Economic Methods of Pharmacoeconomic evaluation

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ABSTRACT

Pharmacoeconomics is a branch of science that helps in the identification, measurement, and comparison of the costs and consequences of a drug therapy for the society. As drugs are heavily priced, it is extremely applicative in government as well as private sector and in pharmaceutical industry for carrying out comparison of various cost consequences. It is also an important tool for optimum resource allocation as well active decision making. The main aim of this article is to give a brief introduction of Pharmacoeconomics, its numerous evaluation methods such as cost benefit analysis, cost minimization analysis, cost utility, cost effectiveness analysis, along with scope and application of Pharmacoeconomics.

1. Introduction

The progress in the healthcare scenario of the population is been immensely contributed by the pharmaceuticals and other therapeutic interventions. In the past several decades, the mortality rates for several diseases have declined substantially due to the introduction of new drug entities [1]. Some data exist regarding the actual costs and corresponding benefits attributed to specific drug therapies. The unavailability of defined methodologies to evaluate medical interventions is one of the major reasons. Perhaps, it can be said that the current focus of the entire healthcare system on reducing costs of pharmaceutical products and services to save costs for the total health-care system is not up to the mark [2]. A sizable amount of drug costs is still accounted as out of pocket expense even if, a growing chunk of drug expenditures is covered by private health insurance and government programs. Thus, not only patients but also to the third-party payers, and governments the affordability of pharmaceutical products and services has become a crucial matter to. Thus, the costs and consequences of drug therapy are necessary to be valued scientifically [3]. Today's health care practitioners are all united by a common desire in defining the value of medicine. As there are serious concerns about rising medication costs and consistent pressure to decrease pharmacy expenditures and budgets clinicians/prescribers, pharmacists, and other health care professionals are answerable towards the value of the pharmaceutical goods and services they can provide. Pharmacoeconomics, or the discipline of placing a value on drug therapy, has evolved since years to clarify this important issue [4].

The description and analysis of the cost of drug therapy to health care systems and society has been defined as Pharmacoeconomics [5]. Pharmacoeconomics is a distinctive part of health economics which involves identification, measurement, and comparison of the costs along with consequences of pharmaceutical products and services. The economic relationship between research and development of a drug, its production and distribution, pricing, storage, and ultimate consumption has been briefly explained by Pharmacoeconomics. The nature or well-being of markets, firms as well as individuals for the applicability of pharmaceutical products, services, and programs is been studied and evaluated. A collection of, descriptive and analytic techniques that evaluate pharmaceutical interventions, spanning from individual patients to the healthcare system is done in Pharmacoeconomics. Thus, aiding the policy makers and the healthcare providers in evaluating the access to rational drug usage. Affordability and post-treatment value are the terms that determine access [6]. To compare pharmaceutical products and treatment options Pharmacoeconomics is the branch of economics that makes use of cost- effectiveness, cost-benefit, cost of-illness, cost-utility and cost-minimization analyses [7].

2. Definitions of important terms

2.1 Economics

To satisfy unlimited wants for outputs economics is the study of the allocation of limited resources or inputs among alternative users. The terms health economics and Pharmacoeconomics are defined by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR)as follows.

2.2 Health economics

‘The field of study that focuses on the cost (inputs) and consequences (outcomes) of health care interventions, such as the use of drugs, devices, procedures, services and programs by evaluating the behavior of individuals, firms, and markets in health care system [8].

2.3 Pharmacoeconomics

‘The field of study which frequently focuses on the costs (inputs) and consequences(outcomes) of that use that evaluates the behavior of individuals, firms and markets relevant to the use of pharmaceutical products, services and programs.’ [8]

3. Scope and need of Pharmacoeconomics

3.1 Need of Pharmacoeconomics

Pertaining to the development and sophistication of health technologies the cost of obtaining appropriate level of healthcare is increasing across the globe. Due to increased life expectancy, improved standard of living and increased demand of quality health care services health care spending has also increased. Medicines are a small but significant proportion of total health care cost. Patients across all nations are affected by high price of medicines. Out of pocket expenditure [9] is been financed in a developing

country like India, total 85% health expenditure is financed [10]. As poor people limited resources and the prices of drugs are high the condition is so bad that they must frequently have to choose between buying medicines or buying food or other necessities. There are numerous factors which influence the drug pricing like the sector in which medicines are purchased i.e private or government sector and often the price is higher in private sector. Another factor is the types of procurement agent: e.g. a public sector purchaser must be different price for the same product. The drug pricing will also be influenced by the distribution route and the patient status. So, medicine prices do matter Pharmacoeconomics has become more important over the past 20 years due to an increased stress on efficient drug therapies for disease thus increasing health costs, Basically, in industry Pharmacoeconomics is useful in determining among specific research and development alternatives. It finds use in determining program benefits and prices paid in government sector and also for designing insurance benefit coverage in private sector [10].

