggling to meet rising costs in health care. They make many efforts to contain drug costs, by price negotiation, patient co-payments or dedicated drug budgets, as well as other tools for cost control, including restricted access or delayed market access to medicines, which is the case in low or middle income countries.1 Given the limitations on healthcare resources, there is increased interest in assessing the value for money, or economic efficiency, of healthcare treatments and programs. This is achieved through economic evaluation, in which the costs and consequences of alternative treatment strategies are compared.2 Pharmacoeconomics is a sub-discipline of health economics, which itself is a relatively new science even economic interest in drug and other treatments of health problems is much older. The term pharmacoeconomics was introduced in 1986, at meeting of pharmacist in Toronto, Canada, when Ray Townsend from the Upjohn company, used the term in presentation. In addition, Ray and few others performed studies since the early eighties...
using the term pharmacoeconomics within the pharmaceutical industry. Pharmacoeconomics, the description and analysis of the costs of drug therapy, can be defined as the branch of economics that uses cost-benefit, cost-effectiveness, cost-minimization, cost-of-illness and cost-util-ity analyses to compare pharmaceutical products and treatment strategies required for the patients.

As it is already mentioned, rising costs of medication is present all over the world. Similar pattern can be found in Bosnia and Herzegovina as well, even some measures by governments and health care authorities in Bosnia and Herzegovina has been taken in last four years. Pharmaceutical expenditure in Bosnia and Herzegovina increases in last few years, as it is shown in Figure 1, and based on annual report on import and trade of medicines issued by Agency for medicines and medical devices in Bosnia and Herzegovina.

**Figure 1.**

Trends in medicines utilization in Bosnia and Herzegovina

<table>
<thead>
<tr>
<th>Year</th>
<th>Foreign producers (BAM)</th>
<th>Domestic producers (BAM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>380.156.195</td>
<td>382.98.475</td>
</tr>
<tr>
<td>2010</td>
<td>424.314.495</td>
<td>410.33.110</td>
</tr>
<tr>
<td>2011</td>
<td>424.842.094</td>
<td>477.01.611</td>
</tr>
<tr>
<td>2012</td>
<td>557.033.055</td>
<td>537.98.021</td>
</tr>
<tr>
<td>2013</td>
<td>438.557.453</td>
<td>481.6.244</td>
</tr>
</tbody>
</table>

**NEED FOR PHARMACOECONOMICS**

Pharmacoeconomics studies had been performed within the pharmaceutical industry since the early eighties and today pharmacoeconomics research is a flourishing industry with many practitioners, a large research and application agenda, several journals and flourishing professional societies including the international society for pharmacoeconomics and outcomes research. Basically the pharmacoeconomics is needful in following manner;

- In Industry- Deciding among specific research and development alternatives.
- In Government- Determining program benefits and prices paid.
- In Private Sector- Designing insurance benefit coverage.

Australia was the first jurisdiction to use pharmacoeconomics studies as part of decision making processes for new drugs. Since 1993, economic analysis has been a requirement in the information submitted by manufacturers on whether new drugs go on the national formulary, ensuring that the drug will be reimbursed in the Australian healthcare system. Following Australia’s lead, several other jurisdictions, including Canada, New Zealand, Norway, Finland, Sweden, and Scotland (in the UK) request economic data as part of their formal decision making procedures for new drugs. In several other jurisdictions, including England, Germany, Hungary, the Netherlands, and Portugal, pharmacoeconomics studies are used, but only for selected new drugs. Alternatively in England, the National Institute for Health and Clinical Excellence (NICE) only requests an economic study if the new drug is likely to have a major impact on the NHS, either because it represents a “breakthrough” in therapy, or because it has a much higher acquisition cost than existing medications for a given medical condition. Finally, in several jurisdictions pharmacoeconomics analyses are not formally required, but are used by manufacturers and decision makers on a voluntary basis, like it is the case in USA, Denmark, France, and Italy.

