ABSTRACT
Pharmacoeconomics can aid the policy makers and the healthcare providers in decision making in evaluating the affordability of and access to rational drug use. Efficiency is a key concept of pharmacoeconomics, and various strategies are suggested for buying the greatest amount of benefits for a given resource use. Pharmacoeconomic evaluation techniques such as cost minimization analysis, cost effectiveness analysis, cost benefit analysis, and cost utilization analysis, which support identification and quantification of cost of drugs, are conducted in a similar way, but vary in measurement of value of health benefits and outcomes. This article provides a brief overview about pharmacoeconomics, its utility with respect to the Indian pharmaceutical industry, and the expanding insurance system in India. Pharmacoeconomic evidences can be utilized to support decisions on licensing, pricing, reimbursement, and maintenance of formulary procedure of pharmaceuticals. For the insurance companies to give better facility at minimum cost, India must develop the platform for pharmacoeconomics with a validating methodology and appropriate training. The role of clinical pharmacists including PharmD graduates are expected to be more beneficial than the conventional pharmacists, as they will be able to apply the principles of economics in daily basis practice in community and hospital pharmacy.

Keywords: Drug costs; drug industry; formularies; health insurance; pharmacoeconomics

INTRODUCTION
Healthcare community is ever more sensitive to costs, as the overall health expenditures are escalating. Accordingly, appraisal of goods and services in healthcare goes beyond evaluation of safety and efficacy in which the economic impact of these goods and services on the cost of healthcare is also considered. As in economics, efficiency is the key concept in the pharmacoeconomics, and this principle helps one to design strategies for buying the greatest amount of benefits for a given resource use.[1]

Resources such as materials and equipments allocated for healthcare are scarce; nevertheless, their possible usages are infinite. Hence, it is a challenge for healthcare professionals to provide quality patient care with minimum cost. Given the limitations on healthcare resources, there is increased interest in assessing the value for money, or economic efficiency of healthcare treatments and programs. Economic evaluation, analyzing costs and outcomes of several alternative therapies can also be a useful approach; though can be very difficult to accomplish.[2]

In an environment where the cost of healthcare is sky rocking, 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.[3] “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
Pharmacoeconomics identifies, measures, and compares the costs and consequences of pharmaceutical products and services. It involves economic evaluation of drug development, drug production, and drug marketing, i.e., all the steps that take place from the time the drug is manufactured to when it reaches the patients.

Pharmacoeconomics
The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) defines pharmacoeconomics as “the field of study that evaluates the behavior of individuals, firms, and markets relevant to the use of pharmaceutical products, services, and programs, and which frequently focuses on the costs (inputs) and consequences (outcomes) of that use.”

Genesis of pharmacoeconomics
Pharmacy was finally recognized as a clinical discipline within the healthcare system in the early 1960s. At this time, disciplines within the pharmaceutical sciences such as clinical pharmacy, drug information, and pharmacokinetics became an important part of pharmacy education and sciences. 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, et al., 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 septicemia. 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.

Initially, defined as “analysis of the costs of drug therapy to healthcare systems and society”, 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.

Methods of pharmacoeconomic analysis
Pharmaceutical studies compare costs, clinical, and humanistic outcomes associated with different therapies. The evaluation mechanisms delineated are often helpful in demonstrating the cost impact of innovative treatments, granting greater acceptance by healthcare providers, administrators, and the public.

There are four major types of pharmacoeconomic analysis:
A: Cost-minimization analysis
B: Cost-effectiveness analysis
C: Cost-benefit analysis
D: Cost-utility analysis

Major types of pharmacoeconomic analysis, formula and application given in Table 1.