3.2 Scope of Pharmacoeconomics

3.2.1 To Pharmaceutical manufacturers

Before a drug is approved for use by the FDA Pharmacoeconomics can be an extremely useful tool. In the drug development process huge amount of resources are spent by the pharmaceutical manufactures. The manufactures can avoid spending vast resources to the development of a drug that lacks to provide competitive advantage if proper pharmacoeconomic research is conducted before preceding to the development. A drug i.e. cost-effective in the present healthcare environment, can have a competitive advantage. Cost effective can mean a drug that is less costly and at least as effective as an alternative; even more effective and costlier than an alternative. To the usual safety and efficacy investigation of a new drug Pharmacoeconomics can be considered as an additional factor of investigation for the launch of the drug. The impact of the disease and existing treatment on the patient's quality of life (QOL) involves specific evaluation such as individual and societal costs of the illness for which the drug is indicated, the costs and consequence of existing treatment methods. Reduction in uncertainties can be achieved thus contributing to the knowledge base that facilitates the decision of whether to further evaluate a treatment via clinical trials. To provide additional information regarding a drugs impact on patient outcome phase III studies may involve cost efficacy and QOL components. The scientific basis of drug therapy decision making will be increases.

3.2.2. Healthcare Practice

To benefit clinical and policy decision making Pharmacoeconomics is used. In every pharmacotherapy decision basis evaluation components; clinical, economic, and humanistic outcomes should be incorporated. Considering just drug acquisition costs would not be of much use. Various clinic decisions, including individual patient treatment, effective formulary management, resource allocation and medication policy has been supported by pharmacoeconomic data. Whether or not a drug should be included or excluded on or from the formulary can also be determined by proper pharmacoeconomic data. Numerous strategies can be used to incorporate Pharmacoeconomics into formulary decision making. Local pharmacoeconomic research can also be utilized as a tool along with published pharmacoeconomic studies and economic modelling techniques that are used [11]. Pharmacoeconomics

can assist in maintaining a balance between cost and patient outcome (quality of care), often resulting in maintaining or improving quality of care, with potential cost savings also the data can be used for effective allocation of resources in hospitals. Pharmacoeconomic research is important to the healthcare practitioner in the cost-conscious environment.

3.2.3. Process and product evaluation

Pharmacists help in drug use evaluation. Ideally, this value should be translated into patient and financial outcomes. Drug use evaluation along with concentrating on inappropriately prescribed therapy and overprescribing, also focuses on the most cost- effective therapy. Conducting cost-effectiveness studies allows an evaluation of total costs and consequences from various perspectives [8].

4. Components of Pharmacoeconomics

The components of Pharmacoeconomics are summarized in the figure 1.1

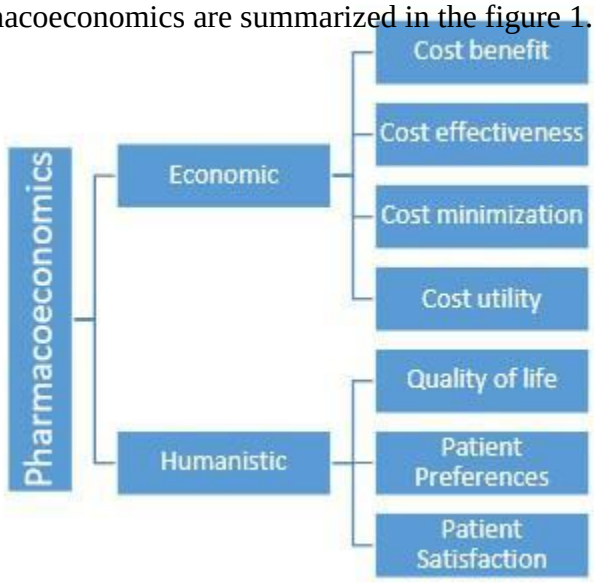

Figure 1.1 Components of Pharmacoeconomics

5. Impact of different costs on pharmacoeconomic evaluation

The two main types of cost considered in a pharmacoeconomic evaluation are financial cost which is the mandatory cost and economic cost. Opportunity cost is the cost i.e. is associated with the benefit foregone when selecting one therapy alternative over the next best [12]. In any cost analysis determination of the various costs involved in a drug invention is the first step. These costs can be direct, indirect and intangible.

