

Pharmacoeconomics Guidelines for India

HealthNetIndia

International Society for Pharmacoeconomics and Outcomes Research

Contributed by;

- Suresh K. Gupta, PhD, Professor Emeritus & Head, Clinical Research (DIPSAR), Advisor To Pharmacovigilance Program of India (PvPI), Delhi Institute of Pharmaceutical Sciences & Research, University of Delhi, New Delhi, India.
- Dixon Thomas, PhD, Professor & Head, Department of Pharmacy Practice, Raghavendra Institute of Pharmaceutical Education & Research, Anantapur, India.
- Denny John, MBA, MPH, Sr. Manager – Knowledge Services, (Health Research & Consulting), Capita India Pvt. Ltd., Mumbai, India.
- A.N. Nagappa, Professor, Manipal University, Udupi, India.
- N. Udupa, Director-Research (Health Sciences). Manipal University, Udupi, India.
- Munish Duvedi, Team Lead, Clinical Operations, GVK Biosciences, Gurgaon, India.
- Jitendar Sharma, PhD, Head-Division of Healthcare Technology & HTA, National Health Systems Resource Center, Ministry of Health & Family Welfare, New Delhi, India.
- Richa Goyal, Consultant (HEOR), Capita India, Mumbai, India.
- Javed Shaikh, Consultant (HEOR), Capita India, Mumbai, India.
- Dávid Dankó, PhD, Research leader, Corvinus University of Budapest, Hungary.
- Y. Padmanabha Reddy, Principal, Raghavendra Institute of Pharmaceutical Education & Research, Anantapur, India.
- Subhash C. Mandal, PhD, Senior Inspector, Directorate of Drugs Control, Govt. of West Bengal, Kolkata, India.
- J.S. Bapna, Professor, Pharmaceutical Management, Indian Institute of Health Management Research, Jaipur, India.

Submitted on August 30, 2014

Contents

1. Introduction
2. Health Technology Assessment
3. PE Guidelines
4. Good Prescribing & Pharmacy Practices
5. References

1. Introduction

Pharmacoeconomics (PE) refers to the scientific discipline that compares the value of one pharmaceutical product or treatment mix to another. It is a sub-discipline of health economics.^{1,2}

A pharmacoeconomic study evaluates the cost (expressed in monetary terms) and effects (expressed in terms of monetary value, effectiveness, efficacy or enhanced quality of life) of a pharmaceutical product. 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 etc.³ In 1993, Australia became the first nation to use pharmacoeconomic analysis as part of the process for deciding whether new drugs should be subsidised by the Federal Government.⁴

The current healthcare delivery system in India is more skewed towards private healthcare utilization. As per WHO's World Health Statistics 2012, almost 60% of

total health expenditure in India was paid by the common man from his own pocket in 2009. The Report states that 39 million Indians are pushed to poverty because of ill health every year. Around 30% in rural India did not go for any treatment for financial constraints. About 47% and 31% of hospital admissions in rural and urban India were financed by loans and sale of assets.⁵ Although attempts have been made by government in terms of health financing coverage in terms of Employees State Insurance Scheme (ESIS), Central Government Health Scheme (CGHS), Universal Health Insurance (UHI) Scheme etc, these have failed to cover the vast number of populations. It is mainly due to the reason that schemes such as ESIS, CGHS etc. are for formal employment sector whereas 70% of India's employed are in the informal sector, thus keeping them out of any "safety net" mechanism. Social security schemes such as UHI Scheme have failed due to lack of awareness about the scheme among the poor, inadequate social marketing efforts and its usage through reimbursement rather than "cashless" transactions. Other schemes such as the RastriyaSwasthyaBimaYojana (RSBY) are eligible for enlisted Below Poverty Line (BPL) populations and listed employment groups, such as domestic workers, street vendors, construction workers etc., and hence are not inclusive for all poor and vulnerable populations in the country.⁶

The economic boom in India has opened up commercial markets for manufacturers of healthcare products, in particular the pharmaceutical industry, cosmetic industry, vaccine manufacturers, medical device/ equipment manufacturers etc. Since health-related decision-making process is often not based on scientific evidence, commercial interests often take priority over scientific concerns, in framing and implementing health policies. In India, a strong price control mechanism is in place through the National Pharmaceutical Pricing Authority.

