## *Clinical Epidemiology*

# Application of Health Economics in Medical Research and Clinical Epidemiology

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Health economics is a science to optimize resource allocation. Therefore, health economics can only be applied when there are choices(1), and there are no dearth of choices in modern medicine. The characteristic feature of health economics is that it deals both with inputs, or costs, and outputs, or consequences(1). In this article, we will be discussing the applications of health economics in medical research and clinical epidemiology with reference to technology assessment.

### Medical Technology and Technology Assessment

All of us involved with the health care are keenly aware of rapid advances in various technologies that are flooding the market. The word technology means drugs, devices, instruments and operations (2) used in health care. Before we can accept a new technology, we have to know how good is it and this issue is addressed by medical research which uses the principles of clinical epidemiology. We also have to know how much better is the new when compared to the old, and this question in answered by health economics. Whenever a new technology is discovered it usually goes through predefined phases of assessment to prove its worth.

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### Phases of Technology Assessment

Each medical technology ideally goes through three phases of assessment. In the first phase there is just an assessment of its technical characteristics. For example, what is the anti-bacterial activity of a new drug, or what is the sensitivity and specificity of a new diagnostic test, or what is the resolution of a new scanning devise, *etc.* In the second phase, the efficacy of a diagnostic or therapeutic technique is assessed. The best evidence for this comes from a randomized controlled trial. However, other observational studies, namely case-control and cohort studies, can provide lesser quality of evidence.

New technology that has been assessed on the basis of epidemiological study designs will hardly ever be applied in the very same setting, much lesser so if it was a clinical trial. Therefore, in third phase, we assess how good this new technology will be in real life situation and in a different set of patients. We also compare the costs and benefits provided by the new and the old technologies. When there are multiple clinical endpoints, we may also try to distinguish the effects of the old versus new on the quality of life.

If new technology is better than the old, it may change the practicing patterns of physicians. But before this can happen, it is better to do an economic analysis to find what would be effect of this change to the payer or provider. Here, payer is usually

the patient and the provider may be a hospital. Stated differently, before a new technology comes into routine practice, it is better to assess its policy implications by employing the principles of health economics.

**Cube of Health Economics**

The basic terminologies used in health economics are shown in the cube in *Fig* 2(3). Three basic concepts involved in economic assessment are: (*i*) Type of analysis that is performed; *(ii)* Types of costs and benefits that are included in the analysis; and *(iii)* Point of view from which the analysis is undertaken. This cube shows how these different considerations come together in an economic assessment. Appreciating the three dimensions is the key to understanding the analysis as a whole.

Three types of analysis may be performed: cost identification, cost-effectiveness and cost-benefit (4). They distinguish whether or not benefits are assessed in the analysis and how these benefits are quantified. If only the costs are assessed, it becomes cost identification study. If the benefits are also assessed in terms of health points, then it is cost-effectiveness analysis. If all the health benefits that are provided are quantified in monetary terms, then it is called cost-benefit analysis.

Three types of costs and benefits may be considered: direct, indirect and intangible. Direct costs are those that can be attributed to the change in health status, *e.g.,* cost of medicines and hospitalization. Indirect costs are those incurred due to illness, *e.g.,* loss of wages and transport costs. Intangible costs are those that cannot be measured in monetary terms but are equally important. For example, response to loss of hair following anticancer therapy or indwelling catheter for continuous ambulatory peritoneal dialysis.

Finally, there are four points of view from which the analysis may be undertaken: that of the patient or that of the provider of health care or that of the payer or that of the society.

**Data for Economic Analysis**

The data that goes into economic analysis comes from the second phase of technology assessment, when the medical research is actually done. Ideally, at this stage we must define our economic objectives and end points and collect data on relevant variables. For example, if we are carrying out a randomized trial of six monthly albendazole for improving nutritional status of preschool children(5), we must anticipate in advance that before this intervention can have policy implications, the health care providers would like to know its cost-effectiveness. To carry out the relevant cost-effectiveness analysis, in phase two itself, we must collect relevant cost data with the data on effectiveness in both the arms of the trial.