5.1 Direct costs

Capital costs, staff costs, drug acquisition costs are the costs considered from the perspective of the healthcare funder. It also includes physician's fees, costs of treating an adverse drug reaction, cost of administering the medication, etc.

5.2 Indirect costs

Loss of productivity, loss of earnings, loss of leisure time and cost of travel to hospital etc are the costs considered from the perspective of society as a whole [13]. This takes place not only the patient but also their family and society into consideration.

5.3 Intangible costs

This involves the worry, pain or other distress; which the family of a patient or the patient might suffer. These costs are not measured in monetary terms but are captured in measures of quality of life. The cost can be measured in following ways:

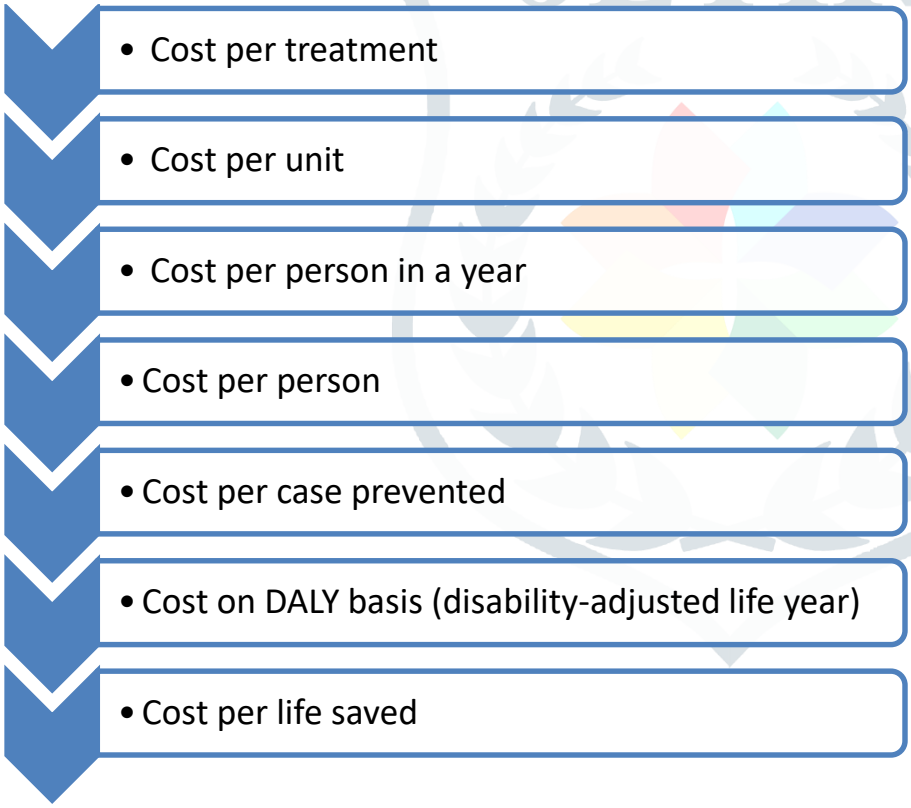

Figure 1.2 Methods of measuring cost

6. Outcomes of Pharmacoeconomic evaluation

Benefits or outcomes are the second fundamental component of a pharmacoeconomic study.
The expected benefits from an intervention might be measured in:

6.1 "Natural" units- The extent to which a particular condition can be healed. e.g. years of strokes prevented, life saved, peptic ulcers healed etc.

6.2 "Utility" units - Utility includes satisfaction, or sense of well-being, and is an attempt to span out of evaluation of quantity of a state of health to even its quality. Direct measurements can be made to estimate utility. Time trade off or standard gambles, or by imputing them from the literature or expert opinion can be certain techniques utilized. They also include measures of quality of life in different disease states [14].

7. Approach to Pharmacoeconomic evaluation

The approach used for Pharmacoeconomic evaluation are mentioned in the figure 1.3.