Most healthcare services in developing countries are provider-driven, in the sense that people have little role in their healthcare decision-making process. This is largely related to limited resources and infrastructure, and the demand-supply imbalance. Thus people in developing countries are often faced with the difficult choice to "take it or leave it". However, this scenario is changing in developing countries where empowerment of people in terms of wealth and education, is increasing. In such countries, many people can access and afford levels of healthcare that are of high

quality, and also provide value-for-money. This is changing the provider-driven systems to demand-generated systems.

Insurance and employer reimbursement of health costs, is also aiding this process. A mix of social, voluntary, private and community-based health insurance plans are available in India. Although the government pays for approximately 20% of drugs used in India, private out-of-pocket expenditure in India on health-care is one of the highest in the world. Increased public funding combined with flexibility of financial transfers from centre to state can greatly improve the performance of state-operated public systems. Just by increasing public healthcare funding would not help the quality of health-care delivery unless there are strictly implemented robust pharmacoeconomics guidelines in place. In New Delhi, Mumbai, and Trivandrum, state authorities have invited the National Institute for Health and Clinical Excellence (NICE) to help in the development of clinical guidelines.^{5,7}

2. Health technology assessment in India

Health technology assessment (HTA) is a rapidly growing field of interest in India. Hope this very first pharmacoeconomic guidelines in India would be a formal framework for assessing pharmaceutical products for the country. *Health Technology Assessment (HTA) is a multidisciplinary field of policy analysis, studying the medical, economic, social and ethical implications of development, diffusion and use of health technology.* HTA would ensure that public funds within India's central government, states and union territories is spent on safe, effective and value-for-money pharmaceuticals to maximise the efficiency of public pharmaceutical spending so that coverage of medicines can be gradually extended across a wider satisfied population. It is well known fact that the healthcare delivery in each country is influenced by local and global politics.⁸

Preparing pharmacoeconomics guidelines will be an important step in order to establish health technology assessment (HTA) in India. Areas in which HTA could be applied in the Indian context include, drug pricing, development of clinical practice

guidelines and prioritizing interventions that represent the greatest value with in a limited budget.

India is planning to be part of universal health coverage scheme by 2022. It is a big capacity building challenge for central and state governments to provide high quality health-care without financial hardship on the healthcare seekers. It is important to focus on preventive and public health strategies aimed at reducing the most important health problems in India. Recent advancements in high quality primary healthcare including maternal and child health services by the State Tamil Nadu is encouraging.

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

- Central and state drug regulators constituting with the pharmacoeconomics advisory groups.
- Implement HTA using pharmacoeconomics guidelines.
- 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.
- Improve access to life-saving medicines and affordability of essential medicines.
- Implementing public-private partnership medical insurance systems linked with Aadhar card.
- Collect healthcare tax and increase spending on health budgets.
- Creating awareness in public and professionals for better resource utilization.
- Consider healthcare as a basic necessity, individual right and responsibility.
- Include pharmacoeconomics principles in medical, pharmacy, nursing, public health and other healthcare professional education.⁹

Public health system of a country is driven by many factors like modernization of healthcare services, burgeoning cost of healthcare, rapidly increasing population and rapid growth of biomedical literature databases in medical sciences. There are different reasons for conducting health technology assessments such as qualifying the product in terms of its applicability in common public, designing mechanism for

healthcare reimbursement or finding pathway to integrate health technology in current health system.

The methodology of HTA differs from countries to countries. For example, NICE conducts HTA to provide recommendations to make sensible choice between available clinical interventions, where as Germany HTA agency considers it as an evidence based documentation purpose. However, main methodology remains same which includes systematic review which is synthesis of critically appraised original articles and clinical studies/trials. This systematic review is followed by cost-effectiveness analysis which is combined representation of clinical effect and coverage cost in form of ratios such as cost benefit, cost utility or cost effectiveness. The market status review is conducted by identifying demand/need, costs of same or similar technologies and patent status. Innovative health technologies not only impacts commercial environment but also sometimes mandates organizational structure changes. This may include recruitment of staff with higher skills or change in role of current personnel depending on use of technology in investigational or established diffusion phase.⁸