Pharmacoeconomics criteria as obligatory part of reimbursement dossier is also introduced in Federation of Bosnia and Herzegovina since 2011, even not applicable in full form, and with many misunderstandings due to lack of educated professionals in this field who could in a first place review and assess submitted studies. Use of pharmacoeconomics studies and criteria in decision making among key decision makers in Bosnia and Herzegovina have been researched by a group of authors and showed that decisions are not made on full pharmacoeconomics studies.

**METHODS OF PHARMACOECONOMIC EVALUATIONS**

As it is mentioned and quoted in definition of pharmacoeconomics, two parts of pharmacoeconomic...
nomic equation are cost and outcomes of the treatment.

**Costs**

Costs involved in pharmacoeconomic evaluation can be mainly divided into financial cost (mandatory cost) and economic cost (resource for which no mandatory payment is made) opportunity cost is the benefit foregone when selecting one therapy alternative over the next best alternative. Economic evaluation therefore represents an essentially symmetrical framework which draws up a balance sheet to compare the costs and benefits of drug therapy. The 'cost' arising from drug therapy relates not to the price paid for a drug, nor even all monetary costs related to its use, but incorporates all the implications of drug therapy including time lost from work and distress.

Based on this, costs in pharmacoeconomics can be categorized as direct (medical and non-medical) indirect and intangible costs.

**Direct medical cost**

This is what is paid for specialized health resources and services. It includes the physician's salaries; the acquisition cost of medicine; consumables associated with drug administration; staff time in preparation and administration of medicines; laboratory costs of monitoring for effectiveness and adverse drug reactions.

**Direct non-medical cost**

This includes cost necessary to enable an individual receive medical care such as lodging, special diet and transportation; lost work time (important to employers) such as acute Otitis media in pediatric patients with professional parents who lost work time during the treatment of their kid.

**Indirect costs**

This is the cost incurred by the patient, family, friends or society. Many of these are difficult to measure, but should be of concern to society as a whole. This includes productivity loss in the society; unpaid care givers; lost wages; expenses of illness borne by patients, relatives, friends, employers and the government and; loss of leisure time.

**Intangible costs**

These are costs related with the patient's pain and suffering; worry and other distress of the family members of a patient; effect on quality of life and health perceptions. For example patients of rheumatoid arthritis, cancer or having terminal illnesses in which quality of life is suffered due to adverse reactions of the drug treatment. These are difficult to measure in monetary terms but represent a considerable concern for both doctors and patients. Quality adjusted life year (QALY) is one method by which intangible costs can be effectively integrated in PE analysis.

**Outcomes**

The second fundamental component of a pharmacoeconomic study is outcomes. What is the effect of alternative drug therapies on disease progression, survival, quality of life?

In assessing outcomes, it is also important to take into account both positive and negative outcomes. Positive outcome is a measure of the drug's efficacy. Negative outcomes include side effects, treatment failure, and the development of drug resistance. Outcome (benefit) measurement aims to be equally comprehensive by incorporating all of the impacts upon the patient's life that arise as a consequence of drug therapy. The benefits derived from an intervention might be measured in:

- 'Natural' units-e.g. years of life saved, strokes prevented, ulcers healed etc.
- 'Utility' units-measuring changes in a patient's satisfaction, or sense of wellbeing in an attempt to evaluate the satisfaction derived from moving from one state of health to another as a consequence of the application of drug therapy.

Such utility measurements are frequently based upon some measurement of quality of life. Many different methods have been proposed to measure quality of life based upon widely different techniques and value systems.

The Quality Adjusted Life Year (QALY) is a summary of quality and quantity of life which attempts
to construct a single summary measure of quality of life.\textsuperscript{17}

\textit{Methods of pharmaco economic evaluations}

There are basically 4 categories or types of pharmaco economic studies. These are presented here in order of detail,

1. Cost-minimization analysis (CMA)
2. Cost-effectiveness analysis (CEA)
3. Cost-utility analysis (CUA)
4. Cost-benefit analysis (CBA)

\textit{Cost-minimization analysis (CMA)}

This involves measuring only costs, usually only to the health service, and is applicable only where the outcomes are identical and need not be considered separately. An example would be prescribing a generic preparation instead of the brand leader (lower cost but same health outcomes).\textsuperscript{18} This form of evaluation is very easily understood and widely applied by doctors. However it cannot be used to evaluate programs or therapies that lead to different outcomes.

