DESIGNING AND CONDUCTING COST-EFFECTIVENESS ANALYSIS STUDIES IN HEALTHCARE

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ABSTRACT

Background: Health economic evaluation is essentials in the era of growing development of new health interventions to improve health of people and healthcare system. It focuses on the comparative analysis of alternative options in terms of both costs and consequences. Economic evaluation using cost-effectiveness analysis (CEA) technique helps the analyst to identify the most cost-effective option for achieving a pre-set objective. It is a method of assessing whether the current mix of interventions is efficient as well as whether a proposed new technology or intervention is appropriate. This article aims to describe the essentials steps in designing and conducting health economic evaluation studies in healthcare settings using CEA technique.

Materials and methods: The content was based on reviewed of various articles searched through both online databases such as google scholar, MEDLINE, PUBMED and CINAHL and manual publication on information pertaining to health economics and CEA.

Results and discussion: There are 4 preliminary considerations and 5 essential steps in conducting CEA. The preliminary consideration includes baseline determination, selecting appropriate outcome, determining the cost perspective and time horizon. The baseline can be no program or existing program or other drugs or surgical procedures for specific treatment of specific diseases. The outcomes need to be the same for all the comparable interventions and can be either single or combined outcomes. Deciding cost perspective either societal or provider perspectives is for the basis of the analysis, which cost will be attributed to the outcomes. Time frame is the amount of time which the analysis is projected while analytic horizon refers to length of time which both costs and outcomes are collected. The first and second steps in conducting CEA are developing research questions that must be clearly defined and designing decision analysis tree to graphically describe the sequence in which intervention occur, how the course of a health condition is affected, complications, and health outcomes may follow. The third steps are measuring both cost and outcome. The fourth steps are calculating cost effectiveness ratio (CER) and incremental cost effectiveness ratio (ICER) and the final steps is testing for uncertainty by conducting sensitivity analysis to test the robustness of the conclusions of an economic evaluation.
Conclusion: Good justification of a program/intervention in terms of costs and its effectiveness must be ascertained prior to implementation, therefore health economic evaluation studies using CEA may facilitate in the decision-making process for efficient resource allocation.

Keywords: health economic, cost-effectiveness analysis, healthcare

1.0 Introduction

Economics has an important part to play in the evaluation of health and healthcare interventions. It has been described in various ways. Economics refers to the way people and society make choices of scarce resources and by choosing to use resources in one way, those same resources will not be available for other potentially beneficial pursuits or in other name called opportunity cost (Shiell, Donaldson, Mitton & Currie, 2002). In more details, economics is defined as the study of “how men and society end up choosing, with or without the use of money, to employ scarce productive resources that could have alternative uses, to produce various commodities and distribute them for consumption, now or in the future, among various people and groups in society” by Paul Samuelson, 1948 (Shiell, et al 2002). It involves the analyses of costs and benefits in improving patterns of resource allocation.

Interest in health economic evaluation has accompanied concerns about rising health care costs, pressures on health care policymakers to allocate resources. There are growing development of new health interventions to improve health of people and healthcare system. Therefore, it needs to demonstrate the economic benefits of their interventions by conducting health economic analysis. Economic model can provide useful and relevance information into how health care can be organised and financed (Kernick, 2003). There are different types of economic evaluation studies which can be divided into full economic evaluation studies, partial economic evaluations studies and single effectiveness studies.

