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**Review Article**

# An algorithmic approach to pharmacoeconomic analyses

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## ABSTRACT

Pharmacoeconomics is defined as the description and analysis of costs of drug therapy to health care systems and society. There are various methods used, such as cost-minimization (CMA), cost-effectiveness (CEA), cost-utility (CUA) and cost-benefit analyses (CBA). Others include willingness-to-pay (WTP) and incremental net benefit (INB) analysis. However, there is lack of knowledge in the proper application of these in a coordinated fashion. The aim is to create an algorithm for health-care professionals in deciding appropriate treatment in a pharmacoeconomic perspective when multiple treatment options are available, ensuring safe and effective health-care services within limited resources. For this we reviewed various literature on pharmacoeconomics and compiled various analytical methods being used, along with their pros and cons, including when they can be applied and not. We used all this information to prepare the algorithm which goes as follows. Step 1: for the given patient condition, find the minimum effectiveness of treatment required and list out the health interventions which can provide it along with their costs, benefits and utility. Step 2: conduct INB analysis using WTP method to rule out those which the patient cannot afford. Step 3: among others, conduct CUA followed by CBA, CEA and CMA in this order. Step 4: the treatment option which doesn't get ruled out at the end of these steps should be considered. If sufficient data is available (which is an important limitation), this algorithm can serve as a powerful tool in optimizing health-care interventions, at least in selective health-care setups.

**Keywords:** Pharmacoeconomics, Cost-effectiveness analysis, Cost-utility analysis

## INTRODUCTION

Pharmacoeconomics is defined as the description and analysis of costs of drug therapy to health care systems and society. It identifies, measures and compares the costs and consequences of pharmaceutical products and services.

There are various methods used for analysing costs in pharmacoeconomics, such as cost-minimization analysis (CMA), cost-effectiveness analysis (CEA), cost-utility analysis (CUA) and cost-benefit analysis (CBA).

Cost-minimization (CMA) is the simplest of the four analyses. When different treatments have the same clinical effect, we choose the one which costs the least.[1]

But when different health care interventions are not expected to produce the same outcomes both the costs and the consequences of the options need to be assessed. T

his can be done by cost-effectiveness analysis (CEA), whereby the costs are compared with outcomes measured in natural units-for example, per life saved, per life-year gained, and per pain- or symptom-free day.[2]

There are two calculations usually used for CEA.[3]

$$Average\ cost - effectiveness\ ratio\ (ACER) = Cost\ of\ treatment / effectiveness\ of\ treatment$$

$$Incremental\ cost - effectiveness\ ratio\ (ICER) = (Cost\ of\ treatment\ A - cost\ of\ treatment\ B) / (effectiveness\ of\ treatment\ A - effectiveness\ of\ treatment\ B)$$

For this study, we use ACER but not ICER, since the other analyses that will be used in the algorithm eliminate its necessity.

Cost-utility analysis (CUA) is a special type of CEA where quality-adjusted life-years (QALYs) are used as the unit of effectiveness. The advantage of this method is that takes into consideration multiple effects of a drug, including the adverse effects, whereas CEA can only be done for one effect of interest.[4]

Another important consideration in pharmacoeconomics is "benefit", which is usually calculated as the cost avoided by the treatment, which includes cost to treat future complications of the disease (if untreated), and loss of wages of the patient.[5]

CBA considers only costs and benefits of a treatment without considering effectiveness. It is usually done in any one of these two ways as per preference.

$$Net\ benefit = Benefit - cost$$

$$Benefit - to - cost\ ratio = Benefit/cost$$

The treatment option producing higher of these values would be opted over the other.[6]

Apart from the above four basic analyses, we use willingness-to-pay (WTP) and incremental net benefit (INB) analysis to take into account patient's affordability of the treatment. WTP is the maximum amount of money a person would be ready to pay for a unit of effectiveness.[7]

$$INB = (WTP \times \Delta\ effectiveness\ of\ treatment) - \Delta\ cost\ of\ treatment$$

The delta (Δ) symbol in the equation usually represents a comparison between two interventions, but it could also be used to compare a treatment with "no treatment". In such case, both the cost and effectiveness of the "no treatment" would be usually taken as 0, reducing the formula to the following.

$$INB = (WTP \times effectiveness\ of\ treatment) - cost\ of\ treatment$$

But for self-resolving conditions, "no treatment" can also be considered to have a numerical value for effectiveness, while the cost is still zero. In our algorithm we compare a treatment only with "no treatment". An INB value greater than or equal to zero suggests that the patient is able to afford the treatment with the particular effectiveness, whereas a treatment with INB lesser than zero cannot be recommended.[8]

Although these and various other methods exist, there is a knowledge gap in when and how these calculations should be used. Hence in our study we propose an algorithm to be useful for health-care service providers in deciding the optimum treatment when multiple treatment options are available. By applying these analyses in the right order, a clinician can rule out those treatment options which have lesser effectiveness, more adverse effects, higher cost and lesser affordability.