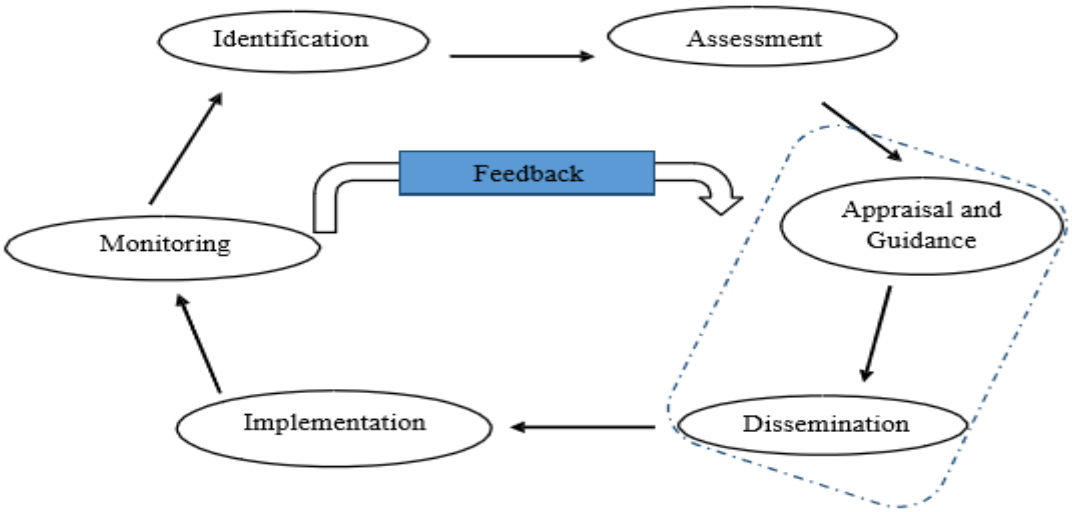

Figure 1.3 Approach to Pharmacoeconomic evaluation

8. Economic Methods of Pharmacoeconomic Evaluation

Methods designed to assess the costs (resources consumed) and consequences (clinical, humanistic) of alternative therapies are included in Pharmacoeconomic evaluations.

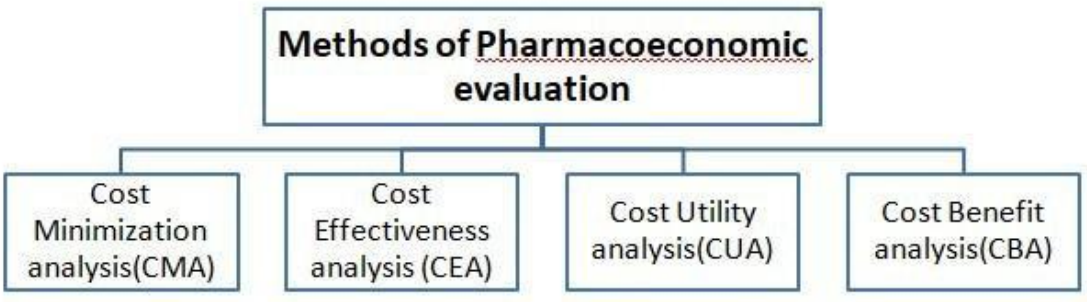

Figure 1.4 Methods of Pharmacoeconomic evaluation

8.1 Cost minimization analysis (CMA)

When comparing two or more therapies cost minimization analysis helps to determine the least costly alternative. In CMA when comparing the costs of the alternatives the therapeutic safety and efficacy should be same. Also, once the therapeutic safety and efficacy of the alternatives is compared with the actual therapy and confirms that it is has an equivalent outcome, the costs can then be known, determined, and compared in terms of money.

CMA is a relatively simple method for evaluating therapy alternatives if the therapeutic equivalence of the alternatives being compared has been proven. A more inclusive method s.a. cost effectiveness analysis is done if not proven. CMA only shows cost savings of one of the therapies over other.

It is only applicable to evaluate using CMA when two or more therapeutically equivalent agents or alternate dosing regimens of the same agent. This method has been used frequently, and its application could expand given the increasing number of “me too” products and generic competition in the pharmaceutical market [15].

8.2 Cost effectiveness analysis (CEA)

When two or more therapeutic approaches have differential effectiveness Cost effectiveness analysis (CEA) is used.