Health Technology Assessments have become increasingly useful, providing evidence on clinical benefit, cost effectiveness, social, legal and regulatory insights leading to identification and uptake of appropriate and safe technologies such as biopharmaceuticals, medical devices, implants, drugs and therapeutic practices. National Health Systems Resource Centre (NHSRC), New Delhi has been interested in HTAs for various interventions. NHSRC suggests a focus on;

1. How to ensure universal access to essential medicines and devices
2. How to write specifications when processing these so that we get the best value for money
3. How to assess technologies that public health systems should adopt for increased effectiveness and those that we should avoid, due to reasons of safety or poor cost effectiveness
4. How to identify areas where new technologies appropriate to our needs are invented and to develop an ecosystem that focus on such innovations.¹⁰

Structured quick assessment (SQA)

The HTA outcomes can be translated into pharmaceutical policy if authorities perform a structured quick assessment (SQA) for all pharmaceuticals which wish to receive public funding from any government program. Ideally, government-funded programs (incl. drug tenders) should only be open to medicinal products which have undergone SQA. It is equally important that all pharmaceuticals with a reimbursement history (i.e. previously reimbursed products) should also be subject to SQA, and different assessment criteria should be accepted and used for on-patent (single-source) and competing (off-patent) drugs. The evaluation process should follow a pragmatic, easy-to-execute, low-resource approach. General assessments must ensure that health technologies meet the above-stated principles by;

- 1) Serving the overall benefit of society by not raising barriers to access,
- 2) Avoiding the need for additional primary data collection and resource-intensive quantitative analysis, and
- 3) Minimizing the burden on state administration, maximizing the speed and quality of evaluation, as well as transparency and unambiguity in policy decisions.

In order to ensure a balanced, informed decision, assessments should also encompass multiple criteria, i.e. clinical, societal and financial aspects, and it should reference to relevant assessments available abroad. Health technologies may be further evaluated on the basis of quality of safety and effectiveness evidence in India, assessment and reimbursement history of the medicine in peer countries, therapeutic value added (e.g. high unmet need, higher effectiveness, favourable side effect profile, convenience of use, improved adherence and better quality of life), service to society (alignment with health policy, alleviation of social burden), and impact on drug budgets (direct and indirect).

For previously reimbursed drugs, assessment criteria may be different, where the quality of local safety and effectiveness evidence in India would be an important factor to consider.

SQA of technologies could be undertaken in any research oriented organization with the Ministry of Health & Family Welfare. Ideally such as institution should have technical collaboration with academia and research institutes for uptake of technical inputs as well to serve nodal points for dissemination within the health system. HTA work in India should primarily be done on a response basis on the priorities that are appropriate to the various health departments with the government decision making". In summary, structured quick assessment (SQA) of pharmaceuticals in India could be a qualification process linked to public funding to ensure safety, effectiveness, patient preferences, and value-for-money public pharmaceutical spending.

Model SQAs could be performed by a competent and independent agency under Department of Healthcare Research (DHR). States and union territories could follow the standard operating procedures developed by the DHR.¹¹

PE guidelines can be useful for these stakeholders to facilitate decision making in following ways:

1. National Pharmaceutical Pricing Authority (NPPA) – National Pharma Pricing Policy;

- Prioritization and Identification of drugs/products in India, which are pharmacoeconomically more important and beneficial.
- Creation of database by sponsoring/conduction PE studies- Pharmacoeconomic Studies and Health Technology Evaluation. Can replicate role of NICE – UK to some extent.
- Help government in identification of areas of pharmaceutical subsidies, import, and identify the areas in research where government can incentivize the research of new drugs and health technologies.

2. Health Insurance – Health policy-makers and health systems research institutions in collaboration with economic policy study institutes need to gather information about the prevailing disease burden at various geographical regions to develop standard treatment guidelines. This would help estimate the costing of health

services for evolving benefit packages and to determine the premium to be levied and subsidies to be given. This will also help to map health care facilities available and the institutional mechanisms, which need to be in place, for implementing health insurance schemes.

