



## AN OVERVIEW OF CHALLENGES, IMPORTANCE AND EVALUATION OF PHARMAECONOMICS: ROLE OF PHARMACIST'S IN HEALTH CARE SYSTEM

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### Abstract

The main goal of the pharmacoeconomics is to address whether an additional gain from a medical intervention is worth paying extra cost based on three aspects of health outcomes: Economic, Clinical and Humanistic outcome known as ECHO Model. By perceiving the principles, methods, and application of pharmacoeconomics, pharmacists will be prepared to make better, more-informed decisions regarding the use of pharmaceutical products and services, that is, decisions that ultimately represent the best interests of the patient, the health care system, and society. Pharmacoeconomics can be applied to any therapeutic area like hospital pharmacy, using a variety of application strategies. As the healthcare sector is progressing day by day the need to develop Pharmacoeconomics area is must. Healthcare sector is not just a small area but it became an industry now. It has more dimensions to explore. So, main goal of this article was to explain it with in a cumulative way by mentioning two examples- where the first one is direct cost that outlays money and then is indirect cost for the productivity effect. Patients also get benefit out of Pharmacoeconomics findings. Pharmacoeconomics research should be strongly supported in a country like India where majority of health care spending is done by the patient's themselves.

**Keywords:** Pharmacoeconomics, ECHO Model, Pharmacist, Pharmacoeconomic evaluation, Healthcare Sector, Pharmaceutical Policy, Drug Commercialization, Cost Utility Analysis, Cost Benefit Analysis, Cost of illness Analysis, Cost Minimization Analysis.

### Introduction

Pharmacoeconomics adopts and applies the principles and methodology of health economics to the field of pharmaceutical policy [1]. Initially, defined as "analysis of the costs of drug therapy to healthcare systems and society", [2, 3] the actual term "pharmacoeconomics" first appeared in the literature in 1986 when Townsend's work was published to highlight the need to develop research activities in this new discipline. In 1992, a journal named "Pharmacoeconomics" was launched [2]. It is the discipline concerned with optimal allocation of resources to maximize population health from the use of medicines [4]. It is currently being used to make formulary decisions (complementing clinical data), design disease management programs and measuring the cost effectiveness of interventions and programs in managed care [1, 5]. Pharmacoeconomic analyses are increasingly used to help decision-makers assess the value of health interventions [6]. Pharmacoeconomics study is primarily for the purpose of drug listing, competitiveness, pricing, and reimbursement [7]. It is a field or a discipline that is used by health care payers to really compare the cost versus

the benefit of alternative drugs. It involves balancing the costs and consequences of pharmaceutical therapies and services. It helps in forming an economic relationship which combines the drug research, its production and distribution, storage, pricing, and further use by the people [8]. In an environment where the cost of healthcare is sky rocketing, insurers are looking for evidence that can support decisions that determine purchasing, contracting, and inclusion of new medications in the formularies. The producers of medications therefore, have to assess the value of the drugs, both in terms of economic worth and clinical efficacy [2, 9]. "Doctors prescribe, patients consume and, increasingly throughout the world, third purchasing parties (government insurance companies) pay the bill with money that they have obtained from increasingly reluctant healthy members of the public" [2,10]. Pharmacoeconomic evaluation therefore makes use of the broad range of techniques used in health economics evaluation to the specific context of medicines management [1, 11]. It can help decision-makers judge whether the therapeutic benefits produced by a new drug are worth the extra costs [12].

Data generated from pharmacoeconomics studies have potential to impact many domains like health insurance, reimbursement under Central and State Government schemes, health policy, import and export of pharmaceutical products, technologies, subsidies on health products and planning of future health care benefit programmes [13,14]. In 1993, Australia became the first nation to use pharmacoeconomic analysis as part of the process for deciding whether new drugs should be subsidized by the Federal Government [13, 15]. In high-income countries pharmacoeconomic analysis is widely used to guide priority-setting decisions for pharmaceuticals [12, 16]. National Institute of Clinical Excellence (NICE) in the UK and the Canadian Agency for Drugs and Technology in Health (CADTH) are examples of institutions which have been established for pharmacoeconomic evaluation of new pharmaceutical products and technologies [12, 17, 18].

Pharmacoeconomics analysis takes into consideration the stakeholders of the pharmaceutical ecosystem. These are mainly clinical professionals, hospital staff, the payer, the formulary committee, academicians, vendor or clinical research organization (CRO), the patient, the regulator, and the general public. Pharmacoeconomics analysis considers the geographic location due to pricing, for example, hospital charges and insurance services [7]. It is a part of health economics and more broadly a part of health technology assessment. It estimates incremental value of pharmaceutical interventions. The term "value" in general refers to the outputs achieved relative to the costs incurred when new is compared with old intervention(s). In healthcare, value can be defined as the patient health outcomes achieved per money spent [19].

Pharmacoeconomics is a branch of health economics related to the most economical and efficient use of pharmaceuticals. Pharmacoeconomics research identifies measures and compares the costs and outcomes of pharmaceutical products and services. Pharmacoeconomics can play a significant role in the efficient allocation of resources in healthcare systems with constrained budgets. The purpose of this article is to provide an introduction of pharmacoeconomics, its various methods of evaluations such as cost of illness analysis, cost minimization analysis, cost benefit analysis, cost utility analysis, cost effectiveness analysis and also discuss challenges, and importance of pharmacoeconomics. And also discuss the ECHO Model with significant examples.

## HISTORY

Pharmacoeconomy is a young interdisciplinary science at the intersection of pharmacy, medicine and economics, focusing on the social aspects and

implications of different types of pharmacotherapy [20]. Pharmacoeconomics is a sub-discipline of the field of health economics, which itself is a relatively new sub-discipline of economics, only formerly appearing in the economics scientific literature since the 1960s [21]. The term Pharmacoeconomics was first time used in public forum was in 1986, at meeting of pharmacist in Toronto, Canada, when Ray Townsend from the Upjohn company, used the term in presentation [22]. Since the early eighties pharmacoeconomics research is a flourishing industry with many practioners, a large research and application agenda, several journals and flourishing professional societies including the international society for pharmacoeconomics and outcomes research [23, 24].

Pharmacoeconomics developed its roots in 1970s. The first book on health economics was published in 1973 and in 1978; McGhan, Rowland, and Bootman from the University of Minnesota introduced the concept of cost-benefit and cost effectiveness analysis. Utilizing sophisticated pharmacokinetic protocols, Bootman published an early pharmacy research article in 1979 in which cost-benefit analysis was employed to appraise the outcomes of individualizing aminoglycoside dosages to severely burned patients with gram-negative septicaemia. In 1983, Ohio State University College of Pharmacy initiated a specialized pharmacy academic program with the objective of providing an overview of the application of cost benefit and cost effective analysis in healthcare, with emphasis on their application to the delivery of pharmaceutical care [23].

