REVIEW ARTICLE

Economic evaluation in the field of mental health: conceptual basis

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Objective: Technological advances in medicine have given rise to a dilemma concerning the use of new health technologies in a context of limited financial resources. In the field of psychiatry, health economic evaluation is a recent method that can assist in choosing interventions with different cost and/or effectiveness for specific populations or conditions. This article introduces clinicians to the fundamental concepts required for critical assessment of health economic evaluations.

Methods: The authors conducted a review with systematic methods to assess the essential theoretical framework of health economic evaluation and mental health in Brazil through textbooks and studies indexed in the PubMed, Cochrane Central, LILACS, NHS CRD, and REBRATS databases. A total of 334 studies were found using the specified terms (MeSH - Mental Health AND Economic, Medical) and filters (Brazil AND Humans); however, only five Brazilian economic evaluations were found.

Results and conclusions: Economic evaluation studies are growing exponentially in the medical literature. Publications focusing on health economics as applied to psychiatry are increasingly common, but Brazilian data are still very incipient. In a country where financial resources are so scarce, economic analyses are necessary to ensure better use of public resources and wider population access to effective health technologies.

Keywords: Health technology assessment; health economics; cost-effectiveness; epidemiology

Introduction

In a scenario where the demand for new health interventions exceeds available financial resources, important decisions must be made. Economic evaluations may represent a useful tool in health policy decision making, helping make processes more rational and fair.[1] Economic analysis of interventions in mental health entails identification, measurement and comparison of costs and outcomes of competing strategies for prevention, diagnosis, or treatment of psychiatric disorders. The main objective is to maximize benefits to society by funding those interventions that generate the best outcomes using available resources.[2]

When they need to recommend, license, buy, or use a particular health intervention, decision makers look for answers to some crucial questions, such as "Is this treatment efficacious and effective?," "Does the intervention improve disease symptoms or patient quality of life?," and "Does the intervention bring benefits for a cost that is worth paying?" This last question can be answered by means of a particular type of economic analysis: cost-effectiveness analysis.[3]

In summary, in view of the challenges imposed by contemporary society (rapid development of new technologies and limited economic resources), evaluation of the efficacy and effectiveness of interventions no longer suffices. Their efficiency must also be evaluated, and only economic analyses allow that. Since economic evaluation is a relatively recent methodology in psychiatry and related fields, the objective of this article is to present the fundamentals of these studies, providing a basis for mental health professionals to conduct their own critical evaluations of the growing literature in this field. The specific objectives of this article are to introduce the types of economic analysis described in the literature, as well as the main components for defining measures of cost, effectiveness and cost-effectiveness. Finally, particular aspects of economic analysis in mental health are discussed, and a brief description of the evaluation of health technologies in Brazil is provided.

Types of economic evaluation

As will be discussed later, the term economic analysis refers to studies where a comparison between two or more interventions is performed, focusing on cost and effectiveness data. However, many published articles only present data on economic costs; these are known as

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incomplete or partial economic evaluations. Such studies can be classified according to which specific costs are being addressed: cost analyses are studies that describe the economic costs involved in one or more interventions, whereas cost-of-illness studies are those that estimate economic costs related to particular diseases.[3]

Another type of analysis, known as cost-minimization analysis, compares the costs of two or more interventions that achieve similar outcomes (in terms of effectiveness). In this situation, the comparisons are made on the basis of cost alone.[3]

This article, however, will focus on complete economic evaluations: those that can provide valuable, concrete information to enable more appropriate decision-making with respect to resource allocation.[4] Complete economic evaluations are indistinctly referred to as cost-effectiveness analysis or cost-effectiveness studies, but they can be more accurately classified into a variety of subtypes, depending on which measure of effectiveness is adopted, as the next section will show.

Main components of an economic analysis

By definition, cost-effectiveness analyses entail a comparison of two or more alternative methods for the treatment of a given disease. These alternatives are usually competing technologies for the treatment of the same disease, known as mutually exclusive interventions - for instance, the choice between different classes of antidepressants to treat depression, or different atypical antipsychotics for schizophrenia. In a comparison between two interventions, one calculates ratios that represent the additional cost required to achieve an extra unit of clinical benefit.

Cost-effectiveness ratio

From a conceptual standpoint, the cost-effectiveness ratio (CER) is the difference in costs between two interventions divided by their difference in effectiveness, usually defined as an unit such as the quality-adjusted life year (QALY)[4]: $CE = (Cost_2 - Cost_1) / (QALY_1 - QALY_2)$.

The outcome measure used as the denominator of the CER defines the type of cost-effectiveness analysis, as shown in Table 1.

Average and incremental cost-effectiveness ratios

An important distinction must be made between average and incremental CER. The average CER is calculated

by dividing the cost per patient of an independent intervention by its outcome. However, the average CER does not compare alternative strategies; this can only be achieved through calculation of the incremental cost-effectiveness ratio (ICER), using the formula shown above. Most methodologically adequate cost-effectiveness studies now published express results as ICERs.[4]

Outcome measures

As mentioned above, the denominator of a CER is the difference in effectiveness between the two interventions that are being compared. To estimate the effectiveness of an intervention, the investigator must first know the health conditions that may occur as a consequence of each intervention, the likelihood that each of these conditions will occur, and the potential duration of these conditions.