Sometimes we come across two different situations. The first situation is one where medical research on a new technology has already been done without the collection of data on appropriate economic variables. If we now plan to do an economic analysis, the economic data have to be imported from the next best available source. The second situation is that when economic analysis is done before the medical trial. Here the data on various clinical end points is assumed. Data on economic end points is derived from different surrogate sources. Various types of modeling techniques are used to then assess the technology. The primary aim of these types of analyses are to argue in favor or against a medical research trial or give a rough guide to the physicians on whether or not to use the technology, prior to the availability of

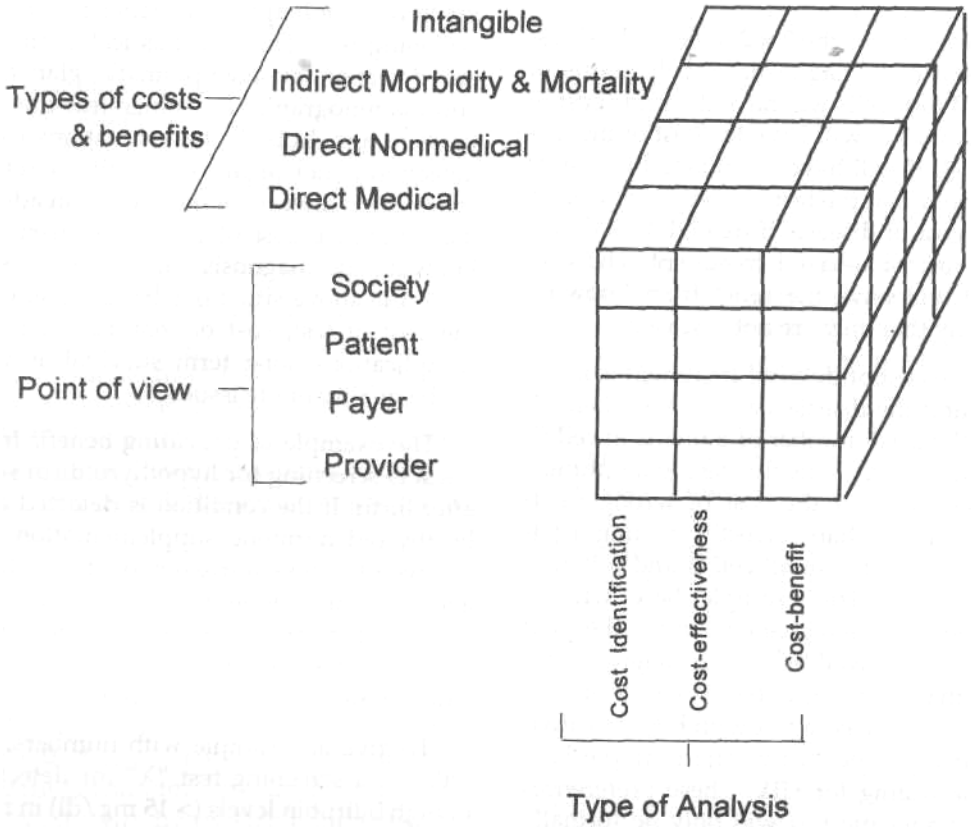


Fig. 1. Cube of health economics

the trial results. For example, if a new drug has been found to effective in the treatment of acquired immunodeficiency syndrome (AIDS), it may be unethical to withhold its use till the data of randomized trial is available. The data on drug efficacy can be assumed and data on cost can be imported from other studies on AIDS patients. By various modeling techniques the incremental cost-effectiveness ratio of this new drug can be calculated. This will be of help to the physicians while making a decision on the use of new drug. Since the estimates of costs and sometimes effects are uncertain, sensitivity analysis has to be done to check for the robustness of the results (1).