3. Central/State Governments can be guided on reimbursement under various mandatory sponsored insurance schemes like CGHS/ESIS. Department of Health Research (DHR), Government of India) is expected to play pioneering role in development of pharmacoeconomics research in India. DHR can somewhat play role similar to NICE in UK. As per the mandate given by Government of India, it states “DHR will promote and provide guidance on research and governance issues, including ethical issues in medical and health research”

4. Public hospitals Procurements: Guidance to States and Centre on free drug distribution in public hospitals.

5. Guide government on subsidy to be provided on technologies, so that medicine bills could be reduced, new technologies could be introduced in management of diseases and import duties waived off on essential pharmacoeconomic drugs.

6. Prescription Advice to practitioners in various therapeutic domains.

7. Creation of national database on the pharmacoeconomics of various drugs and health technologies, which may help healthcare providers, society, and Central Bureau of Health Intelligence.

8. Universal Vaccination Programme: Pharmacoeconomic research can help prioritization of vaccine and biological to be introduced in this programme by demonstrating comparative impact of vaccines. Vaccines are considered as most pharmacoeconomic health interventions.

9. Drug regulatory agency and patent: Drug Controller General of India (DCGI) / Central Drugs Standard Control Organization (CDSCO) is the competent authority to give permission for clinical trial in India. However with the advent of “Me too” drugs

and large generic drug maker have similar claims but before marketing they need to take approval from DCGI. However, similar to American and European drug regulators, CDSCO is also short of experts to review applications and they need to strategically prioritise. It is several times observed that globally various regulatory authorities spend lot of time to review clinical trial application of generic and “Me too” drugs, where as those drug trials which are necessary to be conducted in larger public interest are delayed. Patent system is strict in India. This will also encourage pharma companies to innovate newer molecules and health technologies.

3. PE Guidelines

The guidelines presented below represent to the economic evaluation of pharmaceutical drugs, but can be applied to the following situations: designing and conducting an economic evaluation of a new health technology or healthcare intervention (e.g. screening).

Guideline 1. Study design

The study design for any economic evaluation should have the following framework:

- Clearly defined research question or objectives of analysis
- Audience of the evaluation
- Analysis methods
- Cost determination
- Viewpoint of the analysis
- Analytic horizon
- Intervention to be specified
- Choice of therapeutic alternatives for comparison should be specified
- Target population

The study design could use both a prospective and retrospective study designs.

The economic evaluation of the pharmaceutical drug can be carried out in parallel to a clinical study for measuring ‘efficacy’. This can also be done through modelling methods for documenting ‘effectiveness’.

If all the data required for model calculations is not available for India, then similar parameters from other developing countries could be used, or in certain cases expert opinion can be used if such data is not available. It should be kept in mind that a high degree of transparency would need to be maintained in such cases, and the details should be provided as much as possible.

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines give a much complete framework for designing PE studies.¹²

Guideline 2. Audience of the evaluation

The main audience of an evaluation should be the decision makers, and in the context of India, this may be different from the funders of the evaluation. This can include:

- a) Ministry of Health and Family Welfare
- b) Drug Pricing Control Authority
- c) Government Departments financing large-scale health insurance programs, e.g. Ministry of Labour for Rashtriya Swasthya Bima Yojana (RSBY)
- d) International organisations, such as World Bank, USAID etc.
- e) Non-government aid agencies, e.g. Medicines Sans Frontiers, Bill & Melinda Gates Foundation etc.
- f) Insurance companies
- g) Pharmaceutical companies

Guideline 3. Methods of analysis

Table 1 shows that there are different types of evaluation which can be used to answer different decision questions. However, these are classified according to the type of comparison to the costs and consequences. The choice of method of analysis will depend on the research question, and must be clearly justified.

Table 1: Different types of economic evaluations

Method of analysis	Measurement/assessment of costs	Measurement/assessment of outcomes	Cost-outcome comparisons
--------------------	---------------------------------	------------------------------------	--------------------------

Cost-minimisation analysis (CMA)	Monetary	None	None
Cost-effectiveness analysis (CEA)	Monetary	Natural units	Costs per outcome unit
Cost-utility analysis (CUA)	Monetary	Utility values	Costs per QALY
Cost-benefit analysis (CBA)	Monetary	Monetary	Net costs
Cost- consequence analysis (CCA)	Monetary	Variety of different natural units	Cost per outcome unit

On the basis of these methods of analysis, supplementary questions can also then be considered, such as budget impact or cost impact. This would be particularly important for public agencies such as Ministry of Health, and government departments responsible for financing health insurance programs.