\textit{Cost-effectiveness analysis (CEA)}

The term cost effectiveness is often used loosely to refer to the whole of economic evaluation, but should properly refer to a particular type of evaluation, in which the health benefit can be defined and measured in natural units (e.g. years of life saved, ulcers healed) and the costs are measured in money. It therefore compares therapies with qualitatively similar outcomes in a particular therapeutic area.

For instance, in severe reflux esophagitis, we could consider the costs per patient relieved of symptoms using a proton pump inhibitor compared to those using H2 blockers. CEA is the most commonly applied form of economic analysis in the literature, and especially in drug therapy.\textsuperscript{19}

It does not allow comparisons to be made between two totally different areas of medicine with different outcomes.

\textit{Cost-utility analysis (CUA)}

This is similar to cost effectiveness in that the costs are measured in money and there is a defined outcome.\textsuperscript{20} But here the outcome is a unit of utility (e.g. a QALY).

Since this endpoint is not directly dependent on the disease state, CUA can in theory look at more than one area of medicine, e.g. cost per QALY of coronary artery bypass grafting versus cost per QALY for erythropoietin in renal disease. In practice this is not so easy since the QALY is not a well-defined fixed unit transferable from study to study. We should be particularly wary of attempts to draw up league tables of QALYs to allow comparisons between ranges of therapies. The values in such tables have usually been derived at different times and in different ways and are not comparable.

\textit{Cost-benefit analysis (CBA)}

Here, the benefit is measured as the associated economic benefit of an intervention (e.g. monetary value of returning a worker to employment earlier), and hence both costs and benefits are expressed in money.\textsuperscript{21} CBA may ignore many intangible but very important benefits not measurable in money terms, e.g. relief of anxiety. CBA may also seem to discriminate against those in whom a return to productive employment is unlikely, e.g. the elderly, or the unemployed.

However the virtue of this analysis is that it may allow comparisons to be made between very different areas, and not just medical, e.g. cost benefits of expanding university education (benefits of improved education and hence productivity) compared to establishing a back pain service (enhancing productivity by returning patients to work). This approach is not widely used in health economics, although many economists like it on theoretical grounds and because it removes some of the “sacred cow” protection which surrounds health care. They argue that health should be another commodity, and not necessarily valued more than other possible uses of the resources.

Overview of key above mentioned types of pharmaco economic analysis and their key characteristics are given in Table 1.
LIMITATIONS AND ISSUES IN PHARMACOECONOMIC IMPLEMENTATION IN PRACTICE

Many problems limit our use of health economics in practice. The whole process may be open to bias, in the choice of comparator drug, the assumptions made, or in the selective reporting of results. This suspicion arises because most studies are conducted or funded by pharmaceutical companies. Difference in costs, difference in effects work better obviously are interested in the results, and there is a publication bias towards those studies favorable to sponsoring companies. Health economics is therefore sometimes misused as a marketing ploy. The same problems may however arise in studies funded by health care payers. To a specialist, this is not such a problem since the almost inevitable biases are usually clear. But since economic evaluation is less well understood by doctors and others, bias needs to be minimized. Doctors may tend to equate health economics with rationing or cost cutting, and many therefore reject on principle the whole process as unethical. Since resources are limited within health services, wasting them by inefficiency is wrong, as it reduces the clinician’s ability to give the best possible care to his patients. It therefore seems unethical not to consider the economics of a medical intervention. A key problem is our ability to implement the results of a study. No matter how good a study is, and how cost effective a therapy compared to existing treatment, it may not be possible to achieve its potential benefits because of the existing cumbersome management structures. Three problems are common: first, a short term outlook which limits the application of economic evaluations showing long term savings for the health service in return for increased spending now. Second, many budgets operate in isolation, and it is not easy to move money between them: for instance, prescribing in primary care is often funded separately from hospital services, so any increased spending on drug therapy in primary care cannot be simply funded from a future reduction in hospital admissions. Third, a new intervention may simply not be affordable no matter how cost effective it might be. Finally, health economics and pharmacoconomics is a young science and is slowly developing and testing its methodologies. We do not have space to address all of these concerns here but many of the details of the methods described above are academically and practically controversial. There have been many guidelines developed for the conduct of economic evaluation, recognizing the possibilities of bias and the poor understanding of many potential users about the whole process. Also, very important issue in pharmacoeconomic studies is perspective. A range of potential perspectives can be adopted from the most limited (impact of changes on a single drug budget) to the societal where all indirect costs are studied as well. Given that the aim of economic analysis is to make the best use of all of society’s resources, the societal perspective is considered the most appropriate, but a health care manager with a limited budget might be tempted to place increased
emphasis upon costs that are imposed upon his area. It should be defined by payer or decision maker which or whose perspective should be taken into account when conducting pharmacoeconomic study and making calculations.