Full economic evaluation is a comparative analysis of alternative courses of action in terms of both costs (resource use) and consequences (outcomes, effects) (Drummond, 2005). It is distinguished from economic analyses which focus solely on costs and resource use. Approach to data collection and analysis determined by the decision problem, economic question and viewpoint of the decision maker. The main aim of conducting full economic evaluation studies is to describe, measure and value all relevant alternative courses of action for example intervention A versus comparator B, their resource inputs, and consequences (Drummond, 2005). Full economic evaluation studies include cost minimization which the determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes, cost-effectiveness analysis (CEA) where it compares programmes which have a common health outcome with costs in monetary units and outcome in non-monetary quantitative units, cost utility analysis (CUA) is a form of cost-effectiveness analysis that compares costs in monetary units with outcomes in terms of their utility and cost benefit analysis (CBA) which compares costs and benefits, both of which are quantified in common monetary units. In partial economic evaluation studies, there are no explicit comparisons between alternative interventions in terms of both costs (resource use) and consequences (effects) but it can contribute useful evidence to an understanding of economic aspects of interventions. Example of partial economic evaluation studies includes cost analyses, cost-description studies and cost-outcome descriptions.
Cost-effectiveness analysis in particular has become apparent after the World War II developed by United States Department of Defence (Quade, 1971). For example, CEA was used as tools to assist the United States military in making allocation decisions for weapons among the demands of the various branches of the armed services with different levels of performance and overlapping missions (International Encyclopaedia of Economics of Education, 1995). By the 1960s it had become widely used as a tool for analysing the efficiency of alternative government programs outside of the military. In general, CEA measures the effects of an intervention and its comparators or alternatives interventions in identical units of outcome and usually presented in the form of a ratio which is ‘cost per unit of effect’.

1.1 Cost-effectiveness analysis in healthcare

Cost-effectiveness analysis in healthcare refers to the economic evaluation in which the costs and consequences of alternative interventions are expressed in cost per unit of health outcome (U.S National Library of Medicine, 2016). At present, CEA is commonly used tool to evaluate health care interventions (Kernick, 2003). The analysis is focusing on evaluating the costs of the alternatives and involves the measurement of benefits in a quantifiable manner or natural unit such as lives saved or death prevented, and then compares the effectiveness of alternative options to deliver the health-related project or program. Cost-effectiveness analysis is used to determine technical efficiency whereby the comparison of costs and consequences of competing interventions for a given patient group within a given budget.

The CEA used to identify the most cost-effective option for achieving a pre-set objective or criterion that is not measurable in monetary terms for example some health outcomes. It can determine the most effective option for a fixed amount of funding that has been allocated to achieve a policy objective. Cost-effectiveness analysis is a method of assessing whether the current mix of interventions is efficient as well as whether a proposed new technology or intervention is appropriate. It is therefore suitable for situations where valid and reliable estimation of the benefits of alternative options is not feasible. Instead of attempting to identify and value the benefits, the most cost-effective means of achieving a desired objective is identified. Health economic evaluation using CEA is suited to situations where clear and defensible health goals exist which can be measured in terms of appropriate units. For example, health goals relating to mortality and morbidity effects of interventions are sometimes combined into single units such as Quality-Adjusted Life-Years (QALYs), Disability-Adjusted Life-Years (DALYs), Health Years Equivalent (HYEs), and other health indices. Using QALYs or DALYs promote comparability across studies.

The growing expectations of health services, new technologies, demographic changes and health sector inflation in addition with scarce resources were unable to satisfy all demands and needs of the people at large. Health economic evaluation studies helps to facilitate in decision making process including resources allocation among competing uses in public health. This article aims to describe the essentials steps in designing and conducting health economic evaluation studies in healthcare settings using CEA technique.
2.0 Materials and Methods

The content particularly the essentials steps in designing and conducting the CEA was adapted and modified based on various articles by the World Health Organization (WHO) publication on CEA, published articles and books. The literature searched was performed through both online databases such as Google Scholar, MEDLINE, PUBMED and CINAHL and also manual searches on publication or information pertaining to health economics and CEA using appropriate keywords such as “cost-effectiveness analysis in healthcare”, “designing health economics study”, and “steps in conducting CEA”.

3.0 Results and Discussion

It is importance to use analytic techniques to understand the clinical and economic consequences of strategies to improve health. Cost-effectiveness analysis is commonly used tools to evaluate health programs/interventions to improve health outcome and health-related quality of life. It provides an opportunity to rationalize health policy if the technique and its application were well understood, designed, and implemented. There are five essentials steps in conducting CEA that will be discussed later in this article; developing research questions, designing decision analysis tree, measuring cost and outcome, calculating cost effectiveness ratio (CER) and incremental cost effectiveness ratio (ICER) and testing for uncertainty. Before conducting any CEA studies, there are also preliminary consideration needs to be determined by the researcher/analyst as described below.