Guideline 4. Viewpoints (or perspective) of the analysis

The perspective is the point of view through which the research question is examined and assessed. The choice would be based on the research question, and can have the following two types of perspectives:

- a) Society
- b) Decision-makers, e.g. Ministry, Insurance Companies etc.

In India, as the majority of expenditure is out-of-pocket. It would be highly useful to consider the societal perspective and opportunity costs that are appropriate should also be considered.

Guideline 5. Cost determination

The societal perspective means that the evaluations must include all the costs and benefits, no matter who actually bears the cost or gets the benefits. This means that all costs and benefits outside the health financing/health insurance payment must also be considered. Any direct or indirect cost outside the health financing/health insurance payment must be presented and calculated separately. Thus, three types of costs must be displayed:

- (1) Direct costs in the health insurance/health financing payment

- (2) Cost in (1) plus direct costs not paid by the health financing/health insurance payment system (i.e. health/public system perspective)
- (3) Costs in (2) plus indirect costs outside the health insurance payment system (i.e. the societal perspective)

Direct costs include direct medical and direct non-medical costs. Direct medical costs arise directly from the treatment (e.g. diagnosis, drug therapy, medical care, in-patient treatment, etc). Direct non-medical costs arise from the consequences of treatment (e.g. transport costs, care services etc)

Indirect costs include losses of productivity resulting from illness and premature death. If impairment of capacity to work is to be considered together with absence from the workplace, the procedure must be presented separately.

A marginal consideration should be attempted in order to quantify the costs of an additionally consumed unit. Mean values should only be used if marginal values are not available.

In order to make the whole consumption of resources transparent, unit quantities and prices should be defined. Ideally, the opportunity cost of a resource should be considered. Opportunity costs represent the value of the next best use of resources, and should represent as accurate figures as available. The calculation of the opportunity costs should consider; all identified relevant costs, measurement of amount of resources, and value (or cost) of these resources.

In a competitive market, this value is represented by market prices, e.g. drugs, medical devices etc. If there is no competitive market, then scales of charges or fees or other forms of administrative reimbursement, can be used. In other cases, substitute quantities or 'shadow prices' should be used. If there are no published data for the cost survey, calculations and individual assessments (estimates, mean values, exploration of published data) should be performed.

Losses of productivity should be quantified by the human capital approach, i.e. the period-related income of the patient group concerned. If no specific data are available for the patient group considered, average values can be used from official statistics.

$$\text{Loss of productivity} = \text{Incapacity for work} \times \frac{\text{Wage costs}}{\text{Dependent employees} \times 365 \text{ days}}$$

In determining the loss of productivity; gender, age and social components must be considered, depending on the research question.

In cases where long-term absence from work or death, only the period until the workplace is filled again (by others or by colleagues) (i.e. friction period) is assessed as loss of production. However, the use of the friction cost approach must be justified.

Guideline 6. Analytic horizon

The choice of analytic horizon depends on the research question and can range from a few weeks to several years (e.g. remaining life expectancy). In choosing the time horizon, it should at all events be ensured that the chosen outcome and the resource consumption of the treatment alternatives are observable in this period.

Guideline 7. Specifying the intervention

The interventions to be analysed and the system within which it is delivered need to be described fully and with care. This will help ensure that all resources used are identified and allow others to understand exactly what was evaluated, which is important for considering the generalizability of the results.

Guideline 8. Choice of therapeutic alternatives for comparison should be specified

The aim of comparative economic analyses consists in assessing competing measures. The choice of alternatives must be appropriate to the research question and the state of science. The chosen alternatives should be described as fully as possible and comply with clinical practices in India and other developing countries. The choice of alternative(s) must be justified. Table 2 presents the principal types of comparison options.

