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Health economic evaluation studies are conducted in many different ways, depending on the health outcomes selected.¹ In the present paper, we discuss the main types of outcomes used, presenting their characteristics, how to measure them and the scientific evidences that they support. We also discuss some types of complementary analyses used to test the robustness and reliability of the findings.

Clinical outcomes

Clinical outcomes are the signs and symptoms that result of a condition or its clinical management, and are usually measured in a medical appointment.² Some outcomes are simple to be measured, such as relevant sequelae and death. Others depend on the knowledge on the natural history of the disease, such as diabetic retinopathy. There are also those outcomes resulting from the interventions, such as adverse reactions.

In some cases, health economic evaluation studies prioritize only the outcomes used in clinical trials or those used in reports of the official sanitary department. This choice leads to selective reporting bias, meaning that only the results that worked are enhanced.³ Moreover, the use of surrogate outcomes should be avoided – e.g., biochemical and physiological parameters that are not necessarily related with important results for the patients.⁴ When using surrogate outcomes, it is important to justify its usage through relevant clinical evidence.

One option to enhance the statistical power of clinical researches is the use of combined outcomes.⁵ Many clinical results are grouped in one outcome, such as the presence of one or more comorbidities.

Utility outcomes

The utility is expressed by the preference of the individual for a given health state.⁶ The quality-adjusted life years – QALY and the disability-adjusted life years – DALY are commonly used.

QALY tends to be the most common indicator. It is obtained by applying techniques or tools that measure the impact of the condition in various dimensions.⁷ Among the most common dimensions, we can mention mobility, anxiety and depression, self-care, pain and illness. In Brazil, two tools are validated: the EQ-5D (EuroQol five dimensions questionnaire) and the SF-6D (Short-form 6 dimensions). Indirect techniques on QALY measurement include the time-trade-off, the standard gamble and the visual analog scale.⁶ These strategies use scales or scenario simulation.

DALY describes the quantity of years lost due to disablement and death.⁷ Based on the life expectance, the unproductivity years are reduced as a consequence of a damage and the years of life lost.

Regardless of the method for utility measurement, this measurement is recommended to be performed in representative sample of individuals with interest

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clinical condition. Besides, the utility is influenced by factors intrinsic to the context under investigation, such as the values and perceptions of the society toward adverse situations. Thus, using utility data from other countries may compromise the robustness of the study.

Monetary outcomes

Cost-benefit analyses measure the outcomes in monetary units.¹ This strategy is particularly useful when it is necessary to compare interventions of distinct areas, for instance, between vaccination campaign and acquisition of Intensive Care Units (ICU) beds. However, there are ethical and methodological concerns when attributing monetary value to the human life.

Converting clinical consequences into monetary units requires a balance of individual preferences and social values. The human capital and willingness to pay approaches are the most used.⁸ The procedures aim at estimating costs that could have been avoided in case the intervention and the strategy under investigation had been adopted. Taking as an example the comparison between the malaria rapid-test and the microscopy, the financial benefit to measure could be the costs avoided in consequence of medical-hospital expenses and the productivity loss avoided due to incapacity and early death.⁹

The human capital approach considers that the value of the benefit to health is equal to the profit caused by the intervention or strategy. The salary raise is usually based on the average salary, stratified by sex, age or occupation.

The willingness to pay approach is the most recommended method.⁸ Avoided expenses and how much people decide to spend to reduce the chance of an undesired health event are determined. This way, intangible benefits are also included in the analysis. To deduce the values, surveys with hypothetical scenarios are designed, in order to obtain the payment intention.

Information sources on the outcomes

Reliable clinical guidelines establish the diagnosis criteria, the treatment algorithm and the mechanisms for clinical monitoring. Thus, these documents are the first sources to be consulted when identifying clinically important outcomes.

Regardless of the type of outcome, the data reliability is influenced by the study design. Finding systematic reviews remain the first option to know the consequences

of interventions. It is possible to use data from the local setting whenever this measurement can be conducted. The best measurements come from randomized clinical trials. They are particularly important when they add knowledge on the main intervention or analysis strategy.

In the absence of clinical trials on the topic, one can resort to observation designs. Most recently, researchers have decided to use big databases (big data) and electronic medical records as information sources. The cohort studies are hierarchically superior comparing to case-control, and this latter are preferred to the cross-sectional studies. It is also possible to use specialists' panels, which generate information located in a lower position on the evidence hierarchy.

Complementary analyses

Not only the costs, but also results in health need to be corrected if the time horizon was longer than a year. In order to analyze different time periods, a discount rate must be used, besides the inflation adjustment. In Brazil, there is a suggestion of applying a 5% discount rate.¹⁰

Outcomes are measured in samples, in a way that there is a variety expected for the results, usually expressed through confidence intervals. Such results are used in sensitivity analyses, a subject that will be treated later in these series.

Most of times, it is possible to divide the target population into groups of better or worse prognosis. It can also be interesting to investigate the presence or absence of comorbidities in the analysis. These details increase the external validity of the economic model.

Conclusion

This paper presents the principles adopted in the selection of outcomes to be used in economic evaluation studies. Figure 1 presents a verification list to guide the work. The choice can be either for easily measured outcomes – for example, the occurrence of death –, or others which are more complex to obtain, for being multidimensional, such as life quality.

The choice for a certain outcome reflects the study perspective, the understanding of the clinical course of the disease and the analytical hypothesis. Multi-professional teams tend to make better choices. There is a considerable lack in outcomes research in Brazil. Tools that measure quality of life should be more frequently used, even in the health services routine.

Items	Comments
1. Identify the primary and secondary outcomes that directly answer to the research question	Start with clinical outcomes. Depending on the scenario, the results are pondered in terms of utility (e.g.: quality-adjusted life years – QALY) or monetary values.
2. Define, clearly and objectively, clinical outcomes	The outcomes may reflect the natural history of the disease and the possible effects of the interventions or strategies analyzed. Most of time, the measurement methods must be validated – e.g., recommended by clinical guidance.
3. Inform the measurement tools in cost-utility studies	The tools need to reflect the specific conditions of the clinical course of the disease or treatment. The suggestion is to measure the quality-adjusted life years (QALY). There are direct and indirect estimates (see text).
4. Specify the measurement method in cost-benefit studies	The clinical results are converted to monetary values. The suggestion is to use of the willingness to pay approach.
5. Consider additional analysis	Identify the important clinical population groups or subgroups. Perform sensitivity analyses considering the variation observed, using confidence intervals, for example. Adjust the outcome projections for periods longer than one year, by applying discount rates.

Figure 1 – Items to be verified when identifying and measuring outcomes on health economic evaluation studies

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