## METHODS

We reviewed various literature on pharmacoeconomics which are publically accessible such as textbooks and published articles and compiled various pharmacoeconomic analytical methods being used, along with the pros and cons of each of them, including when they can be applied and not. We used the obtained information to prepare the algorithm.

## RESULTS

The algorithm goes as follows (Figure 1).

The first step in deciding a treatment among many available options is to find the minimum effectiveness required to treat the patient's condition. Then rule out all those interventions which provide sub-threshold effectiveness. Now the remaining ones all have effectiveness either equal to or more than the threshold effectiveness required.

Once we have the list of which treatments work, we need to find out which among these the patient is ready to pay for. For this, first we need to find out how much (maximum) the patient is ready to pay for one unit of effectiveness (willingness-to-pay). We then multiply this value with the effectiveness of a treatment option, to find the cost that the patient is ready to pay for this particular treatment option. If the actual price of the particular treatment is more than this value (INB<0), the patient might not want to pay for it, and hence not recommendable. If the actual price is equal to the calculated value (INB=0), it means the maximum amount the patient is ready to pay is exactly the cost of the treatment, hence it can still be recommended. But if the actual price of the treatment is less than the calculated value (INB>0), it would be cost-friendlier.

After ruling out all those drugs with INB<0, we get drugs which are both effective and affordable. But some of these could have adverse effects as well, and some drugs might have added benefits. To take into account all these aspects, we do cost-utility analysis (CUA), wherein the QALY gained by the treatment could be considered as a comprehensive measure of the various effects/adverse effects of the drug/treatment. Drugs/interventions which

have a higher cost-utility ratio will be chosen for the next analysis. Now some of the treatment options after CUA may yield almost the same value.

So, we do cost-benefit (CBA) analysis with those to make sure their monetary benefit is also higher, apart from just health benefits.