(Cost effectiveness = cost/output)
Where,

Cost: direct and indirect costs for the therapy

Output: benefit to the patient

The incremental cost-effectiveness analyses assess the difference between the two therapies. Cost-effectiveness analysis (CEA) involves a larger look at drug costs. Measurement of cost is done in terms of money and outcome is measured in terms of benefits or the level of effectiveness

CEA in this manner estimates the incremental expense of accomplishing an incremental medical advantage communicated as a specific wellbeing result that changes as indicated by the sign for the therapy given. CEA gives a structure to think about at least two choice alternatives by analyzing the proportion of the expenses and the health benefits between the options. The general objective of CEA is to give a solitary measure, the ICER (incremental cost effective ratio) which relates the measure of advantage determined by making an alternate therapy decision to the differential expense of that alternative.

When two options are being compared, the ICER is calculated by the formula [17]:

(Cost (treatment 2) - Cost (treatment 1)/Effectiveness (treatment 2) - Effectiveness (treatment 1))

Ordinarily, these health results are estimated as lives saved, years gained, or an assortment of other clinical or health results. In contrast to CEA, CBA investigates both the expenses and benefits of interventions in monetary terms. CEA looks at therapeutic techniques through the count of the ICER, a measure of the expense of changes in health results. When information on effectiveness and costs are available analyses can be done on clinical trial data by using decision analysis models. Due to the variety of health outcomes that can be used as the effectiveness term in these analyses and to the absence of a definitive criterion for "cost- effective" interpretation of CEA results can be challenging [18].

8.3 Cost utility analysis (CUA)

Cost utility analysis is a technique used to evaluate interventions or drugs having variety of outcomes can be compared. CUA is suitable technique to compare various project and treatments options which increases life with serious side effects such as chemotherapy used in cancer, those which reduces rate of morbidity rather than mortality such as arthritis treatment, and when HRQOL is an important health outcome being examined. It is not used frequently in comparison to other methods of economic evaluation due to of an agreement issues on measuring utilities, trouble in comparing quality adjusted life years between patients and populations, and trouble in quantifying patient preferences. While comparing different treatment options Pharmacoeconomics wishes to incorporate a measure of preference of patient or value of life measures. Cost utility analysis is a technique which compares options of treatment which integrates preferences of patients. It gives comparison of several factors such as quality, cost and no of patient years. Measurement of cost is done. in dollars, and therapeutic effect is not measured in physical units but by using patient- weighted utilities [19]. Usually measurement of utility used is a quality-adjusted life year (QALY) obtained. It is a common measure for status of health used in CUA, which combines rate of morbidity and mortality data. The results obtained from cost utility analysis can also be expressed in the form of ratio, a cost-utility ratio (C:U ratio). The ratio is translated in the form of cost/QALY gained. The preferred treatment alternative is that with the lowest cost per QALY (or another health-status utility). QALY refers to all the years with proper health which is compared with total no of years experienced. For eg, person with no disease have a 1.0 QALY, whereas person with some disease may have lower QALY i.e 0.5 QALY it varies based on the disease [20].In this the incremental cost of a project from a point of view is compared to the incremental health improvement expressed in the unit of (QALYs) [21]. CUA measures cost in terms of quality and quantity of life. Unlike cost benefit analysis cost utility analysis measures the comparison of variety of procedures giving different treatments.

8.4 Cost benefit analysis (CBA)

A type of economic analyses in which both the costs and consequences are determined in monetary terms is known as cost benefit analysis (CBA). The benefit obtained from the treatment in monetary terms is considered as the numerator. In the denominator, the investment for the treatment therapy again in monetary terms is considered. In CBA, both incremental costs and outcomes are valued in monetary terms and thus, a direct calculation of the net monetary cost in achieving a treatment can be done. The cost of the productive value to society can be determined as gain in life-years. Numerous techniques like

willingness-to- pay is used to analyse the gains in quality of life. Willingness-to-pay is the amount that a person is willing to pay for a benefit in quality-of-life.
Amongst all economic evaluation techniques, CBA is the most tough and comprehensive in nature. Completely varied interventions can be compared which makes it is useful in resource allocation activities. Identification, measurement, and comparison of the costs and benefits of a program or treatment alternative can be made. Treatment options in which the costs and benefits do not occur simultaneously can be easily compared using this technique. However, programs with different aims can also be compared with the help of CBA as all benefits are transformed into dollars and then the programs can be evaluated. Discounting of future cost as well as benefits are done to their present value. A ration known as benefit to cost ratio is utilized to express these costs and benefits. However, it is extremely challenging to calculate the benefits in terms of economy. It is easy to convert certain benefits where as others require subjective judgement. Intangible benefits (anxiety, stress, pain) are tough to express in economic terms, thus they aren't included in CBA analysis.