It is believed that pharmacoeconomics will obtain the same level of recognition when its application in clinical setting is more complete. In other words, when pharmacy practitioners begin to apply the results of pharmacoeconomic research to therapeutic decision making, thus positively influencing patient outcomes, the disciple will become an increasingly critical component of the pharmacy curriculum [25].

## IMPORTANCE

Efficacy and safety are crucial considerations in judging drugs, for example, whether or not to include them in a local formulary. More and more, pharmacoeconomic aspects are becoming of additional importance [26]. Pharmacoeconomics should be viewed as a tool that compliments other strategies in making choices and/or ensuring efficient use of resources [27]. The demand for and the cost of health care are increasing in all countries as the improvement in and sophistication of health technologies. Cost of medicines are growing constantly as new medicines are marketed and are under patent law, preference of drug therapy over invasive therapy, discovering various off label uses of existing drugs and

the irrational drug prescription. All over the world patients are affected by high price of medicines. In a developing country like India 85% of total health expenditure is financed by house-hold out-of-pocket expenditure. Many poor people frequently face a choice between buying medicines or buying food or other necessities due to limited resources and high pricing of drug. So medicine prices do matter [28]. Pharmacoeconomics is used at all stages in the development of medicines by the pharmaceutical industry, when medicines are researched, produced and marketed. Some countries insist on pharmacoeconomic evaluations as part of the licensing process [29].

**Importance of Pharmacoeconomics has become more important over the past 20 years, due to an increased emphasis on efficient drug therapies for disease, which increase health costs, as follows-**

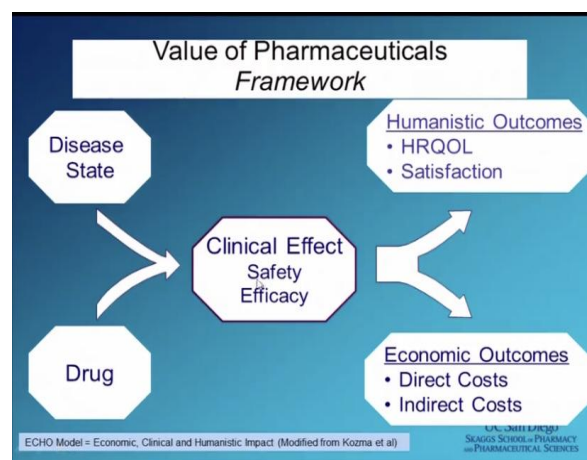
1. Rising health expenditures have led to the necessity to find the optimal therapy at the lowest price. Pharmacoeconomics is an innovative method that aims to decrease health expenditures, whilst optimising healthcare results
2. Pharmaceutical expenditures, which constitute a large part of healthcare expenditures, have been increasing much faster than total healthcare expenditures.
3. Numerous drug alternatives and empowered consumers also fuel the need for economic evaluations of pharmaceutical products.
4. The increasing cost of healthcare products and services has become a great concern for patients, healthcare professionals, insurers, politicians and the public.
5. This increasing concern has prompted demand for the use of economic evaluations of alternative healthcare outcomes. This escalation in healthcare spending is due to increased life expectancy, increased technology, increased expectations, increased standards of living and an increased demand in healthcare quality and services.
6. Healthcare resources are not easily accessible and affordable to many patients; therefore Pharmacoeconomic evaluations play an important role in the allocation of these resources.
7. The basic task of economic evaluation is to identify, measure, value, and compare the costs and consequences of the alternatives being considered [30].
8. Without systematic analysis, it is difficult to clearly identify clearly the relevant alternatives [31].
9. The perspective (or viewpoint) assumed in an analysis is important. A programme that looks unattractive from

one perspective may look significantly better when other perspective is considered [31].

10. Pharmaco-economics is an essential tool in the pharmaceuticals procurement realm. It monetizes clinical outcomes and provides the most objective and accurate guidance for drug purchases [32].

### ECHO MODEL

The main goal of the pharmacoeconomics is to addresses whether an additional gain from a medical intervention is worth paying extra cost based on three aspects of health outcomes: Economic, Clinical and Humanistic outcome known as ECHO Model [19]. The economic, clinical and humanistic outcomes (ECHO) model for a pharmacoeconomics evaluation views the drug as some combination of its clinical, economic and humanistic attributes. Safety and effectiveness are no longer the only salient attributes of a drug; the effect on total health resource utilization, cost and quality of life must be evaluated [33]. It depicts the value of a pharmaceutical product or service as a combination of traditional clinical-based outcomes with more contemporary measures of economic efficiency and quality. This integrated approach provides a theoretical basis for considering potential trade-offs among economic, clinical, and humanistic variables in optimizing the allocation of health care resources [34].



**Figure 1: ECHO MODEL [35]**

Every clinical trial starts with the disease state and it combines a group of patients with a drug and in which the clinical effect observed is safety first, were there any adverse effect or is it causing any harm to the patients? And if not then the next thing to look at is efficacy, does the drug actually work? Is it producing a reduced symptoms or improved mortality, this is where the clinical trial ends and next comes the pharmacoeconomics phase; the Humanistic Outcomes includes Health Related Quality Of Life (HRQOL), does it improve patient's quality of life because of the improved

safety and efficacy? And then because of this improved safety and efficacy what happened to the economic outcomes, which is divided into Direct Cost and Indirect Cost. The clinical effect safety and efficacy is driving the Humanistic and Economic Outcomes.

Value of Pharmaceuticals Framework		
Economic (Resource Utilization)	Clinical	Humanistic
<b>Direct Costs</b> e.g. Drug Physician visits Hospitalization Nursing time Transportation	<b>Safety</b> e.g. Headaches Nausea Stroke	<b>Quality of Life</b> Health-Related vs. Overall, Global
<b>Indirect Costs</b> Lost days of work Reduced Productivity Patient, Provider, System	<b>Efficacy</b> e.g. Reduced Symptoms Cured Patients Saved Lives Years Gained	<b>Patient satisfaction</b> e.g. With Treatment With Provider
		<b>Patient preferences</b> e.g. Treatment Mode Disease State

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**Figure 2:** Value of Pharmaceuticals Framework [35]

So here is a chart that gives some examples of exactly what is direct cost, indirect cost and different other variables.

So the economic sign is also called as resource utilization because these are resources that are utilized, so direct costs are things for which you actually outlay money like drugs, this is directly related to either treatment or to the disease itself, so the drug is directly related to the physician visits, hospitalization, nursing time, transportation. Indirect cost in pharmacoeconomics is related to the disease or its productivity like lost days of work, reduced productivity, patient provider system, the clinical outcomes consists of safety which include Headache, Nausea or it could be also big things like stroke, and efficacy which include cured patients number of saved lives. On the Humanistic side the most common humanistic outcome that is measured is quality of life; its health related quality of life. Patient satisfaction could be with the treatment itself or it could be with the provider or with the system.