3.1 Preliminary consideration before conducting CEA

Before conducting CEA studies, there are four preliminary considerations need to be identified includes baseline determination, selecting appropriate outcome, determining the cost perspective and time frame and analytic horizon (Gift, & Marrazzo, 2007).

3.1.1 Baseline determination

The first consideration is to determine the baseline to which the alternative program to be compare. It can be no program or existing program. In healthcare settings or clinical medicine, we need to decide what treatment options and comparator will be considered in the analysis. Options may include other alternative method to deliver health education, other drugs for specific treatment of specific diseases, alternative to surgical procedures or medical and health interventions.

3.1.2 Select appropriate outcome

Secondly is to select appropriate outcome. It needs to be the same outcomes for all the comparable program/interventions and must be clearly defined. It also must be clarified through discussions with key stakeholders, including policy makers, funders, service providers and users (Byford, McDaid, & Sefton, 2003). Choosing an outcome measures depend on the objectives of the evaluation and the objectives of the intervention. Health outcomes or effects in CEA can be expressed as single measure of health outcome or
combined measures. How the outcome is measured will be discussed under step 3 of conducting CEA.

3.1.3 Determine the cost perspectives

The third consideration is to decide whose cost perspective will serve as the basis for the analysis before conducting CEA studies. The study perspective refers to the viewpoint the study will take to quantify costs and outcomes, which costs will be included and which cost will be attributed to the outcomes. It can be societal perspectives, provider perspective, funder perspectives or organization perspectives. The perspective is reflected in the research question and goals of the analysis (Stothers, 2007).

3.1.4 Time frame and analytic horizon

The fourth or final preliminary consideration is we need to determine the time frame that is defined as amount of time over which the analysis is projected. Analytic horizon or the length of time in which outcomes and costs are collected also need be ascertained. A decision needs to be made prior conducting CEA. It is recommended that the time frame required to collect costs must be long enough to observe the effectiveness of the intervention/program and to avoid capturing only cycles or patterns in costs for example costs affected by seasonal effects (Honeycutt, Clayton, Khavjou, Finkelstein, Prabhu, Blitstein, Evans, and Renaud, 2006). The year of price in which costs are valued usually based on most recent year of the study data. For example, if a study is comparing 2 strategies, one implemented in 2000 and one implemented in 2002, costs would be valued in terms of prices in 2002 (WHO, 2002).

3.2 Conducting CEA

The essentials steps in conducting CEA are showed in Figure 1. The details explanation of each steps will be discussed below.

**Figure 1:** Essential steps in conducting CEA studies

3.2.1 Step 1: Developing research question

In CEA, a research question should be clearly defined that compares the consequences of various treatment options in terms of costs. For example, comparing two methods of delivering health education among tuberculosis patients to promote treatment success, one is using technology-based methods for example WhatsApp application or Facebook and compare with current existing health education using face-to-face method. The research question will be,
“Is the technology-based health education intervention program being cost-effective in promoting treatment success among tuberculosis patients as compared to face-to-face health education intervention?”

The formulation of research question is depending on the perspective that can be societal/provider/clinician/program/funding source perspective. Apart of that, it is also important to consider the time frame, effectiveness measures such as cases of disease detected and cases of infection successfully treated, relevant treatment options and relevant outcomes in the process of developing research questions (Stothers, 2007).

3.2.2 Step 2: Designing decision analysis tree

Decision analysis is a process of quantifying programmatic alternatives for systematic analysis (Gift, et al, 2007). It graphically describes the sequence in which interventions occur, how the course of a health condition is affected, complications, and health outcomes may follow. Designing a decision analysis tree can be done manually or using a specific software such as the TreeAge software. Apart of that, Markov model also is used to formulate a decision analysis in CEA study (Komorowski & Raffa, 2016). It is especially used for the modelling conditions that have events that may occur repeatedly over time or for modelling predictable events that occur over time, for example screening for disease at fixed intervals (Glick, 2007).