The weaknesses and strengths of options can be systematically estimated using CBA analysis. Alternative that is best in terms of going through with it in terms of benefits obtained in labor, cost savings and time can be determined. There are two main purposes of CBA:
1.To determine effective decision/ investment in terms of its feasibility.

2. To provide a method for comparing Projects can be compared using CBA. Total expected cost of each alternative against the total expected benefits are compared, to see if the benefits outweigh the costs, and by how much.

CBA has certain similarities to cost-effectiveness analysis. Benefits and costs are adjusted for the time value of money, so that all flows of project cost and flows of benefits over time are determined on a common basis in terms of their "net present value." A healthcare decision maker would choose that alternative that has the highest net benefit or the greatest benefit-to- cost (B:C) ratio.
The program or treatment is of value if the B:C ratio is more than 1the benefits outweigh the cost.

The benefits equal the cost if the B:C ratio equals 1. The benefits are equivalent to the cost.

The program or treatment is not beneficial in economic terms, if the B:C ratio is less than 1. The cost outweighs the benefits.

Valuing health benefits in economic terms can be difficult and controversial. Sometimes expressing health benefits as monetary units can be inappropriate and unaccepted. Thus, unless done appropriately, CBA should not be employed. CBA can also be used in not only documenting but also justifying the worth of an existing clinical service or the potential value of a new one. CBA can also help in determining the service that provides maximum return on investment thus help in proper resource allocation [22].

9. Pharmacoeconomic evaluation of Biosimilars used in Cancer treatment

In cancer therapy, use of biologics has seen the light of the day, thus healthcare costs globally are highly driven by the cost of cancer treatment. Biologics although extremely effective but are highly expensive. However, by using biosimilars, patient accessibility to biological therapies has increased as there is a reduction in the cost of treatment. Several factors like safety and efficacy of biosimilars in comparison to biologic drugs, costs involved in manufacturing and development, monitoring safety, and pricing policies undertaken by government or institutes can influence the overall pharmacoeconomic evaluation of biosimilars. In US, the use of biosimilars depends on numerous considerations like pharmacovigilance and safety profiles, affordable pricing and the education of professionals and patients [23,24]. In Germany, the Netherlands and the United Kingdom, as there was an availability of a lower cost biosimilar to G-CSF, a 10% to 20% increase in the use of a G- CSF agent was found. Also, G-CSF was used in the early stages of the therapy, thus a transition of its use as a secondary to primary prophylactic agent against febrile neutropenia was observed [25]. Thus, it can be said if biosimilars are made more affordable, they have the potential to provide patients with greater access to biologic drugs.

Numerous Pharmacoeconomic considerations are made by numerous countries for effective use of biosimilars [26]. Many countries have developed guidelines specifying standards for conduction of economic evaluations that are to be included in reimbursement applications. Properties of the biosimilars and reference biologics determine the pharmacoeconomic studies that are the most pertinent to biosimilars [27].