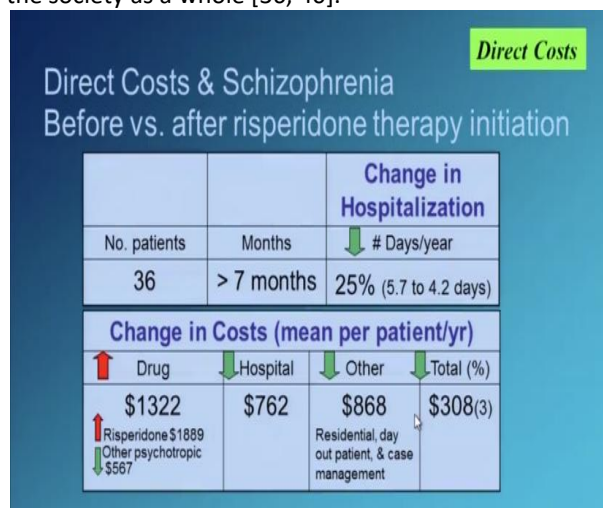
**So here are two examples the first one is direct cost that outlays money and then is indirect cost for the productivity effect:**

### 1. Direct cost and Schizophrenia Before VS after Risperidone Therapy Initiation

Schizophrenia is a disorder of the brain which affects how a person thinks, feels, and perceives reality [36,37] and significantly decreases the quality of life of patients [36,38].

Schizophrenia represents one of the leading public health issues in psychiatry [39]. Individuals with schizophrenia use a substantial amount of healthcare

services. This condition imposes a significant economic burden on both the patients and their families and on the society as a whole [36, 40].



**Figure 3:** Example of Direct Cost- Before vs. after risperidone therapy initiation in Schizophrenia patients. [41]

This is a study in Schizophrenia patient and what they feel before and after risperidone therapy initiation. This is a small trail with 36 patients in which they will receive risperidone therapy for more than 7 months. This produces improved safety and efficacy effects and also improves the symptomatology. Moreover this drug is more convenient economically as well as some other ways specifically hospitalization and there were changes in the days of hospitalization from before and after, the number of days per year showed reduction upto 25%. Before the risperidone therapy that group of patient had an average of 5.7 days in hospital versus 4.7 days after they had done the risperidone kit therapy. So if one is spending money on risperidone therapy they are saving hospital costs.

Further it is observed that the cost of the drug actually went up and the risperidone costs \$1889, but the use of other psychotropic drugs was eliminated, so these costs went down by \$587, so the drug cost ended up increasing by \$1322. The decrease in average cost for the hospital was \$762. And there are also some other savings, residential day care, outpatient kind of care, case management there was a reduction in those services as well. In total the reduction in cost was \$308 per patient. Though risperidone cost is more but it's saving money elsewhere in the health care system.

### 2. Indirect cost and migraine

Migraine is a common and highly disabling neurological disorder associated with a high socioeconomic burden. Effective migraine management depends on adequate patient education: to avoid unrealistic expectations, the condition must be carefully explained to the patient soon as it is diagnosed [42]. It is a frequent disease with



a point prevalence of 20% in women and 8% in men. Therefore, guidelines for the treatment of migraine attacks and the prevention by drug treatment or behavioral therapy have great practical importance [43]. Naratriptan is a promising new oral therapy for acute migraine; it may successfully treat patients who poorly tolerate other triptan therapies or have longer duration migraine headaches [44].

It treats migraine headaches when it occurs, it is not a prophylactic.

Productivity & Migraine		
	Indirect Costs	
Mean	Customary	Naratriptan
# Attacks/pt	35.2	35.2
Duration (hrs)	608.4 hrs.	383 hrs.
Work time lost (hrs/Can \$)	51.4 hrs. (\$851)	32.8 hrs. (\$544)
Unpaid work time lost (hrs/Can \$)	19.9 hrs. (\$228)	12.6 hrs. (\$145)
Leisure time lost (hrs/Can \$)	46.2 hrs. (\$0)	29.6 hrs. (\$0)
Total	117.50 (\$1,080)	75.00 (\$689)

**Figure 4:** Comparison of Effect on productivity when Migraine is treated using Naratriptan and when treated customarily. [45]

This study looked at the cost and it used a clinical trial and put it into a cost model. And it was done for a 1 year period in Canada. And the findings were, there are two columns here; customary treatment and Naratriptan treatment, so the mean number of attacks per patient for both is same there is no difference because Naratriptan does not prevent headaches it just makes it shorter. So the duration of headaches were reduced by 220.4 hours. The economic or the indirect cost analysis is the work time lost in which the customary group lost 51 hours and the Naratriptan group lost 32 hours and then the unpaid work time which also saw reduction in the hours when the customary and Naratriptan group is compared. And finally the leisure time lost (when at home and not working) saw a reduction in time by 16.6 hours and then the total work time lost was 117.50 mean versus 75 mean for the Naratriptan.

So Naratriptan decreases the amount of time the people have migraine headache, and also improves productivity.

#### PHARMACOECONOMICS: EVALUATION METHODS

The basic task of economic evaluation is to identify, measure, value and compare the cost and the consequences of the alternatives being considered [46]. The various methods of pharmacoeconomic

evaluation are cost-of-illness analysis, cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-benefit analysis (CBA) and cost-utility analysis (CUA) [47]. All these approaches consider the cost of the medical intervention itself together with the accompanying costs, but they differ in how they measure the outcome or utility of an intervention [48]. These methods vary primarily in the way effectiveness is valued. For example, for cost-minimization analysis, it is assumed there is no difference in drug effectiveness or side effects. In cost-effectiveness analysis, effectiveness is measured in natural, clinically derived units such as heart attacks avoided or life years saved. In cost-benefit analysis, a monetary value is assigned to effectiveness. And in cost-utility analysis – the recommended approach from an academic perspective – effectiveness is measured in quality-adjusted life-years (QALYs), which account for improvements in both life expectancy and quality of life [49].

The Cost minimization analysis (CMA) assumes that the effects of the two interventions being compared are equal and therefore compares costs. Cost effectiveness analysis (CEA) is used when the effects of the two interventions being compared are different (i.e., one intervention is superior to the other). Cost-utility analysis (CUA) is a special type of cost effectiveness analysis, in which the outcome is expressed as a utility measure (e.g., quality-adjusted life year [QALY]). Cost-benefit analysis (CBA) is derived from transport economics; both costs and benefits are expressed in monetary terms. For assessing pharmaceuticals, the first three types of evaluation are commonly used. Cost benefit analysis is far more challenging to carry out and interpret for health interventions, so papers describing cost-benefit analyses of pharmaceuticals should be interpreted with care [50]. For physicians, these economic analyses can help inform cost-effective care, such as in determining treatment strategies in RA and osteoarthritis, and assessing the risk of fragility fractures in osteoporosis [51].