**Applications of Health Economics in Different Situations**

To clarify the applications of health economics in medical technology assessment, we will discuss its use in the following situations:

1. When a new diagnostic test has been developed.
2. When we want to launch a new screening test.
3. When we want to launch a preventive strategy.
4. In resource allocation when planning a policy.

*Diagnostic Test*

*Table I* shows the 2x2 table for basic assessment of a diagnostic test. In terms of cost, all four cells will have the same cost of testing. Cell A will have the cost of the disease, cell B will have the intangible cost of being told that the test is positive as well as direct cost of disease, if treated. Cell C will incur cost of delayed treatment. Those in cell D will have the relief from knowing correctly that they are not diseased.

If the cost of delayed treatment is much more and the disease can be fatal, then we want the least number of patients in cell C, therefore a very sensitive test will optimize our resources. If the cost of wrong treatment is more than correctly treating a patient, we need a small cell B and a highly specific test. The example here will be treatment for malignancy. And if the pain of missed as well as wrong diagnosis are high, that is, being either in cell B or C is bad, we will need a test with high sensitivity and high specificity. The example here will be testing for HIV. These preferences for a diagnostic test will only be formally known through technology assessments which uses the principles of health economics.

*Screening Test*

From a diagnostic test we go *on* to a screening test. The aspects of a diagnostic test do carry over, but the difference here is that the subjects are not diseased *(Table II).* The test is intended to be applied to larger populations. As proportion that will be truly diseased is small, there will be many false positives. Going back to the 2x2 table for screening test *(Table II),* many people will fall in cell B.

The next logical question is how can we alter and for how much longer can we alter the long term outcomes of a disease by detecting it early. If the available intervention is not helpful it is better not do the screening test. The two classical examples are detection of asymptomatic glancoma and mammography in women less than 50 years of age. In both these situations early detection is not of much benefit, therefore screening is a waste of money. It can add to the intangible cost of pain and misery of knowing the diagnosis early. Decisions in both the above situations have considered the cost of test, cost of treatment and its complications, long term survival as well as the quality of life issues.

The example of providing benefit from a test is screening for hypothyroidism soon after birth. If the condition is detected early, thyroid hormone supplementation can be given to prevent irreversible brain damage. From an economist's point of view the question is whether we have the monetary resources to screen a large number of neonates to provide benefit to a few.

To give an example with numbers, we will use a screening test "X" for detection of high bilirubin levels (> 15 mg/dl) in neo-

**TABLE I**-2x2 *Table for Basic Assessment of a Diagnostic Test.*

| | Disease | |
|---|---|---|
| Test | Yes | No |
| Positive | A | B |
| Negative | C | D |

**TABLE II**-2 x 2 *Table for Assessment of a Screening Test.*

| | Population | |
|---|---|---|
| Test | Disease | No disease |
| Positive | A | B |
| Negative | C | D |

nates in the first week of life. High bilirubin level can cause long term damage to babies. The screening test has a sensitivity of 68.6% and specificity of 65.7% *(Table III).* The cost of test is Rs 20. The cost of hospital stay of mother and baby is Rs. 100. We do expect more of false positives and a bigger cell B. We see this in *Table III.* But what we have to consider is the cost of a false negative and false positive test. If all test negatives are discharged, then being a false negative means that the baby will be readmitted or the diagnosis of high serum bilirubin will be missed. The consequences of missed diagnosis means a small risk of intellectual impairment and a smaller risk of kernic-terus. If we are willing to take this risk, then we will discharge 61% of the test negatives.

*Treatment*

Now, let us consider a disease for which a new modality of treatment has been identified. And we want to know how efficient is this new intervention when compared to the old one; or, how much benefit does a patient get and for how much cost. *Table IV* shows the two by two table for assessment of interventions. New treatment will be traditionally good if (A/A+B) is greater than (C/C+D). In terms of health care, new treatment will dominate over the old one if it is cheaper than the old one and also cures more people.