A basic decision tree has three nodes; decision nodes, chances nodes and end nodes that are connected by branches (Werner, Wheeler & Burd, 2012). The nodes represent points in time. A decision node is a time when a decision is made. A chance node is a time when the result of an uncertain event/consequences become known and end nodes indicates that the problem is completed where all decisions have been resolved (Werner, Wheeler & Burd, 2012). The decision analysis tree structure is showed in Figure 2. Begin with the clinical decision, conventionally on the left, working to the right, draw lines leading from the clinical decision for each possible pathway. A square represents each decision point or node; each chance point (when outcome is uncertain) is represented by a circle and triangle nodes represent the end/final outcome. The probability of an outcome is written below the line for each uncertainty consequences.
Figure 2: Decision analysis tree structure

Figure 3 below illustrated another example of a decision tree used in the economic analysis of a trials to evaluate cost-effectiveness of technology-based health education intervention to promote treatment success among PTB patients. The comparator is current direct face-to-face method to deliver health education among pulmonary tuberculosis patient. The effectiveness outcome measured is the treatment success according to WHO definition for the outcome of a PTB patients. It is the sum of cured and treatment completed.

Figure 3: Example of a decision tree used in the economic analysis of a trials for tuberculosis program

3.2.3 Step 3: Measuring Cost and Outcome

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i. Cost Measurement

Measuring costs of a resource is depending whether it is financial costs or economic costs (Gift, et al, 2007). Financial or budgetary costs refers to the actual money spent on the resources, while economic costs or real cost are the value of a resource in its most productive alternative use or the best foregone use of the resources (opportunity cost) (Gift, et al, 2007). Measuring program costs involves two major components which are identifying type of costs and quantifying costs.

a. Identifying type of costs

Type of costs that need to be included in the analysis of cost-effectiveness involves the determination of evaluation perspectives and costs to develop and implement a program/intervention.

An intervention/program can be evaluated from multiple perspectives; however, in many studies normally the costs analysis is considering either the provider perspectives or societal perspectives (Honeycutt, et al, 2006). Identifying the perspective will determine how costs being identify, quantify and measure. To evaluate an intervention/program from provider perspectives, relevant costs data must be collected as comprehensively as possible. This includes the actual expenditures to provide and implement the health intervention and the value of donated resources or resources not funded by the program. The reason behind why the value of donated resources and resources not funded by the program must be quantified is because the donated resources may become insufficient if the program is to be implemented in a new community or expanded to more participants in the same community, to ensure that the costs between programs in different communities are comparable and the effectiveness of the program can be affected if exclude the value of donated resources.

Evaluation from societal perspective, the opportunity costs and the costs of accessing health interventions such as resources used by patients and their families to obtain an intervention must be included. Opportunity costs are those costs associated with the value of resources in their next best use (Honeycutt, et al, 2006). Example of opportunity costs are the value of time that patients lost to other activities when they need to come to clinic to seek or obtain the intervention (WHO, 2003). Apart of that, in societal perspective costs evaluation, all resources used to access the health intervention such as the cost of taking a taxi to a clinic, or special food for diets connected with therapy also must be included in measuring cost.

The development costs of an intervention/program are the costs required to start up a program and are those costs incurred before a program is implemented (Honeycutt, et al, 2006). These include the capital costs such as building. The implementation costs are the ongoing costs required to provide or implement the program activities. They can either be fixed costs or variable costs depend on the volume of the program activity. Examples of ongoing fixed costs are monthly rent or advertising costs. Examples of ongoing variable costs are medical examination costs or costs for incentives given to participants.
b. Quantifying costs

Quantifying costs should be done based on the actual expenditure or commitments either through receipts, contract or wages paid. To quantify costs, the first primary steps are to ascertain the main activities that the intervention/program performs (Honeycutt, et al, 2006). Examples of the activities are recruiting the participant, training healthcare provider, developing intervention module and providing intervention to participant. All these activities need to be further categorized under program development, program implementation, or both (Honeycutt, et al, 2006). This is to be able to separately measure start-up and ongoing costs.