The choice of the evaluation method depends on the nature of outcomes and the context in which the choices need to be made [52]. As disease state management continues to emerge as a cost-management, quality assurance strategy, formularies perse will wane in importance and pharmacoeconomics and outcomes data will increase in relevance as health professionals endeavor to find the most efficient and effective combinations of medical care [53]. Pharmacoeconomic evidences can be utilized to support decisions on licensing, pricing, reimbursement, and maintenance of formulary procedure of pharmaceuticals [54].

### Cost-Of-Illness Analysis (COI)

A cost of illness (COI) evaluation identifies and estimates the overall cost of particular disease for a defined population [55-59]. It involves identifying all the direct and indirect costs of a particular disease or illness within a healthcare system. It yields a total cost of a disease that can be compared to the cost of implementing a preventive or treatment strategy [46]. It is often referred to as burden of illness and involves measuring the direct and indirect costs attributable to a specific disease. The costs of various diseases, including diabetes, mental disorders, and cancer, in the United States have been estimated. By successfully identifying the direct and indirect costs of an illness, one can determine the relative value of a treatment or prevention strategy. For example, by determining the cost of a particular disease to society, the cost of a prevention strategy could be subtracted from this to yield the benefit of implementing this strategy nationwide. COI evaluation is not used to compare competing treatment alternatives but to provide an estimation of the financial burden of a disease. Thus, the value of prevention and treatment strategies can be measured against this illness cost [60].

### Cost Minimization Analysis (CMA)

Cost minimization analysis compares the cost of two similar interventions to ascertain which less expensive [61] is. It also reflects the cost of preparing and administering a dose. This method of cost evaluation is the one used most often in evaluating the cost of a specific drug. This method can only be used to compare two products that have been shown to be equivalent in dose and therapeutic effect [62]. One of the classical examples of this is a decision to prescribe a generic drug instead of brand name drug, which will achieve the same effect at lower cost [63, 64]. For a generic medication to be approved for market, the manufacturer must demonstrate to the Food and Drug Administration (FDA) that its product is bioequivalent to the initially branded medication. Therefore, when comparing medications that are the same chemical entity, the same dose, and have the same pharmaceutical properties as each other (brand versus generic or generic made by one company compared with a generic made by another company), only the cost of the medication itself needs to be compared because outcomes should be the same [65]. Another example of a CMA analysis includes measuring the costs of receiving the same medication in different settings. For example, researchers could measure the costs of receiving intravenous antibiotics in a hospital and compare this with receiving the same antibiotics (at the same doses) at home via a home health care service [65]. Therefore, this method is most useful for comparing generic and

therapeutic equivalents drugs. In many cases, there is no reliable equivalence between two products and if therapeutic equivalence cannot be demonstrated, then cost-minimization analysis is inappropriate [62].

### To perform a CMA, the following costs should be identified, measured, and then valued—

- Acquisition cost of the medicine
- Pharmacy, nursing, and physician costs (if they contribute significantly to the cost of using the medicine)
- Cost of equipment and supplies (e.g., syringes, needles, IV sets, sterile water for dilution)
- Cost of laboratory services (if a significant cost is involved)
- Indirect costs (such as time off work), but only if they can be measured and valued reliably [50].

By performing CMA it is evident that same drug molecule varying in costs has same drug strength content. Therefore it is assumed that these medications produce similar clinical outcomes. Considering the cost of medication as a factor for medication non-adherence, prescribing cheaper drugs to patients would increase adherence among patients resulting in better therapeutic outcomes. While prescribing the drugs to patients, physicians should also keep this information in mind to reduce health-economic burden on society [63].

### Cost Effective Analysis (CEA)

In applied health economics, a cost effectiveness analysis (CEA) is used to simultaneously compare the costs and outcomes of different interventions. In a CEA, a single clinical outcome is used to measure effectiveness, such as cure or remission, or avoidance of an event, for example, hospitalization [66]. It measures the resources expended for a given endpoint. The endpoint may be years of life gained, years of good vision gained, disability-free years, level of vision gained (such as 20/25), or any other endpoint [61].

The questions such analyses aim to answer are: how much does the new intervention cost compared with current practice and is it more effective; and if so, how much more? Cost-effectiveness analyses aim to provide the same information commonly used for making decisions about purchasing decisions in everyday life. If a new strategy or potential purchase is more effective and less costly than the currently available option, it is almost certainly worth doing, and in general such a strategy is called “dominant.” Likewise, if the new strategy is less effective and more costly, no one is likely to use it. However, the more usual outcome of a cost-effectiveness analysis of a health technology is that the

new technology may be more effective, but also more costly [67]. Good justification of a program/intervention in terms of costs and its effectiveness must be ascertained prior to implementation, therefore health economic evaluation studies using CEA may facilitate in the decision-making process for efficient resource allocation [68].

CEA involves a broader look at drug costs. Cost is measured in monetary terms and effectiveness is measured independently and may be measured in terms of a clinical outcome for, e.g., number of lives saved or complications prevented or diseases cured. CEA thus measures the incremental cost of achieving an incremental health benefit expressed as a particular health outcome that varies according to the indication for the drug. CEA provides a framework to compare two or more decision options by examining the ratio of the differences in costs and the differences in health effectiveness between options [62].

It measures effectiveness in natural units like decrease in uric acid level, decrease in blood glucose and the costs in money. The therapies with qualitatively similar outcomes are compared.

**The average cost-effectiveness ratio (ACER) or an incremental cost effectiveness ratio (ICER) is used to compare the treatment alternatives [69] and which may be calculated by the following equations-**

**ACER= Net Cost / Net Health Benefit**

**ICER = (Cost of drug A - Cost of drug B) / (Benefits of drug A – Benefits of drug B) = Difference in costs (A-B) / Difference in benefits (A-B)**

Cost-effectiveness is, by nature, incremental. Thus, it is necessary to look at the added costs compared with a control group. Selection of the appropriate control group is a challenge itself. At times, the appropriate control is placebo, and at other times, it is active therapy; the appropriate control is dependent on the clinical question being asked [70]. Cost-effectiveness analysis is not uniformly applied in the healthcare system. Decision makers often adopt new treatments without knowing if they are cost-effective. Even when cost-effectiveness has been studied, decision makers may not be able to interpret the data, or they may not agree with the results. Despite this limitation, cost-effectiveness is increasingly used to inform healthcare decision makers [71].