Healthcare and financing system in India
The Indian pharmaceutical industry is a hub where medications can be produced at a low price and still be of international quality. It witnessed a robust growth from the production turnover of about 1.14 billion dollars in 1990 to over 22.73 billion dollars in 2009-10, comprising about Rs, 14.1 billion dollars of domestic market and 9.38 billion dollars of exports. In terms of production, the India pharma industry ranks 3rd on a global scale, whereas in terms of turnover worth, it ranks 14th. Medication prices are among the lowest prices in the world. However, the overall expenses associated with medications continue to soar in the country. Although India is a producer of abundance of quality drug at low cost, only one third of its population has access to essential medicines.

More than 68% (Census 2011) of the population lives in villages and work on farms or perform other menial jobs and are paid on a day to day basis. In rural areas comprised of villages and small towns, primary health-centers and community health-centers are put into service by the state government. On the breadline, the rural population heavily depend on the government funded hospitals for procuring healthcare.

In India, allopathic and alternative medicine healthcare practices (Ayurveda, Unani, Siddha, and Homeopathy) operate side by side. Many patients switch from one practice to another when relief is not adequate. The quality of healthcare services is much better in the urban areas compared with rural areas. Some rural areas might have very minimalistic healthcare. The practice of procuring private healthcare for many people is on the rise. The challenge that the Indian government faces is to make healthcare affordable for the majority of people in the country who cannot afford healthcare. Allopathic medications have a big market in India. In 2004, 5.2% of nominal GDP was spent on producing allopathic medications which is equivalent to US $34.9 billion. In 2005-2009, it grew by 12% per annum, i.e., 5.5% of nominal GDP which is equivalent to US $60.9 billion. As far as the ratio of doctors and
nurses to the population is concerned, it is 5.9 doctors, 0.8 nurses, and 0.47 midwives for 1,000 people, which adds up to 1.86 health workers for every 1000 population.

The statistics provided by the Union Ministry of Health and Family Welfare's Health Information of India state that in 2004, there were 67,576 government doctors in India who provided healthcare to 15,980 people.

Out of the $24 million spent on healthcare in India, about 77% money is spent on private healthcare, and the rest is out of pocket expenditure.

Despite the significant expenditure on healthcare, India's healthcare system faces several challenges. For instance, the public sector expenditure is 21%, i.e. US $5.04 million, and the external aids amount to the remaining 2%, i.e., US $0.48 million.

Limited number of people have health insurance in India. The major issues that govern insurance penetration are the extent and type of coverage. About 10% of the total population has insurance through health financing schemes. The ironic situation is that the insurers leave out the poor and the ill population as they cannot afford the prepayment schemes. The insurance that people purchase voluntarily accounts for Rs. 4 billion, i.e., US $86.3 million, and is estimated to grow at a very fast pace.

### Applications of pharmacoeconomics

Historically, the principles of pharmacoeconomics were applied in the field of hospital pharmacy activities. The cost effectiveness data were used to support the addition or deletion of a drug to or from a hospital formulary. At present, the pharmacoeconomic assessment of formulary actions has become a standardized part of many pharmacy and therapeutic committees.

### Pharmacoeconomic studies find value in

1. Fixing the price of a new drug and re-fixing the price of an existing drug.
2. Finalizing a drug formulary.
3. Creating data for promotional materials of medicines.
4. Compliance of requirement for drug license.
5. Including a drug in the medical/insurance reimbursement schemes.
6. Introduction of new schemes and programs in hospital pharmacy and clinical pharmacy.
7. Drug development and clinical trials.

### Pharmacoeconomics and drug development

In India, the estimate for the development of New Chemical Entity (NCE) is often quoted at US $90-100 million due to lower input costs. For every 10,000 NCE in discovery, ten enter preclinical development, five enter human trials, and only one might be approved. Accordingly, large amount of money spent on pursuing a useless chemical entity is borne by the consumer. Pharmacoeconomic studies may be planned and conducted at the clinical development stages (phases 1 to 3) and post-marketing research stage (phase 4). Subsequently, studies may need to be conducted at several stages of pharmaceutical research.