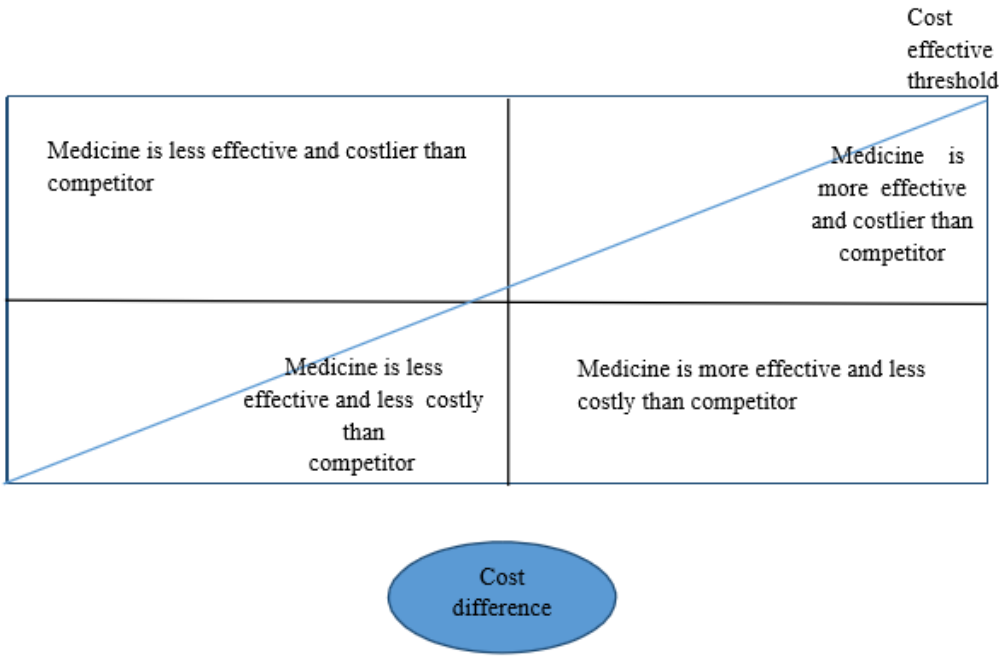

Figure 1.4 Cost effectiveness plane

In the literature, only few articles are available that talk about the pharmacoeconomic analyses of biosimilars, especially biosimilars containing monoclonal antibodies. Only few cost-minimization analyses have been documented for biosimilars in certain countries like United Kingdom (UK). One of the examples can be of tbo-filgrastim by Teva. Tbo-filgrastim is a short-acting G-CSF product. In Europe, Tbo-filgrastim is marketed under the trade name Tevagrastim that is a biosimilar to G-CSF. As, at the time of FDA submission, a US biosimilar pathway was not in place, Teva markets tbo-filgrastim

as an innovator product in the United States [28]. Identification of treatment strategies that are beneficial to patients in terms of therapeutic value and cost can be done by healthcare professionals by making use of cost-minimization analyses. For example, in a study the benefits of the use of high-cost versus low-cost bypassing agents that have demonstrated similar efficacy profiles in surgical patients with hemophilia were compared. In the study authors examined drug cost and dosing for surgical procedures over 14-days. A total cost saving of $470,000 was achieved with the use of the lower-cost bypassing agent which also showed a 58% decrease in total drug cost [29]. Cost-minimization models may provide insight into the value of biosimilars in terms of cost and clinical benefit thus increasing the acceptance of biosimilars. Cost-minimization analyses from two phase III trials in the UK for biosimilars to epoietin alfa in patients with chronic renal failure demonstrated clinical equivalence for the biosimilar epoietin zeta, compared with epoietin alfa. It was concluded that epoietin zeta has an equivalent efficacy in terms of maintenance of hemoglobin concentration that is economical according to a cost-minimization analysis. Another study in patients with breast cancer, witnessed a cost-savings of £322 per patient over an 84-day period for a biosimilar to filgrastim for the prevention of neutropenia [26]. Although currently there are limited number of results of cost-minimization analyses, these results may suggest a role of biosimilars in addressing constantly escalating cancer treatment costs without compromising on efficacy and safety to patients with cancer.

Conclusion

In the period of rising costs related to healthcare, the science centres around value for money concept. For this, there is an earnest need to build up a science based on investigation of costs and outcomes of drug treatment to healthcare framework and society. Pharmacoeconomics is that science which intend to qualify the estimation of pharmacotherapy through comparing costs and results. By understanding the strategies, principles and applications of Pharmacoeconomics, healthcare experts will be prompting to make more educated choices that help in the welfare of the patient, the healthcare system, and society. Henceforth Pharmacoeconomics is also socioeconomic in nature as it relates patients, society and economy, to drug therapy. Currently, different pharmacoeconomic techniques can be used as a powerful model for effective formulary management, individual patient treatment, prescription strategy assurance, and allocation of resources. Financial, humanistic, and clinical results ought to be considered utilizing pharmacoeconomic strategies, for better decision making whenever possible.

However, Pharmacoeconomics can be challenging to implement. It would be beneficial to constitute Pharmacoeconomics advisory groups for both state and central drug regulators. Also, immense concentration is required on both direct and indirect services so that the burden of diseases can be decreased. Some measures can be undertaken to achieve it, which include, decreasing the poverty, improving nutrition, developing health-care infrastructure and preventing transmission of diseases by appropriate treatment and immunization. Another important thing to be done is to improve patient access. It is extremely essential to create awareness in healthcare professionals and common public better utilization of resources. Thus, Pharmacoeconomic principles should be included in pharmacy, medical, public health as well as other health-care professional education.

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