#### **Cost Benefit Analysis (CBA)**

Cost benefit analysis is the most comprehensive and the most difficult of all economic evaluation techniques [72]. The term CBA is often informally used to refer to any analysis used in decision-making that compares the

expected costs and benefits (both in monetary terms) of an investment. In principle, to be regarded as complete, a CBA should capture all benefits due to an intervention, valuing them either at their market value or at the level of consumption that individuals are willing to forego to obtain those [73]. CBA is best used in conjunction with traditional evaluation approaches rather than as a replacement approach. The use of CBA can help an evaluator to be more confident in stating the evaluation findings, particularly in social policy settings where the use and importance of CBA is growing [74]. It clearly embraces an enormous field. It offers clear guidelines for the evaluation of government decisions in such varied fields as tax, trade, or incomes policies; the provision of public goods; the distribution of rationed commodities; or the licensing of private investment [75]. It offers the opportunity to capture many benefits of public health interventions such as vaccination that may not naturally fit into a CEA framework. Other approaches, such as cost-consequences analysis and multiple criteria decision analysis, also admit a wider range of outcomes, but do not offer a straightforward way to synthesize multiple outcomes into a single measure [73].

These costs and benefits are expressed as a ratio (benefit to cost ratio), a net benefit or net cost. A clinical decision maker would choose the program or treatment alternative with the highest net benefit or the greatest benefit to cost (B/C) ratio [55, 76].

**Guidelines for the interpretation of this ratio are indicated as [55, 77-79]:**

If B/C ratio >1, the program or treatment is of value. The benefits realized by the program or treatment alternative outweigh the cost providing it.

If B/C ratio = 1, the benefits equal the cost. The benefits realized by the program or treatment alternative are equivalent to the cost of providing it.

If B/C ratio <1, the program or treatment is not economically beneficial. The cost of providing the program or treatment alternative outweigh the benefits realized by it.

The most difficult and challenging part of CBA lies in calculating the benefits in economic terms. Some benefits are easy to convert, others need subjective judgment. CBA may ignore intangible benefits (pain, anxiety, and stress) that are difficult to express in monetary terms. It may also discriminate against the unproductive population or the dependent population, e.g. the elderly [72].

### Cost Utility Analysis (CUA)

Cost-utility analysis is the most sophisticated form of pharmacoeconomic analysis that takes into account the improvement in quality of life and/or length of life conferred by an intervention for the resources expended [80]. It is like CEA in that there is a defined outcome and the cost to reach that outcome is measured in monetary terms. However in this case the outcome does not have to be measured on a common natural scale. Outcome in CUA in terms of changes in patient wellbeing (utility) and since such an outcome measure is not disease specific, CUA can in theory compare the 'value' of health interventions over more than one area of medicine (e.g. coronary artery bypass grafting versus the use of erythropoietin in treating anemia in chronic renal failure) [81].

CUAs show the relationship between the resources used (costs) and the health benefits achieved (measured as quality-adjusted life-years [QALYs]) for an intervention compared with an alternative strategy. Because CUAs allow for comparisons across a broad spectrum of interventions, conditions, and populations, such tools are useful to aid health care decision making [82]. As pressures to contain costs of medical care have escalated, cost-utility analysis (CUA) has received both critical acclaim and scrutiny as a methodology to inform decision makers regarding the economic value of health care interventions [83-89]. It is a popular choice of economic evaluation to inform health care decisions. CUA is used when the effectiveness of competing treatment alternatives involves both quality and length of life aspects [90,91].

Despite the theoretical advantages of CUA, certain methodological problems persist that require caution in its application. While QALYs are the best known summarization measure of utility, objections to their use have been raised. For example, it is often difficult to compare QALYs across people, because individuals' preferences over health states may differ according to whether or not they are in that state. Methods for eliciting preferences continue to undergo refinement for general applicability. In addition, and very importantly, some of the best known quality of life indices- whether generic or disease specific - which have been developed but cannot readily be transformed into QALYs. [92].

### CHALLENGES

Pharmacoeconomics is the part of health economics that focuses on the economic evaluation of pharmaceuticals. Health outcomes research, and patient-reported outcomes (PRO) in particular, aim at understanding patient value in terms of impact of disease and its treatment on physical functioning and psychosocial wellbeing, known also as "health-related quality of life" (HRQL). PRO's are usually measured by

self-reported questionnaires, thereby reflecting the patient's own viewpoint on the value of a new medicinal product. In many clinical development studies, HRQL is nowadays routinely measured to help establish the product's value for purposes of pricing and reimbursement. Despite this growing interest, both disciplines face numerous challenges going forward. Today, economic evaluation of new medicines is mandatory in many countries, so the question is no longer whether or not pharmacoeconomics is here to stay. But challenges remain mainly related to methodological issues. In contrast, I believe the jury is still out on HRQL and PRO research. A recent survey suggests that although clinicians recognize the importance of PRO's, limited experience and information is a barrier to the use of quality of life assessment in their own clinical practice [93].

The main challenges for pharmacoeconomics are:

1. Establishing guidelines or standards of practice.
2. Creating a cadre of trained producers and consumers of pharmacoeconomic work.
3. Continuing education on the relevant features of this discipline for practitioners, government officials, private sector executives.
4. Stable funding to support applied pharmacoeconomic research [1, 94].
5. Rise of non-communicable diseases, and growing patient expectations [95, 96].

Challenges in developing and implementing pharmacoeconomics guideline could be managed by involvement of all stakeholders. Some suggestions are as follow:

2. Concentrate on both direct and indirect services to decrease the burden of ailments such as improving nutrition, decrease poverty, develop infrastructure for healthcare and living healthy and prevent transmission of diseases by treating patients and immunizing public.
3. Improve access to life-saving medicines and affordability of essential medicines.
4. Consider healthcare as a basic necessity, individual right and responsibility.
5. Include pharmacoeconomics principles in medical, pharmacy, nursing, public health and other healthcare professional education [13].

### CONCLUSION

In the era of healthcare innovations and rising medical costs, the pharmacoeconomics focuses on 'value for money'; it evaluates the costs and effects of a pharmaceutical product. Pharmacoeconomic acts as



socioeconomic too, it relates patients, society and economy to drug therapy, various pharmacoeconomics methods can be applied for effective formulary management, individual patient treatments, medication policy, determination and resource allocation. Economic, Clinical and Humanistic outcomes is considered and valued using pharmacoeconomic evaluation methods, to inform local decision making whenever possible. By understanding the principles, methods, and application of pharmacoeconomics, pharmacists will be prepared to make better, more-informed decisions regarding the use of pharmaceutical products and services, that is, decisions that ultimately represent the best interests of the patient, the health care system, and society. Pharmacoeconomics can be applied to any therapeutic area like hospital pharmacy, using a variety of application strategies. As the healthcare sector is progressing day by day the need to develop Pharmacoeconomics area is must. Healthcare sector is not just a small area but it became an industry now. It has more dimensions to explore. Patients also get benefit out of Pharmacoeconomics findings. Pharmacoeconomics research should be strongly supported in a country like India where majority of health care spending is done by the patient's themselves.