### Phase 1 trials

The initial clinical trial endeavors to determine the toxicity profile of the drug of interest in humans. It is during this stage that cost of illness studies should be accomplished to aid in deciding whether to further develop the drug and gather background data for future pharmacoeconomic evaluations or not.

### Table 1: Major types of pharmacoeconomic analysis-definition, formula and applications

| Economic analysis | Definition | Formula/example | Applications |
|-------------------|------------|-----------------|--------------|
| Cost minimization analysis | Compares interventions with similar outcomes and determines the optimal strategy based on costs | Drug A: Cost ($)=3000, Benefits (life year)=2.5 | CMA shows cost savings of the treatment programme over another. It aids formulary decision making |
| Cost effectiveness analysis | Compares strategies on the basis of dollars/pounds/other currencies per physical unit of improvement in clinical outcome (e.g., life-years gained, mm HG blood pressure reduction) | Cost effectiveness ratio=Net cost of intervention/net change in health effect | CEA is useful in comparing cost with health outcomes for individual patients. It provides data to endorse drug policy formulary system and individual patient treatment decisions |
| Cost benefit analysis | Translates all outcomes of interest into monetary units (e.g., dollars). Used primarily to make resource allocation decisions when effectiveness of interventions does not need questioning | Net benefit=net benefits-net costs. If net benefit=0, then program is cost beneficial | CBA is used mainly at the macro level for policy decisions on health care program |
| Cost utilization analysis | Compares strategies on the basis of dollars per unit of health, adjusted for preferences or quality | Cost/Quality ratio=Costs/quality adjusted life years (QALYs/DALYs/DALE) | CUA compares treatment program with different outcomes and various health programs. The basic goal is to improve QOL |

CMA = Cost minimization analysis, CEA = Cost effectiveness analysis, CBA = Cost benefit analysis, CUA = Cost utilization analysis, QALYs = Quality adjusted life years, DALYs = Disability adjusted life years, DALE = Disability adjusted life expectancy, QOL = Quality of life
of illness data may also aid in the development of preliminary models to assess the clinical benefits that must be achieved to have a marketable product.

**Phase 2 trials**

In phase 2 trials, the drug is administered to a limited number of patients with the target disease. During this phase, cost of illness studies can begin or continue, as can preliminary development of quality of life and recourse utilization instruments. Models can be refined as more information is available about the clinical aspects of the drug.

**Phase 3 trials**

Cost of illness data can be an important factor that can determine the marketability of drugs. In the phase 3 clinical trials, the drugs are administered to the patients similarly as they would be when they are marketed. At this stage, the discussion, planning, and pharmacoeconomic studies are of prime importance. It is recommended that clinical studies presenting pharmacoeconomic evaluation be conducted along with efficacy evaluation of the drugs. Even though pharmacoeconomic evaluations might be time consuming and may delay the new drug application (NDA) process, they should be done unless the drug is very innovative and has no other alternatives.

**Phase 4 trials**

Phase 4 trials consist of the post-marketing phase. Pharmacoeconomics can be applied to retrospective and prospective studies involving the drug. Pharmacoeconomic evaluations provide information about cost and outcomes of drugs in real life settings unlike clinical trials that are conducted in controlled settings. Pharmacoeconomic evaluations conducted during clinical trials give information about the efficacy of drugs, which in turn provide an approximation to the real world. Pharmacoeconomic evaluations and clinical trials can be conducted in conjunction with each other in several ways:

1. A clinical trial can be designed to test the safety and efficacy of a drug, followed by a pharmacoeconomic evaluation.
2. A clinical trial can be designed to conduct a pharmacoeconomic evaluation.
3. Clinical data collected prospectively in a clinical trial can be used to conduct a retrospective or prospective pharmacoeconomic evaluation.

**Compliance of requirement for drug license and pharmacoeconomics**

Evidence about drug quality, efficacy, and safety is an essential requirement for drug licensing and regulation. Given the ever-increasing healthcare costs, this evidence needs to be backed by evidence of cost-effectiveness as well. In simple words, evidence comparing the effectiveness of available treatments for a particular disease condition and their related costs need to be presented to the federal body before they are introduced in the market.