Then, costs within each activity can be sub-categorized into several resource components such as manpower, contracted services, materials and supplies, buildings and facilities, and donated or readily available resources (Honeycutt, et al, 2006). The number of resource components is not fixed. Costs for each activity should be collected based on the resource components. For example, the manpower cost is calculated based on time spent on the performing program activities including salaries and other benefits. Contracted service costs include costs for program activities provided by external services. All the bills related to the contracted services must be appropriately keeping track. The costs of materials and supplies include costs for purchases to support program activities such as stationary and glucometer for glucose monitoring. The costs of buildings and facilities include rent and/or mortgage payments, as well as their physical maintenance and operating costs including utilities, taxes, and insurance. The labour and resources donated or not funded by the program also must be quantified. For example, if a program involves volunteers among nurses, the value of the volunteers is estimated by determining the market salary, or average wage, of a similarly qualified nurse.

There are several methods of costing such as by activity-based costing or micro-costing technique. We do not include the detail technique of costing in this article. This paper intended to share the basic steps in measuring cost in CEA.

ii. Outcome measurement

Outcome data can come from many sources depending on the outcome of interest pre-identified before conducting the CEA studies under the preliminary considerations section. Measuring outcome or estimating health effects can be done directly such as by calculating number of disease-prevented or incident cases of a specific disease in an intervention group compared to a control group over a given follow-up period (Gift, et al, 2007). There are several ways of measuring health outcomes in CEA. It can be categorised into single measure (natural unit) or combined measures of health outcome. Single measure of health outcome, for example, a program that focus on the reducing the acute asthma attack among patients with bronchial asthma, the unit of outcome measures will be the number of acute asthmatic attack among those patients in the study. The methods used to obtain the results of outcome measure of interest include data from routine service records, diaries, qualitative interviews and quantitative methods (Byford, et al, 2003). Apart of that, the outcome can be categorized into three; clinical unit such as mmHg reduction, HbA1c and cholesterol level; quantitative unit such as live-saved or life-year gained; qualitative such as direct and indirect measures such as EQ-5D, SF-36, Visual Analog Score, Standard Gamble and Time Trade-off.
DALYs is one of combined measure of health outcome. It is most common outcome metric used to explained CEA and World Health Organization (WHO) has recommended it is best to express population effectiveness in terms of DALYs (WHO, 2003). In general, DALYs refers to the total of years of potential life lost due to premature mortality and the years of productive life lost due to disability (Murray & Lopez, 1996). One DALY is one lost year of healthy life (Murray & Lopez, 1996). The formula for DALYs is as follows,

\[
\text{DALY} = \text{YLL} + \text{YLD},
\]

Where,

- \( \text{YLL} \) = years of life lost due to premature mortality.
- \( \text{YLD} \) = years lived with disability.

Quantifying burden of disease in terms of DALYs, the first step is to determine the YLL metric which corresponds to the number of deaths multiplied by the standard life expectancy at the age at which death occurs, and it can be rated according to social preferences, the formula is,

\[
\text{YLL} = N \times L
\]

Where,

- \( N \) = number of deaths.
- \( L \) = standard life expectancy at age of death (in years).

To estimate YLD on a population basis, the number of disability cases is multiplied by the average duration of the disease and a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead). The basic formula for one disabling event is,

\[
\text{YLD} = I \times DW \times L
\]

Where,

- \( I \) = number of incident cases.
- \( DW \) = disability weight.
- \( L \) = average duration of disability (years).

**Concept of discounting**

The value of costs and benefits incurred today more than those that they may incur in the future (Cellini & Kee, 2015). It is both standard and recommended practice in CEA studies to assume a time preference by applying a discount rate to both the costs and benefits of different programs under evaluation (WHO, 2003). Discounting refers to the process of adjusting the value of costs or benefits that occur at different points of time in the future so that they may all be compared as if they had occurred at the same time (Shiell, et al, 2002). Discounting is necessary if there is a preference to defer costs until tomorrow or to enjoy benefits today (positive time preference) (Shiell, et al, 2002).

In CEA, analysts use what is known as a social discount rate \((r)\), to calculate the present value of costs and benefits. All monetary values in CEA studies can be convert either to their present value or their equivalent value at the beginning of the project, in year 1 (Cellini & Kee, 2015). Although there is little agreement over what \(r\) value to use, it is important that analysis is performed using a common discount rate to ensure comparability across studies. For that reason, the base case analysis recommended by WHO-CHOICE collaboration using a 3% discount rate for both costs and health effects, with age-weighting (WHO, 2003). In the
sensitivity analysis, WHO has recommended testing the sensitivity of the results to a 0% discount rate for health effects and a 6% discount rate for costs (WHO, 2003).