## REFERENCES

- Surendra G. Gattani, Pharmacoeconomics: A Review, Asian Journal of Pharmaceutical and Clinicals Research, 2009, 2(3): 15-26.
- J Res Pharm Pract, Akram Ahmad, Isha Patel, Sundaranjan Parimilakrishnan, Guru Prasad Mohanta, Hae Chung Chung, Jongwha Chang, The role of pharmacoeconomics in current Indian healthcare system, 2013, 2(1):3-9.
- Parthasarathi G, Nyfort-Hansen K, Nahata MC., A Textbook of Clinical Pharmacy Practice, Essential Concepts and Skills, Pharmacoeconomics, Orient Longman Private Limited, 2007, 378.
- Br J Clin Pharmacol, Dyfrig A Hughes, Pharmacoeconomics, 2012; 73(6): 968–972.
- Purkiss R, Pharmacoeconomics – the importance for pharmacist, 2006; 13: 34.
- Dixon Thomas, Mickael Hiligsmann, Denny John, Ola Ghaleb Al Ahdab, Hong Li, Pharmacoeconomic Analyses and Modeling, Clinical pharmacy drug information pharmacovigilance pharmacoeconomics and clinical research,18 (Elsevier, 2019), 261-275.
- Odilia Osakwe, Clinical Development: Ethics and Realities, 9 (Elsevier, 2016), 191-220.
- Mahendra rai, Richa Goyal, Pharmacoeconomics in healthcares, Pharmaceutical medicine and translational clinical research, 33 (Elsevier, 2018), 465-472.
- MeiJen Ho, Joish NV, Biskupiak EJ, The role of pharmacoeconomics in formulary management: Triptan case study for migraine, Pharmacy and Therapeutics Journal, 2005;30:46.
- Bennett PN, Brown MJ, Topics in drug therapy, Clinical Pharmacology, 9th ed, Edinburgh, Churchill Livingstone, 2003, 24.
- Wally T, Haycox A, Bolond A, Pharmacoeconomics, Churchill Livingstone publication, 1st edition, 1-14.
- Mori, A.T., Robberstad, B. Pharmacoeconomics and its implication on priority-setting for essential medicines in Tanzania: a systematic review. BMC Med Inform Decis Mak 12, 2012, 110.
- Pharmacoeconomic & outcomes research guidelines for India, PEOR guideline. (available from: [https://www.ispor.org/docs/default-source/asia-consortium/peguidelines\\_india\\_march2016.pdf?sfvrsn=23205d6d\\_2](https://www.ispor.org/docs/default-source/asia-consortium/peguidelines_india_march2016.pdf?sfvrsn=23205d6d_2))
- Gordon G. Liu, Karen Eggleston, Teh-wei Hu, Emerging health economics and outcomes research in the Asia-Pacific region, 2008, 11:S1–S2.
- Garman L. The Dual Burden of Disease in India, What's Going on at GRAVIS. 2013. Available from: <https://gravisindia.wordpress.com/2013/04/15/the-dual-burden-of-disease-in-india/>
- Ander Anell, Priority setting for pharmaceuticals, The European Journal of health economics, 2004, volume 5, 28-35.
- National Institute for Health and Clinical Excellence: Guide to the methods of technology appraisal, Pharmacoeconomics, 26, (Springer Link, 2008), 725-727.
- CADTH: Guidelines for the economic evaluation of health technologies. 2006, Ottawa, Canada: Canadian Agency for Drugs and Technologies in Health. ([https://www.cadth.ca/media/pdf/186\\_EconomicGuidelines\\_e.pdf](https://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf))
- Piyameth Dilokthornsakul, Dixon Thomas, Lawrence Brown, Nathorn Chaiyakunapruk, Chapter 19 – Interpreting Pharmacoeconomic Findings, Clinical Pharmacy drug information pharmacovigilance pharmacoeconomics and clinical research, 19 (Elsevier, 2019), 277-287.
- Dominik Grega, Jozef Kolar, Historical analysis of pharmacoeconomics terms, 2019, Volume 119, 1643-1654.
- Dev Priya, Suresh Purohit, B.L.Pandey, Prabhat Upadhyay, A Brief Description of Pharmacoeconomics, 2015, Volume 3, Issue 11, 20-32.
- <https://www.pharmatutor.org/articles/brief-review-need-of-pharmacoeconomics-in-indian-health-care-system>
- Sonia Scaria, Remya Raju, Sijimol Joseph, Athria A. Nair, Pharmacoeconomics: Principles, methods and Indian scenario, 2015, 37-46.
- Mauskopf JA, Why Study Pharmacoeconomics, Expert. Rev. Pharmacoeconomics outcomes Res. 2001, 1(1): 1-3.
- J Lyle Bootman, Raymond J Townsend, William F McGhan, Chapter 1, Introduction to pharmacoeconomics, Principles of pharmacoeconomics. ([http://fbemoodle.emu.edu.tr/pluginfile.php/36065/mod\\_resource/content/1/chp1-introduction%20to%20pharmacoeconomics.pdf](http://fbemoodle.emu.edu.tr/pluginfile.php/36065/mod_resource/content/1/chp1-introduction%20to%20pharmacoeconomics.pdf))
- Postma MJ, Pharmacoeconomic research, Pharma world sci, 2003, 25(6):245-6.
- <https://wolterskluwer.com/company/newsroom/news/health/2010/09/special-issue-of-pharmacoeconomics-to-focus-on-comparative-effectiveness-research.html>
- Hinchagri SS, Halakatti P.K., Devar SB, Biradar BS, Kankanwadi SK, Patil SD. „Need Of Pharmacoeconomics In Indian Health Care System. A Brief Review“. Pharmatutor-Art-I.D 1277, 2015.
- Ron Purkiss, Pharmacoeconomics- the importance for pharmacists, Hospital Pharmacist, Vol. 13, p34, URI: 10021363, 2006. (<https://www.pharmaceutical-journal.com/news-and-analysis/pharmacoeconomics-the-importance-for-pharmacists/10021363.article?firstPass=false>)
- Debjit Bhowmik S.Duraivel, Rajalakshmi A.N, K.P.Sampath Kumar, Pharmacoeconomic: A Review, Elixir Pharmacy, 69 (2014) 23672-23675.
- George W. Torrance, Greg L Stoddart, Karl Claxton, Mark J Sculpher, Michael F Drummond, Methods of economic evaluation of health care programmes, 4th Edition.