**Discounting** of cost and outcomes (benefits) is also of huge importance in order to get as much as possible accurate information for decision making. This is particularly important when subject of study is intervention with long-term impact (surgical interventions or chronic therapies) since future cost or benefits should be adapted to present value. Sensitivity analysis is one of the obligatory tools for handling uncertainty of final results, especially in model-based pharmacoeconomic evaluations. A sensitivity analysis explores the extent to which the conclusion derived from a study is dependent on the underlying assumptions or upon data that may be subject to measurement errors, e.g. resource use or clinical benefits.

Further and detailed explanation of discounting, modeling and sensitivity analysis are out of this article scope, and could be separately discussed and explained as specific topics.

**PHARMACOECONOMIC PERSPECTIVES IN BOSNIA AND HERZEGOVINA**

In Bosnia and Herzegovina, pharmacoconomics is slowly entering health care system but, beside all above mentioned limitations concerning globally recognized issues, we face with basic problem of proper understanding of pharmacoconomics uses. In 2011 ISPOR Bosnia and Herzegovina Regional Chapter has been established, gathering experts and professionals interested into this field and providing different programs on education into this field through conferences, courses and online learning programs.

Even pharmacoeconomic as a term and concept has been introduced into rulebooks defining reimbursement application by health authorities, still it is not put in force in decision making. According to existing legislation, pharmaceutical industry should submit cost-effectiveness and budget impact analysis as part of reimbursement submission dossier. Even it is not precisely defined which aspects should be included, but generally it should be payer perspective. There is no defined decision rule, so threshold is not officially set. Decentralized system of health care financing also limits implementation of pharmaco economics. Beside lack of data on costs and procedures, pharmaceutical spending and transparency in decision making, there is a problem of setting proper framework for conducting studies, expectation form the system and negotiation plan.

Main obstacle for full implementation of pharmaco economics in practice in Bosnia and Herzegovina is a lack of experts who could perform, review and understand pharmacoconomic studies results.

In that term, key and most important activity should be focused on education of experts. None of the faculties in Bosnia and Herzegovina still do not have pharmaco economics as a subject included in curricula. This could be huge opportunity for pharmaceutical faculties to provide such education through undergraduate or postgraduate programs. Pharmaceutical faculty in Sarajevo, has introduced subject dealing with pharmaco economics but it is far away from good practices in education in this field. Also, there is specialization program for pharmacists covering pharmaceutical informatics and pharmaco economics, but analyzing program and curricula it could be found that only term “pharmacoeconomics” relates to this field, including none of pharmaco economics issues. Research conducted among graduating pharmacy students at Pharmaceutical faculty in Sarajevo found that students do not get enough familiar and do not feel confident to conduct and understand pharmacoeconomic studies.

**CONCLUSIONS**

It is obvious that pharmacoeconomic application in real world improve decision making on public financing of medicines and other procedures. It is well established science with important role in health care system even more in low and middle income countries where health care resources are scarce. It is important that those developing, or seeking to use, expensive new medicines understand pharmaco economics methods and how these can be used to demonstrate value for money.
Pharmacoeconomic is acts as socioeconomics; it relates patients, society, and economy, to drug therapy.

Education in this field is a must, and it would be great chance for pharmaceutical faculties to create sustainable programs and include subject of pharmacoeconomics in their undergraduate and even post-graduate programs.

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