Australia was the first country to form evidence based guidelines about medication reimbursement on the basis of cost-effectiveness research. Since 1993, the Australian Pharmaceutical Benefit Scheme enforces the production of evidence about economic evaluation of the drug before its introduction in the market. The drug manufacturer provides the submission form to the Pharmaceutical Benefits Advisory Committee for inclusion of the drug in the reimbursement list who then verify the evidence provided by the manufacturer. The committee provides recommendations to the health ministry about drug inclusion in the reimbursement list on the basis of evidence about its cost effectiveness. The final decision making by the policy makers about the cost-effectiveness of the drug is determined by the following factors:

1. The importance of the clinical area
2. The availability of alternative treatments
3. The likely effect of listing on the healthcare system and other therapeutic activities
4. The investment of the sponsor in primary research.

The committee is willing to introduce a “breakthrough” medication which might be a bit pricey, provided the manufacturer has invested considerably in its development and production in contrast to ‘me-too drugs’ which have similar counterpart's existent in the market. In spite of this, relative cost effectiveness is an important criterion. So, many other countries like UK, Belgium, Finland, Norway, Portugal, Sweden and Hungary also follow a similar process such as Australia. The Netherlands also introduced a formal process of economic evaluation in 2005. Germany has an institution for economic evaluation research and Spain has regional centers that perform health technology assessment. In Denmark, France, and Italy, pharmaceutical companies provide data about economic evaluation on a voluntary basis. These data when provided are given importance and consideration. Food and Drug Administration (FDA) in United States and Central Drug Standard Control Organization (CDSCO) in India do not require an economic analysis for Drug approval. A new drug has to be approved for a program based on pharmacoeconomic analysis.

**The formulary system**

Formulary creation involves preparing, updating, and using a list of essential medications with their detailed information (formulary manual) and standard treatment guidelines (STGs). A formulary list is an
indicator of good pharmaceutical practice and rational drug usage. The formulary consists of appropriate therapies and cost-effective medications which are of a good quality. It is a precise list which makes the process of procuring, storing, distributing, and using the drugs very easy.[21] The medications that are part of a formulary, have the following advantages:

1. Availability of cost contained quality drugs: When medications are purchased in bulk, there is more price competition and “economies of scale” for procuring, storing, and distributing the quality drugs. This makes it possible to provide drugs at subsidized rates to people who require them the most.

2. Provision of quality care: Healthcare personnel can be better trained to provide cost effective medications. Usage of cost-effective drugs will also make the practitioners prescribe fewer drugs whose drug interactions and adverse reactions they are aware of. This in turn will improve the provision of quality care as the selection of medication is evidence based.

The formulary system, right from the national level to the institutional level, can be strengthened with the help of studies in the areas. It will also help for the rationalization of the drug procurement system in the country and for the practical implementation of the standard treatment protocols.

HEALTH INSURANCE AND PHARMACOECONOMICS IN INDIA

In the Indian health insurance system, mostly inpatient services are covered, so it is necessary to stay for a day in the hospital to claim the insurance. This, instead of saving costs leads to cost inflation. It is necessary to have some mechanism in place, whereby the insurers can strike a contract with healthcare providers and healthcare systems that can help in cost containment.[21,22] There is an added need for insurance systems that encourage consumer to contain costs by providing incentives as well as contain their health expenditure.[23] In case of members with multiple coverage, it is necessary that the benefits offered and liability achieved are coordinated and regulated. There needs to be further expansion of insurance services other than inpatient services, and more focus should be placed on preventive care and wellness programs.[24]

By implementing pharmacoeconomic principle in the hospital administration and treatment protocols, both the patients and the insurance industry will benefit. Patients will receive better quality healthcare at reduced costs, and the insurance companies will be able to provide enhanced care to their clients at minimum cost.