- ([https://books.google.co.in/books?hl=en&lr=&id=yZSCwAAQB AJ&oi=fnd&pg=PP1&dq=.+George+W.+Torrance,+Greg+L+Stoddart,+Karl+Claxton,+Mark+J+Sculpher,+Michael+F+Drummond,+Methods+of+economic+evaluation+of+health+care+programmes,+4th+Edition.&ots=\\_aVapD6nFM&sig=3vNnkdr373vDQFdoxPN94eqRkY&redir\\_esc=y#v=onepage&q=.%20George%20W.%20Torrance%20Greg%20L%20Stoddart%20Karl%20Claxton%20Mark%20J%20Sculpher%20Michael%20F%20Drummond%20Methods%20of%20economic%20evaluation%20of%20health%20care%20programmes%204th%20Edition.&f=false](https://books.google.co.in/books?hl=en&lr=&id=yZSCwAAQB AJ&oi=fnd&pg=PP1&dq=.+George+W.+Torrance,+Greg+L+Stoddart,+Karl+Claxton,+Mark+J+Sculpher,+Michael+F+Drummond,+Methods+of+economic+evaluation+of+health+care+programmes,+4th+Edition.&ots=_aVapD6nFM&sig=3vNnkdr373vDQFdoxPN94eqRkY&redir_esc=y#v=onepage&q=.%20George%20W.%20Torrance%20Greg%20L%20Stoddart%20Karl%20Claxton%20Mark%20J%20Sculpher%20Michael%20F%20Drummond%20Methods%20of%20economic%20evaluation%20of%20health%20care%20programmes%204th%20Edition.&f=false))
32. Albert I Wertheimer, The Importance of Pharmacoeconomics, 2014, 2:1.
  33. C.E. Reeder, Overview of Pharmacoeconomics and pharmaceutical outcomes evaluations, American Journal of health-system pharmacy, 1995, 52, S5-S8.
  34. Clin Ther, Kozma CM, Reeder CE, Schulz RM, Economic, Clinical and humanistic outcomes: a planning model for pharmaco-economic research, 1993, 15(6): 1121-32.
  35. Drug Commercialization course (coursera), Jan D. Hirsch, University of California. (<https://www.coursera.org/learn/drug-commercialization>)
  36. A Fasseeh, B Nemeth, A Molnar, F-U Fricke, M Horvath, K Koczian, A Gotze, Z Kalo, A systematic review of the indirect costs of schizophrenia in Europe, European journal of public health, 2018, 28, 1043-1049.
  37. Available from: <https://emedicine.medscape.com/article/288259-overview>
  38. Saarni SI, Viertiös, Perälä, et al, Quality of life of people with schizophrenia, bipolar disorder and other psychotic disorders, Br J Psychiatry, 2010, 197:386 – 94.
  39. G. Kovacs , T. Almasi a , A. Millier, M. Toumi , M. Horvath , Kristof Koczian , A. Gotze, Z. Kaloa , A.T. Zempenyi a, Direct healthcare cost of schizophrenia – European overview, European psychiatry, Elsevier, 2018, volume 48, 79-92.
  40. Mancuso A, Specchia ML, Lovato E, et al., Economic burden of schizophrenia: the European situation. A scientific literature review, Eur J Public Health, 2014, 24(suppl-2):352.
  41. C Carter, M Stevens, M Durkin, Effects of risperidone therapy on the use of mental health care resources in Salt Lake country, Utah, 1998, 20(2):352-63.
  42. Fabio Antonaci, Natascia Ghiotto, Shizheng Wu, Ennio Pucci, Alfredo Costa, Recent advances in migraine therapy, springerplus, 2016, 5:637.
  43. Hans-Christoph Diener, Dagny Holle-Lee, Steffen Nagel, Thomas Dresler, Charly Gaul, Hartmut Gobel, Katja Heinze- Kuhn, Tim Jurgens, Peter Kroop, Bianca Meyer, Arne May, Laura Schulte, Kasia Solbach, Andreas Straube, Katharina Kamm, Stephanie Forderreuther, Andreas Gantenbein, Jens Petersen, Peter Sandor, Christian Lampl, Treatment of migraine attacks and prevention of migraine: Guidelines by the German migraine and headache society and the German society of neurology, 2019, 3:1.
  44. Dulli DA, Ann Pharmacother, Naratriptan: an alternative for migraine, 1999, 33(6):704-11.
  45. J J Caro, D Getsios, G Raggio, G Caro, L Black, Treatment of Migraine in Canada with Naratriptan: A cost effective analysis, 2001, 41(5):456-64.
  46. Available from: <https://www.scribd.com/document/307161801/TYPES-OF-ECONOMIC-AND-HUMANISTIC-OUTCOMES-ASSESSMENTS>
  47. Nishanthi Anandabaskar, Pharmacoeconomics, Introduction to basics of Pharmacology and Toxicology, 2019, 297-301.
  48. Vasilios Fragoulakis, Christina Mitropoulou, Marc S Williams, George P Patrinos, Economic evaluation and genomic medicine: what can they learn from each other, 3(Elsevier, 2015), 27-36.
  49. David L. Veenstra, Economic issue and genomic medicine, Volume 1, 2013, 440-446.
  50. Available from: [https://www.who.int/medicines/technical\\_briefing/tbs/06-TG\\_Evaluating-drug-costs\\_final-08.pdf?ua=1](https://www.who.int/medicines/technical_briefing/tbs/06-TG_Evaluating-drug-costs_final-08.pdf?ua=1)
  51. John B. Wong, principles of health and application to rheumatic disorders, Rheumatology, 6th edition, 2015. (<https://www.sciencedirect.com/book/9780323091381/rheumatology#book-description>)
  52. Ahuja J, Gupta M, Gupta AK, Kholi K, Pharmacoeconomics, The national medical journal of india, 2004, 17(2):80-83.
  53. C.E. Reeder, Overview of pharmaco-economics and pharmaceutical outcomes evaluations, American Journal of Health- System Pharmacy, 1995, Volume 52, S5-S8.
  54. Prasanna kumar desu, Sri Lakshmi G, Sai Shankar, Desu Prasanna Kumar, Venkateswara Rao, Pharmacoeconomics: An Overview, Universal Journal of Pharmacy, 2018, 7 (3).. ([https://www.researchgate.net/publication/330193884\\_PHARMACOECONOMICS\\_AN\\_OVERVIEW](https://www.researchgate.net/publication/330193884_PHARMACOECONOMICS_AN_OVERVIEW))
  55. Ojaswi Ghadge, Anubha Khale, Pharmacoeconomics- A brief review, 2012, 29-36.
  56. JL Bootman, RJ Townsend, WF McGhan, Principles of Pharmacoeconomics, 3rd Ed. Cincinnati, (Harvey Whitney Books, 2005), 432-459.
  57. Available from: <http://www.scribd.com/doc/15998679/Pharmacoeconomics-Accessed>
  58. Available from: <http://www.accesspharmacy.com/content.aspx?aID=7965070-Accessed>
  59. Weinstein MC, Stason WB., Foundations of cost-effectiveness analysis for health and medical practices, New England journal of medicines, 1997, 296:716-22.
  60. Available from: <https://www.pharmatutor.org/articles/pharmacoeconomics-the-cost-of-health?page=1>
  61. Gary C Brown, Melissa M Brown, Value- based medicine and pharmacoeconomics, 2016, 55:381-90.
  62. Mahendra Rai, Richa Goyal, Pharmacoeconomics in healthcare, Pharmaceutical medicine and translational clinical research, 2018,465-472.
  63. Jainam V., Patni Kalyani N., Deshpande Shrikalp S., Pharmacoeconomic evaluation, cost minimization analysis of anti-diabetic therapy in Gujarat, International journal of medical research & health science, 2016, 5:3.
  64. Walley T, Haycox A, Boland A, Pharmacoeconomics, Churchill Livingstone (Elsevier Science, 2003). (<https://www.elsevier.com/books/pharmacoeconomics/walley/978-0-443-07240-6>)
  65. Available from: [http://downloads.lww.com/wolterskluwer\\_vitalstream\\_com/sample-content/9780781765442\\_Rascati/samples/Chaper04.pdf](http://downloads.lww.com/wolterskluwer_vitalstream_com/sample-content/9780781765442_Rascati/samples/Chaper04.pdf)
  66. Available from: <http://www.pharmideas.com/pharmacoeconomics>
  67. Afshin Farzaneh-Far, Juerg Schwitter, Raymond Y. Kwong, 49 - Cost- effectiveness analysis for cardiovascular magnetic resonance imaging, Cardiovascular magnetic resonance (3rd edition), A companion to Braunwald's heart disease, 2019, 568-573.
  68. Rosliza Abdul Manaf, Muhamad Hanafiah Juni, Faisal Ibrahim, Noor Haslinda Ismail, Designing and conducting cost-effectiveness analysis studies in healthcare, International journal of public health and clinical sciences, 4(5), 2017, 62-76.
  69. Dr. Sabita Paudel, Short communication outlook of pharmacoeconomics and its status in Nepal, 14(1) 2018, 56-58.
  70. William S. Weintraub, David J. Cohen, The limits of cost-effectiveness analysis, 2009, 2:55-58.
  71. Available from: <https://www.herc.research.va.gov/include/page.asp?id=cost-effectiveness-analysis>