The issue of dominance is further explained in *Fig. 2.* Suppose we compare two interventions, A and B, for a common condition. If A costs less than B, but A has more effects than B, then A dominates; and vice-versa for B. But what if the new treatment is cheaper and cures less? Should we still adopt it? Here, we have to consider who pays and how much is the person willing to pay and with how much certainity does the person want a cure. These question can only be answered after economic assessment has compared these choices.

To complicate the issue, the cure rates may be biased if the two treatment modalities were not compared by randomized trial. Also, the outcome may not be as clear as "cure" and "no cure". The outcomes may be various degrees of clinical improvement or cosmetic disfigurement due to surgery. Thus, we now have to consider patient's preferences. For this we can use quality adjusted life years as the outcome of interest and our final analysis will show the amount of money that we are willing to pay for each unit of quality adjusted life years that we gain.

*Preventive Strategy*

Let us consider a preventive strategy. Usually, we launch a preventive strategy after we have demonstrated by medical trials or literature reviews that prevention works, and have shown by economic assessments that it is cheaper than all other alternatives or saves money. But once this has been done, prevention basically gets decentralized (2). It goes in the hands of public themselves and to adopt it is dependent on their desires; for example, smoking

**TABLE III-** *Example of a Screening Test "X" for High Serum Bilirubin (≥ 15 mg/dl)*

| | Disease | No disease | |
|---|---|---|---|
| Test | 24 | 82 | Sensitivity: 68.6% |
| Test | 11 | 157 | Specificity: 65.7% |

**TABLE** IV- *2x 2 Tables for Assessment New Treatment Modality*

| | Outcome | |
|---|---|---|
| | Cured | Not cured |
| New treatment | A | B |
| Old treatment | C | D |

| Effects | Costs | |
|---|---|---|
| | A<B | A>B |
| A>B | A Dominant | Incremental cost-effectiveness analysis |
| A<B | Incremental cost-effectiveness analysis | B Dominant |

Fig. *2. Economic comparison of intervention issue of dominance.*

cessation, diet and aspirin for angina. Even the best quality of health economic assessment may not convince a person to adopt a preventive strategy. So, thereafter, no simple assessment can calculate its incremental cost-effectiveness ratio in the real life situation.

*Resource Allocation*

Like with preventive strategy, economic assessment is needed before resource allocation can be done at any level to ensure efficiency. It is also recommended before any program is launched and while programs are going on. To do such types of analysis, we have to identify all costs, including the program costs. Considerations must be made for long term costs and benefits and opportunity costs (1).

For this, we will take the example of giving 6-monthly albendazole to preschool children (5). Suppose this means that 10 million children each year have to be treated and assuming that the annual treatment cost is Rs. 4, then the intervention cost to treat 10 million children will be Rs. 40 million. Now Rs. 40 million was just the cost of intervention. To this has to be added the program cost of drug delivery. Based on the results of the randomized trial (5), the effectiveness will be an extra 1-2 kilograms weight gain with intervention. Weight gain with intervention will result in a reduction in proportion of underweight children and this may also result in a reduction in mortality related to or confounded by malnutrition.

Going back to the question with which we started: will we do this intervention? The question is as yet unanswered, because we have also to know from where will this money come. Stated differently, the opportunity cost (1) of implementing six monthly albendazole for preschool children has to be considered. If we fund this program, the money will have to be taken away from somewhere else. Now we have to consider the consequences of taking away money from that place. All these sets of issues are dealt with at the level of policy planning. AH the principles of clinical epidemiology and health economics are employed for this purpose.

## Conclusion

Health economics is very meaningful for a country like India where medical resources are scarce. Economic assessment is a part of good quality medical research. Both together are required for technology assessment. Therefore, while planning research, we must decide our economic aims and objectives lay down our hypothesis, calculate sample size for economic outcomes and define variables for economic data collection. In an ideal research world, clinical and economic data are collected simultaneously. Therefore, clinical epidemiology and health economics are an inseparable part of medical research. Good quality epidemiological and cost data, when combined, give the most reliable estimates of cost-effectiveness. To keep in pace with the advances going on, we have to keep re-analyzing older technologies as the newer ones keep coming in.

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