Table 2: Potential range of options against which to compare interventions

1. Current practice

- a. Single principal type(s) of intervention
 - b. Mix of interventions
 2. Best available alternative (e.g. as represented by clinical guidelines or low-cost alternatives)
 3. Do nothing
 - a. Without the new intervention
 - b. Without any care
 4. Alternative levels of intensity for the new intervention
-

Source: Adapted from Castor and Ganiats (1999)

Guideline 9. Target population

The target population is the group for whom the intervention is intended, and this can vary by age, sex, disease and geography. It is also important to identify whether there are subgroups for which separate analysis should be undertaken, such as for different age groups, urban-rural, ethnic groups etc.

Guideline 10. Outcome parameters

In order to state the effectiveness of a medicine, data from clinical trials can be applied to economic models using real and clear assumption. All assumptions must be scientifically reviewed and explained in detail. The reliability and validity of important variables in the models must be examined.

Economic evaluations must be based on complete data for effectiveness and side effects, which are obtained from reviewing and obtaining the existing data of all treatments for a specific indication. Conducting a systematic review using a relevant database will be necessary, listing the databases used, key words used for the inquiry, and inclusion and exclusion criteria of literature. Moreover, unpublished reports that examine treatment conditions of indicators can also be presented.

Wherever possible, a summary table using meta-analysis of all selected literature can increase the accuracy of estimating the differences between the medicine and its comparator. Meta-analysis will also be helpful in finding some characteristics of the medicine that are of clinical importance but cannot be observed in randomized clinical trials. However, while conducting meta-analysis care must be taken to clearly describe the statistical methods adopted.

Source of effectiveness data can be from experimental research or observational research. If no such research is available, expert opinion can be taken. However, the evidence of lower value data can be adopted in an economic evaluation only when the evidence of higher value data does not exist. The methods of choosing experts and collecting their opinions must be described in detail in the evaluation reports.

The values of clinical data can be ordered as follows:

- A) Systematic reviews/Meta-analysis of randomized controlled trails
 - I. Randomized controlled clinical trials
 - II. Controlled clinical trial with pseudo-randomization
 - III. Controlled clinical trial without randomization

- B) Systematic reviews/Meta-analysis of observational studies
 - IV. Cohort prospective studies with parallel control
 - V. Cohort prospective studies with historical control
 - VI. Cohort retrospective study with parallel control
 - VII. Epidemiological case- controlled studies retrospective
 - VIII. Studies of a “before and after” type
 - IX. Expert opinion (Delphi methodology, committee later report and descriptive studies)

As the relationship between clinical outcome parameters and subjective patient well-being is only very indirect, in specific indications- particularly where the medical treatment does not hold out the prospect of either a cure or a significant prolongation of life- the health-related quality of life is the appropriate outcome indicator.

If the quality of life is to serve as an outcome variable, it must be ensured that the variable measured is also an appropriate measure for comparing the chosen treatment alternatives. Outcomes of this kind, in other words utilities, can be determined in the following way:

- specific scales (rank scales),
- game theory procedures (e.g. standard gamble, time-trade off, etc),

- psychometric scale procedures which include generic and disease-specific procedures as well as one-dimensional and multidimensional instruments.

These individual measures are suitable for combining with quantitative objective measurements such as survival time in the form of quality adjusted life years (QALYs), and can be applied to cost-utility analysis (CUA). The utilities of health states can be determined by patient themselves or the general population. If utilities are determined by the general population, the evaluations based on them are considered as “from the societal perspective”. QALY is currently the most widely used and recommended outcome measure. For pharmaceutical manufactures, it is recommended that QALY be used in the main analysis and other effects be used in the secondary analysis. The World Bank & World Health Organization (WHO) suggested adopting disability-adjusted life-year (DALY) as an alternative to QALY. Using DALY world statistics on Global Burden of Diseases (GBD) are released by WHO since 1990.

In other cases economically oriented outcome measures such as hospital days, days of incapacity for work etc. can also be chosen.

Guideline 11. Incremental cost-effectiveness

The incremental cost-effectiveness shows the difference in the cost-effectiveness of two alternatives or the additional costs of the net effect. Health economic analyses should include the description of the modelling techniques for calculating the incremental cost-effectiveness.

To develop models, the structure and the theoretical framework of the models should be explained explicitly, and they should be presented through diagrams (for example, decision trees, Markov models). All data sources used must be described exactly, their choice justified and their suitability and validity assessed. This involves scrutinizing both internal and external validity.