72. Jaya Ahuja, Madhur Gupta, Ajay Kumar Gupta, Kamlesh Kohli, Pharmacoeconomic, The national medical journal of India, 2004, Volume 17, 80-83.
73. Minah Park, Mark Jit, Joseph T. Wu, Cost-benefit analysis of vaccination: a comparative analysis of eight approaches for valuing changes to mortality and morbidity risks, 2018, 16:139.
74. John Liddle, Matt Wright, Bronte Koop, Cost-benefit analysis explained, Volume 15, 2015, 33-38.
75. Jean Dreze, Nicholas Stern, Chapter 14 Theory of cost benefit analysis, Handbook of public economics, 1987, Volume 2, 909-989.
76. P Belien, Healthcare systems. A New European Model? 2000, 85.
77. Available from: <http://www.scribd.com/doc/15998679/Pharmacoeconomics-Accessed>
78. Available from: <http://www.accesspharmacy.com/content.aspx?aID=7965070-Accessed>
79. Helper CD, Strand LM, Opportunities and responsibilities in pharmaceutical care, American Journal of hospital pharmacy, 1990, 47:533-543.
80. Gary C. Brown, Melissa M. Brown, Value based medicine and pharmacoeconomics, Retinal pharmacotherapy, (Elsevier, 52), 2010, 356-361.
81. Br J Clin Pharmacol, T. Walley, A. Haycox, Pharmacoeconomics: Basic concepts and terminology, 1997, 43:343-348.
82. Teja Thorat, Pei-Jung Lin Peter J, Newmann, The state of cost utility analyses in Asia: A Systematic Review, Value in Health Regional Issues, 2015, 7-13.
83. Christine M. McDonough, Anna N. A. Tosteson, Measuring preferences for cost-utility analysis: How choice of method may influence decision-making, 2007, 25(2), 93-106.
84. Luce BR, What will it take to make cost-effectiveness analysis acceptable in the Unites States?, Medical care, (Pubmed 2005), 44-48.
85. Neumann PJ, Why don't Americans use cost-effectiveness analysis? American journal of managed care, Pubmed, 2004, 10:308-312.
86. Neumann PJ, Greenberg D, Olchanski NV, Stone PW, Rosen AB, Growth and quality of the cost-utility literature, Value in health, Pubmed, 2005, 8(1):3-9.
87. Neumann PJ, Divi N, Beinfled MT, Levine BS Keenan PS, Halpern FF, et al., Medicare's national coverage decisions, Quality of evidence and review times, Health affairs, Pubmed, 2005, 24(1), 243-254.
88. Thorpe KE, The rise in health care spending and what to do about it, Health affairs, 2005, 24(6), 1436-1445.
89. Foote SB, Neumann PJ, The impact of Medicare modernization on coverage policy: Recommendations for reform, The American journal of managed care, Pubmed, 2005, 11(3), 14-142.
90. Jeffery S. Hoch, Anneliese Poetz, Economics and healthcare understanding cost utility analysis in healthcare, University of Toronto Medical Journal, volume 83, number 1, December 2005, 126-130. ([https://www.researchgate.net/publication/50854724\\_Understanding\\_Cost-utility\\_Analysis\\_in\\_Health\\_Care](https://www.researchgate.net/publication/50854724_Understanding_Cost-utility_Analysis_in_Health_Care))
91. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL, Methods for the economic evaluation of health care programmes, 2005, 3rd edition, 137-209.
92. Br J Clin Pharmacol, T. Walley, A. Haycox, Pharmacoeconomics: Basic concepts and terminology, 1997, 43:343-348.
93. Dominique Dubois, Grand challenges in Pharmacoeconomics and health outcomes, PubMed, 2010.
94. Lyles A, Recent trends in pharmacoeconomics: Needs and unmet needs, European journal of pharmaceutical sciences, 2008, 34: S7-S24.
95. Mihajlo Jakovljevic, Nick Verhaeghe, Kyriakos Souliotis, Editorial: Challenges of Pharmacoeconomics in global health arena, PubMed Central, 2018, 6:368. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6315142/>)
96. Murata C, Yamada T, Chen C-C, Ojima T, Hirai H, Kondo K, Barriers to health care among the elderly in Japan, Pubmed Central, Int J Environ Res Public Health, 2010, 7:1330-41.