3.2.4 Step 4: Calculating cost-effectiveness ratio (CER) and incremental cost-effectiveness ratio (ICER)

Cost-effectiveness analysis seeks to recognize how much dollars on the costs of an intervention/program. Linking costs and effects can be achieved in the form of a ratio, to provide an overall indication of cost-effectiveness in a way that will inform decision-making (WHO, 2008). CER can be calculated once cost and outcome data are gathered. CER obtained by dividing costs by what we term units of effectiveness as formula below,

\[ \text{CER} = \frac{\text{Total Cost}}{\text{Units of Effectiveness}} \]

A unit of effectiveness refers to a measure of any quantifiable outcome central to the program’s objectives. For example, a health education program aims at promoting treatment success among tuberculosis patients would likely consider the number of cases with treatment success to be the most important outcome. Above calculation is basically represents the average cost-effectiveness ratio (ACER) which the denominator represents positive outcomes from an intervention while the numerator represents the cost of obtaining these outcomes. Interventions with lower ACERs are relatively more efficient (Gift, et al, 2007). CER simply represents a measure of how efficiently the proposed intervention can produce an additional unit of effect, e.g. DALY averted or QALY gained (WHO, 2008).

ICER is more important than ACER value to the determine the cost-effectiveness of interventions because economic analysis is concerned with how much we are paying for each extra unit of effectiveness by undertaking the new intervention (Cellini & Kee, 2015, Byford, et al, 2003). The ICER is calculated by ordering the interventions from least to most effective in terms of outcomes achieved, then for each intervention dividing the change in cost from the next-least-effective intervention by the change in outcomes achieved (Gift, et al, 2007). The formula can be expressed as follows,

\[ \text{ICER} = \frac{\text{Costs}_B - \text{Cost}_A}{\text{Effectiveness}_B - \text{Effectiveness}_A} \]

Where,

- \( \text{Cost}_B \) = Cost of new intervention
- \( \text{Cost}_A \) = Cost of comparison intervention
- \( \text{Effectiveness}_B \) = Effectiveness of new intervention
- \( \text{Effectiveness}_A \) = Effectiveness of comparison intervention

For example, if intervention A costs RM80 and produces 10 effectiveness outcomes, and intervention B costs RM150 and produces 25 effectiveness outcomes, then the ICER will be \((\text{RM150} - \text{RM80}) / (25 - 10) = \text{RM}4.7\) per outcome. Thus, it costs RM4.7 per additional effectiveness outcome achieved when picking intervention B over intervention A. In this case, intervention B would dominate intervention A, making it the best investment of prevention.
dollars, based solely on cost-effectiveness results. Also note that the ACER for B, RM150/25 = RM6 per outcome and ACER for A, RM80/10 =RM8, does not show the true trade off when considering B instead of A.

3.2.5 Step 5: Test for uncertainty (Sensitivity analysis)

All estimates of costs and effects are subject to uncertainty. Therefore, a good health economic evaluation studies should involve assessing the impact of the uncertainties in the parameter values used and factors that determine how model outputs depend on model inputs affects the conclusions (WHO, 2008). There are 3 types of uncertainties, parameter uncertainty which is due to sample variation around estimates of variables used to calculate a CER, such as unit costs, adherence rates, and the efficacy of an intervention, model uncertainty and generalizability uncertainty which relates to the need to extrapolate the results of studies.

The principal methods for handling uncertainty are by conducting a sensitivity analysis. Sensitivity analysis is a method to test the robustness of the conclusions of an economic evaluation and involves systematic assessment of the impact of changes in the assumptions made (Byford, et al, 2003). In other words, certain variables in the analysis, such as individual cost items, are varied and cost-effectiveness reassessed based on new values (Byford, et al, 2003). The sources of data for ranges used in the sensitivity analysis are usually gathered either from the literature or data collected as a part of the study (Gift, et al, 2007). Generally, it is common to use the 95% confidence interval from the data collected in the study or from previously reported studies for a given factor such as the prevalence of disease in a population, or the accuracy of a given diagnostic test to define the sensitivity analysis range (Gift, et al, 2007). Example a CEA studies for a tuberculosis program; the sensitivity analysis is done using the range in costs estimated in the sensitivity analysis for the cost of managing a patient to treatment completion and using a range of effectiveness estimates from other literature from other countries/regions or from pilot projects (WHO, 2002).