In India, economic data is not systematically recorded or published. For this reason, health economic evaluations should refer primarily to data from the following sources:

1. Five year Plans, Committee Reports, National Health Policy (NHP), National Sample Survey Organization (NSSO), Economic Census, National Rural Health Mission (NRHM), Public Budgets (Central and State). The new government under the leadership of Sri. Narendra Modi shall revise the planning commission system.
2. Insurance Companies Annual Reports, ESIS, CGHS, Railways, Mines, Plantations, Labour Yearbook
3. Primary studies on cost of illness, cost of care etc, done by organisations such as WHO, World Bank, NGOs etc.
4. Data from cost calculation by hospitals
5. Cost estimates from Delphi model surveys
6. Empirical surveys
7. Expert opinion

Epidemiological surveys performed directly in India or related to India are extremely rare. However, the data sources could be from:

- 1) Published data or data surveys from India
- 2) Published data from comparable developing countries (e.g. Bangladesh, Sri Lanka, Central Africa etc)
- 3) Other available data (e.g. Global Burden of Disease)
- 4) Expert opinion

Guideline 12. Discounting

Often, in health economic analysis, costs and/or outcomes are considered over a period of more than a year. If this is the case, the calculation of current values is necessary, i.e. long-term considerations require discounting of the costs and benefits at a particular reference point - usually the time at which the study is setup. Discounting allows two different treatment alternatives in which costs and benefits of a particular reference point generally occur at different times to be compared.

As an annual discount, a rate of 5% is adopted, while a sensitivity analysis with lower and higher rates (e.g. 3% and 10%) should verify the robustness of the results. Non-monetary outcomes should be discounted in a separate calculation.

Guideline 13. Uncertainty

Data for a health economic analysis are derived from various sources (e.g. pooled data sets, meta-analyses, unverifiable assumptions). As this is to some extent incomplete and affected by uncertainties, assumptions are frequently made about certain parameter values. Stochastic approaches such as deterministic sensitivity analyses should examine the effect of uncertain and/or estimated parameters on the outcome of the evaluation. Ranges of variation are defined for the variation in exogenous parameters. The definition of the plausible range of variation is based on the following options, depending on the study design for sensitivity analyses:

- (1) Confidence intervals from clinical studies, statistical studies,
- (2) Assumptions from the scientific literature,
- (3) Expert opinions, etc.

A sensitivity analysis is unnecessary if the parameters have already been presented with their dispersion. The results of the sensitivity analysis must be discussed critically.

Guideline 14. Equity

In any economic evaluations used for allocating resources, the equity is an important factor. The equity assumptions for the base case in economic evaluations means that all patients, in clinical trials, and economic evaluations, have a fair participatory opportunity and obtain the expected treatment and outcomes. For example, in the cost-effectiveness analysis (CEA), the cost per life saved or life-years gained is based on the assumption that all lives are equal, regardless of their age, co-morbidities or other states. In cost-utility analysis (CUA), everyone's increase in QALY is of the same value, no matter who the person is, i.e. an additional QALY of a 40-year old man and that of an 80-year old man are equally preferable.

Guideline 15. Presentation of the results

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines need to be followed in publishing the PE study reports. The results and procedure of the health economic evaluation must be reproduced transparently. The results should be presented in the same way as for a publication in journals (peer review) (details of the author, sponsoring, etc). Negative results also should be published.

Descriptions relevant to the research question and significant results should be presented in an aggregated and disaggregated way (e.g. according to cost components, perspectives, etc). The different viewpoints should be presented comparatively. An additional clear and brief description of the results should present the cost-effective (i.e. dominant) strategy.