Indian pharmacy practice and pharmacoeconomics

As third largest producer of drugs by volume, Indian pharmaceutical industry has diversity of medicines; yet, brand name prescriptions are the rule of the day. Formulary system is very weak and treatment protocols exist only in theory. The resources are scarce and competing programs are plenty in healthcare. The concept of healthcare insurance is yet to be popularized in the country.[1] Given the issues prevalent in the Indian healthcare system, pharmacoeconomics has many applications. Pharmacoeconomics can aid in decision making when evaluating the affordability of and access to the right medication to the right patient at the right time, comparing two drugs in the same therapeutic class or drugs with similar mechanism of action, and in establishing accountability that the claims by a manufacturer regarding a drug are justified.

Practicing pharmacists in community, hospital, and clinical settings in India can benefit considerably from the application of the principles of pharmacoeconomic into their normal practice settings. Proper application of pharmacoeconomics will empower the pharmacy practitioners and administrators to make better and more informed decisions regarding products and services they provide. Pharmacotherapy decisions traditionally depended solely on clinical outcomes like safety and efficacy, but pharmacoeconomics teaches us that there are three basic outcomes to be considered clinical, economic, and humanistic in drug therapy. It is accepted by all that appropriate drug selection decisions could not be made today based on acquisition costs only. Applied pharmacoeconomics can help in decision making, in assessing the affordability of medicines to the patients, access to the medicines when needed, and comparing various products for treatment of a disease. It will provide evidence contraindicating the promotion of certain types of high-cost medicines and services.

Pharmacoeconomics has use in health policy decision making and can be applied by a number of healthcare professionals such as policy makers, primary healthcare providers, health-care administrators, and health managers. Available in large quantities, Indian primary care providers are often bombarded with many new drugs of the same category, in addition to the existing drugs. Introduction of new drugs can confuse the doctors and administrators for the judicious selection and rational use of medicines. When introducing new medications, its outcome should be equal or more effective compared to the existing drug and shall have some economic or related advantage.

Evidence about pharmacoeconomics can aid pharmacists and policy makers in the decision-making process about the use of medications and healthcare services. With clinical training about self-medication,
Ayush physicians, i.e., Ayurvedic and Naturopathic physicians focus more on diagnostic rather than therapeutic skills, and they do not know much about the drugs, i.e., the brand name, the strength, the formulation, and the dose in specific conditions. Pharmacological and pharmacoeconomic knowledge is acquired and can be applied in practical prescribing skills. Conventional pharmacists also don’t know much about proper medication use. Present qualification of pharmacist in India is Diploma in pharmacy (2-year study, plus 500 h practical training in hospital) and B.Pharm 4-year degree program and its curriculum does not provide sufficient information, practice, and knowledge about pharmacoeconomics. To overcome such a dilemma, the government of India introduced a new program in pharmacy education named PharmD (2008), which highlights the principles of pharmacoeconomics in its syllabus. Consequently, we can expect the future M.pharm pharmacy practice and new generation of clinical pharmacists and PharmD graduates to be more beneficial than conventional pharmacist as they can be expected to implement the principles of economics in daily basis practice in community and hospital pharmacy.

CONCLUSION

With ever increasing healthcare costs, value added care provided to the patients by individual healthcare institution needs to be further researched. The development of pharmacoeconomics is at an infancy stage in India at the moment, despite the rapid growth of clinical research. India is an affordable destination for conducting clinical research for many western countries. The India Chapter of ISPOR has been formed, but it needs to develop the platform for pharmacoeconomics. We hope in India clinical pharmacists including PharmD graduates be more beneficial than conventional pharmacists as they can implement the principles of economics in daily basis practice in community and hospital pharmacy.

AUTHORS’ CONTRIBUTION

All authors have significantly contributed to the project in terms of conceptualization, writing and reviewing the entire document.

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