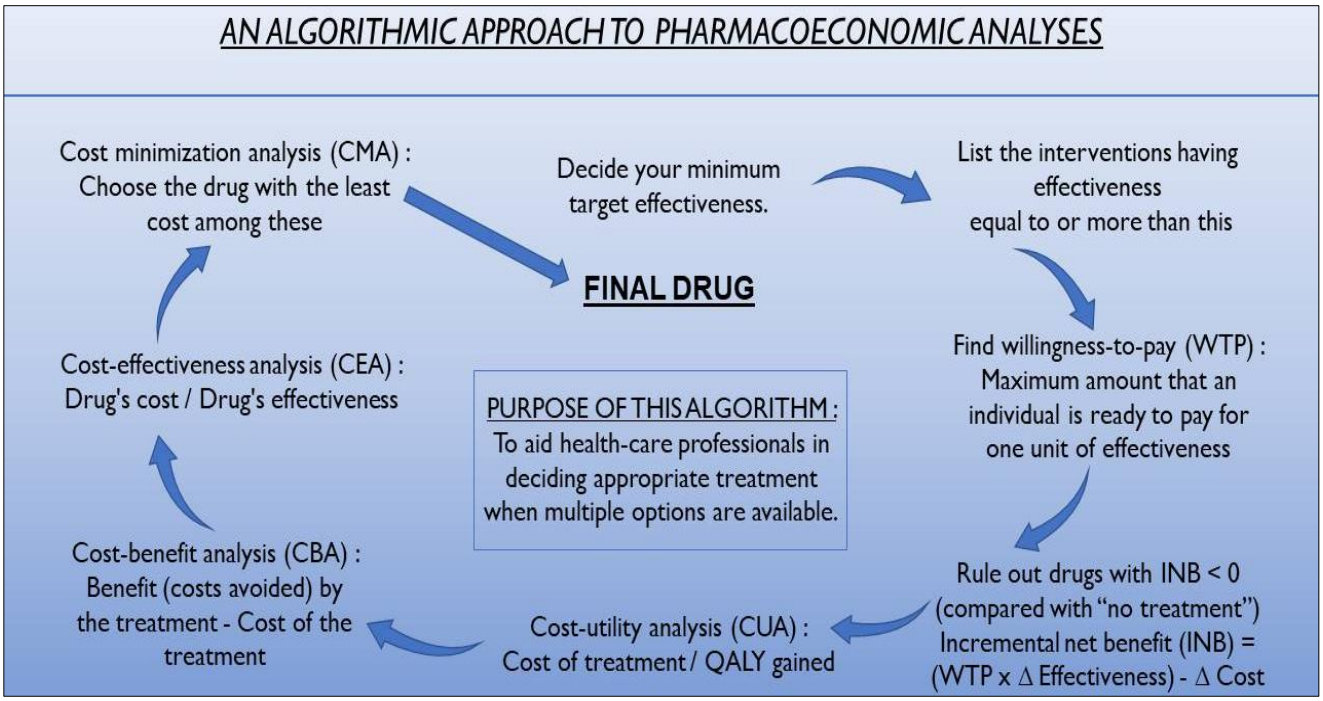


**Figure 1: Algorithmic approach to pharmacoeconimic analyses.**

Since CBA could be done by calculating either net benefit or benefit-cost ratio, sometimes these might give contradictory results, i.e., among two drugs one might have higher net benefit but a lesser benefit-cost ratio. To cover up for these discrepancies, we can do CEA by calculating the cost-effectiveness ratio. While calculating CUA we used a comprehensive measure of effectiveness, whereas now we can focus on the specific effectiveness of the treatment since we have covered all the vital aspects of selecting a drug, i.e., affordability, cost-benefit, long term health-benefit and fewer adverse events.

Among those treatments which might have almost the same cost-effectiveness ratio, we can choose the one drug/treatment/intervention which is simply the least costly (CMA). This would be the treatment option recommendable to the patient.

## DISCUSSION

The processes involved in obtaining the necessary variables to be used in the algorithm may be tedious. For example, consider the first step where we decide target effectiveness and using it, the drugs and their dosages. This may not be simple, especially in this era of precision medicine where therapeutic drug monitoring and pharmacogenomics are used to guide drug dosing. Further these can get complicated by factors such as patient compliance, and drug interactions.[9-12] Applying the value of variables such as WTP in the algorithm may present dilemma because of existence of multiple ways to calculate it, each method having their own pros and cons and producing a different value.[13]

The wide variability in cost of drugs depending on manufacturer, etc. necessitates us to use only cost of those drugs in the algorithm that we are actively prescribing.[14,15] We cannot use set values unless it is a hospital/setup where a particular drug is always obtained from a particular manufacturer.[16] Even in such cases the drugs' set cost in the algorithm need to be updated pertaining to their increase with time.[17]

Finding the utility value for QALY calculation has same drawbacks as WTP value: the existence of different methods for calculating them with each producing different values.[18] Additional drawbacks of QALY include the various criticisms over its reliability.[19,20]

For CBA, often only direct benefits can be calculated. The indirect and intangible benefit values are difficult to valuate and hence might be impossible to conduct a "true CBA".[21]

In spite of these fine inadequacies, the algorithm would still be very much useful if the measurement of the variables involved are well defined in the given clinical setup. Although some software's and guidelines are in place on how to conduct pharmacoeconomic analyses in decision making, either these are focussed on single analyses or they

are vague/unconvincing in dictating exactly how and why to conduct the series of analyses to reach the final decision.[22-24]

## CONCLUSION

We have presented a simple and powerful algorithm to provide an unambiguous method for treatment decision making. Lack of availability of data/tedious processes of collecting data necessary to do the calculations (for QALY, WTP, CBA), existence of multiple ways to calculate the involved variables, inconsistencies in the value of variables (drug/treatment cost) limit its usage. However, in certain health-care setups, the services provided would be narrow and uniform. Hence the information necessary to do the analyses could be easily extracted in these kinds of setups. This data, which is individualized for the particular hospital/health-care setup, can then be used to create personalized software applications for quick and automated analyses resulting in unambiguous treatment decision-making. It can also be used to guide standardized regimen making by national and international authorities for public health programmes.

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