Variables can be tested one at a time (one-way sensitivity analysis), two at a time (two-way sensitivity analysis), or more at a time. In one-way sensitivity analysis, the variables estimates are varied one at a time, keeping all other variables constant and the impact on the study findings is assessed (WHO, 2008). Multi-way sensitivity analysis explores the impact on the results of changing the value of two or more parameters at the same time, for example disease incidence and vaccine price (WHO, 2008). It becomes difficult to visualize n-way sensitivity analyses when the number of variables exceeds three (Gift, et al, 2007).

Probabilistic sensitivity analysis is another kind of sensitivity analysis using statistical methods whereby the probability distributions are applied to specified ranges for the key variables and samples are drawn at random from these distributions to generate an empirical distribution of the CER (WHO, 2008). Therefore, the impact of uncertainty surrounding one variable or around multiple variables can be explored (WHO, 2008). This type of sensitivity analysis is becoming widely used in model-based economic evaluations (WHO, 2008).
4.0 Challenges and limitation of CEA in healthcare

Health economic evaluation using CEA involves multiple assumptions and often produces uncertain results. Estimates of the costs and benefits associated with alternative interventions rely on data to the extent that they are available, relevant, and accurate, but also rely on judgments, values, assumptions, and extrapolations. When undertaking economic evaluation, the sources of uncertainty should be identified, characterized, and communicated clearly, for example by conducting sensitivity analysis. Reporting on the uncertainties and conducting a complete set of sensitivity analyses are important components of any evaluation and in the making of any conclusion of the studies. The presentation of benefits and costs of an intervention must be made carefully and should not be expressed as though they are precise measures of actual economic costs and benefits.

Meanwhile, CEA does not identify the benefits of actions or the willingness of society to pay for improvements (Brouwer and Georgiou, 2012). This refers to the maximum amount of goods or services or equivalent money income that an individual is willing to forego. Willingness to pay is usually hard to determine because health benefits are always not explicitly traded. Moreover, CEA only looks at one outcome at one time. Other external factors contribute to the outcome was not considered and other external benefit from the intervention also not taken into consideration in the analysis.

Apart of that, several other challenges have emerged into concerns to this wider use of CEA in healthcare settings. Generally, any decision in resources allocation must also consider social context such as prioritizing the sick, improve equity and equality in health, or addressing the well-being of future generations in order to significantly affects the entire health sector at large (WHO, 2003). The issue of health equity is absence in CEA studies and misallocation of resources could happen. In addition to that, the cost and time required to evaluate the large set of interventions needed to use CEA to identify opportunities to enhance allocative efficiency may be prohibitive (WHO, 2003). This become a challenge to low- and middle-income countries with scarce resources to carry-out health economic evaluation studies and providing affordable and timely information on the costs and effects of a wide array of interventions to inform policy. The general approach to determine the level of cost-effectiveness across interventions is using thresholds based on per capita gross domestic product (GDP). Under this approach an intervention that, per DALY avoided, costs less than three times the national annual GDP per capita is considered cost–effective, whereas one that costs less than once the national annual GDP per capita is considered highly cost–effective (WHO, 2003).

5.0 Conclusion

The growing expectations and demands from people for better healthcare services require a new proposed health intervention that showed both adequately effective and efficient. CEA is one way to evaluate effectiveness of health interventions or programs, for organization to gain efficiency. Good justification of a program/intervention in terms of costs and its effectiveness must be ascertained prior to implementation, therefore health economic
evaluation studies using CEA may facilitate in the decision-making process for efficient allocation of resources among various competing healthcare program.

**Author’s contribution**

Author 1 : information gathering, preparation and drafting of manuscript  
Author 2 : final review and editing of manuscript  
Author 3 : review of manuscript  
Author 4 : review of manuscript

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