4. Good Prescribing & Pharmacy Practices

Pharmacoeconomics (PE) principles are vital parts of good prescribing practices. Many of the developing economies either do not have national pharmacoeconomic guidelines or they are poorly implemented. National drug price controls shall stabilize the cost of medicines in different brands and schemes, which shall decrease confusion in prescribers for selecting medicines. Variation in price for drugs and different brands are huge.¹³

The basic purpose of separating medicine prescribing and dispensing is to ensure independence in the choice of medicines. Incentive or remuneration for prescribing should be discouraged; prescribing from essential medicines list need to be encouraged so that over prescribing or unnecessary prescribing of costly medicines could be avoided. Pharmacy and therapeutic committees could perform routine resource utilization and patient based PE studies to develop and update clinical guidelines as part of implementing good prescribing practices.¹³ Restrictions on reimbursement also play a major role in avoiding overprescribing and additional costs. Conflict of interest policies need to be enforced in medical education, conferences, and continuing medical education. Influence of pharmaceutical

marketing shall not bias good prescribing practices. It is advisable that pharmaceutical marketing should be limited to the purchase department of health care facilities. Prescribers shall seek drug information through unbiased drug information services, so that prescribers and dispensers could have independence in their decision making on medicines in discussion with consumers, which will improve medication adherence.¹⁴⁻¹⁶

Further research and development of PE guidelines are needed in institutional and regional levels in India based on pharmacoeconomics, clinical interventions, health care delivery systems, and clinical outcomes. A combination of ethical and scientific reform could help in planning & implementation of good PE practices in India.

5. References

1. Mueller C, Shur C, O'Connell J. Prescription Drug Spending: The Impact of Age and Chronic Disease Status. *American Journal of Public Health*. 1997; 87 (10): 1626–29.
2. Arnold RJG and Ekins S, Time for cooperation in health economics among the modeling community, *PharmacoEconomics*. 2010; 28(8):609-613.
3. Mandal CS, Pharmacoeconomics- Regulatory perspective and its relevance in Indian Context. *Pharma Times*. 2013; 45(5): 18-20.
4. Birkett DJ, Mitchell AS, McManus P. A cost-effectiveness approach to drug subsidy and pricing in Australia. *Health Aff (Millwood)*. 2001;20(3):104-14.
5. Press Information Bureau. GOI. India Embarks on Universal Health Coverage during 12th Plan. Available at: <http://pib.nic.in/newsite/erelease.aspx?relid=88129> (Accessed on 27-08-2014).
6. Gerard La Forgia & Somil Nagpal. Government-Sponsored Health Insurance in India: Are You Covered? The World Bank, 2012. Available at: <http://documents.worldbank.org/curated/en/2012/08/16653451/government-sponsored-health-insurance-india-covered> (Accessed on 10-02-2014)
7. NICE. International projects. Available at: <http://www.nice.org.uk/aboutnice/niceinternational/projects/NICEInternationalProjects.jsp?textonly=true> (Accessed on 02-01-2014).

8. INHATA. HTA resources. Available at: <http://www.inahta.org/HTA/> (Accessed on 02-01-2014).
9. Thomas D, Zachariah S, Padmanabha Reddy Y, Alvarez-Uria G. Development of Pharmacoeconomics guidelines in India. *Perspect Clin Res.* 2014; 5(2):54.
10. NHSRC. Healthcare technology. Available at: http://nhsrcindia.org/index.php?option=com_content&view=article&id=173&Itemid=642 (Accessed on 02-01-2014).
11. Thomas D, Danko D, Structured Quick Assessment of Pharmaceuticals in India. *News Across Asia.* 2013; 2(3):3.
12. ISPOR. CHEERS: Good reporting practices. Available at: <http://www.ispor.org/taskforces/economicpubguidelines.asp> (Accessed on 21-02-2014).
13. Fleetcroft, R., Cookson, R., Steel, N. & Howe, A. Correlation between prescribing quality and pharmaceutical costs in English primary care: national cross-sectional analysis. *Br. J. Gen. Pract. J. R. Coll. Gen. Pract.* 2011; 61, e556–564.
14. Thomas, D, Seetharam, G. & Alvarez-Uria, G. Essential medicines concept for quality assurance of health care facilities. *J. Pharm. Bioallied Sci.* 2012; 4, 172.
15. Mishra SI, Gioia D, Childress S, Barnet B & Webster RL. Adherence to medication regimens among low-income patients with multiple comorbid chronic conditions. *Health Soc. Work* 2011; 36, 249–258.
16. IPA. Good Pharmacy Practice Guidelines. Available at: http://www.ipapharma.org/html/GPP_Guidelines_IPA2002.pdf (Accessed on 21-02-2014).