A detailed description of the entire chain of events that may occur, can be provided by a decision tree. Figure 1 demonstrates, as an example, a decision tree for treatment of attention-deficit hyperactivity disorder (ADHD) with immediate-release methylphenidate (MPH-IR) in Brazilian children and adolescents.

To conduct a cost-effectiveness analysis, the investigator must calculate a numeric estimate for each of the outcomes presented at the final branch of the decision tree, as shown above. In medical specialties other than psychiatry, these events of interest are often measured as reductions in mortality rate, years of life saved, or increased survival. In the field of mental health, however, these measures rarely apply, as the diagnosed conditions are usually both chronic and nonlethal.[5] In this context, other outcome measures could be used, such as disease-free days, remission rates, and relapse rates.

However, the clinical outcomes listed above may not be enough to assess the benefit of an intervention, because: a) they are measured in different units, thus precluding comparison between different treatment strategies; and b) all are objective measures, usually measured by the investigator, and do not take into account patients' opinions of their own condition. Subjective measures are essential in the field of mental health, as psychological distress can only be truly evaluated from the standpoint of the individual that is experiencing it. Therefore, in recent decades, international guidelines for cost-effectiveness studies[6] and international health technology assessment agencies, such as the UK National Institute of Clinical Excellence (NICE) (2010), have recommended the use of quality of life measures as the outcomes of choice for assessment of effectiveness in economic evaluations.

Quality of life

In order to be appropriate for use in economic analysis, a quality-of-life measure must meet some criteria: a) it must yield a single score; b) it must be based on individual preference for a certain health state; c) conventionally, it must be measured on a scale of 0 to 1, where 1 represents full health and 0 represents death. The scores

Table 1 Types of cost-effectiveness analysis

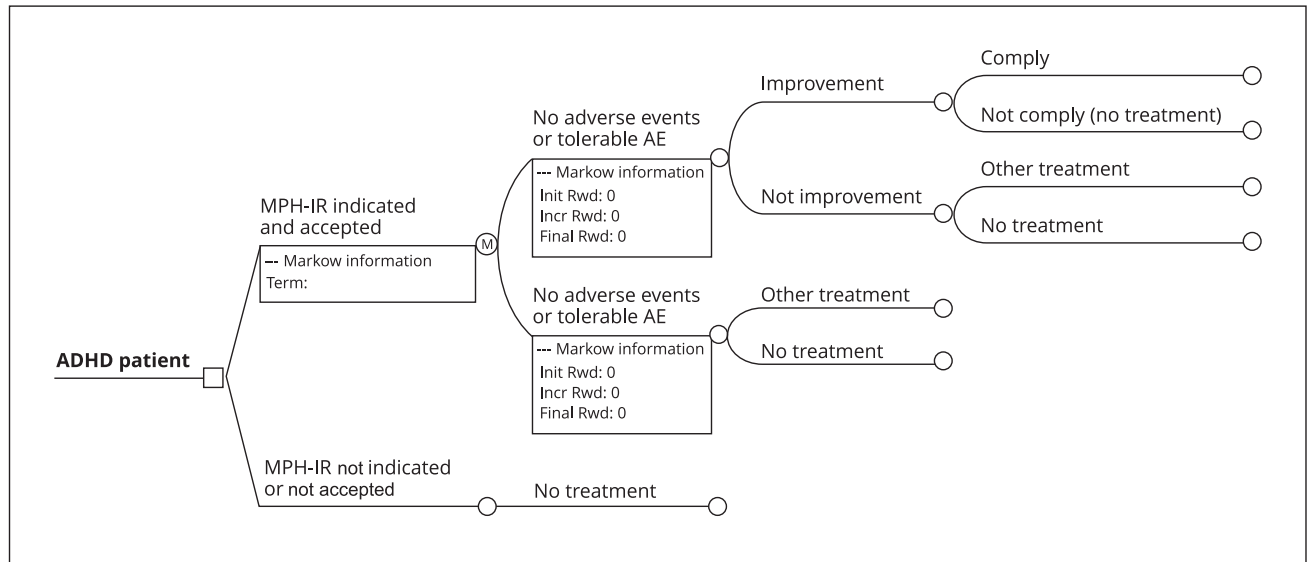| Type of analysis	Outcome	Result
Cost effectiveness	Natural units	Cost/work days lost to illness Cost/unit of improvement on a given scale
Cost utility	Quality of life	Cost/QALY
Cost-benefit	Monetary units	Cost/outcome expressed as dollars, pounds, reais etc.

QALY = quality-adjusted life year.

Figure 1 Decision tree for treatment of attention deficit-hyperactivity disorder (ADHD) with immediate-release methylphenidate (MPH-IR) in Brazilian children and adolescents. AE = adverse events; Rwd = reward.

generated by these instruments are known as preference-based measures or utility measures. When combined with survival data, these figures enable estimation of QALY, which are used to represent effectiveness in cost-utility studies.

The main advantages of the QALY as an outcome measure are that it enables comparison of different studies, as it is always measured in the same unit, and the fact that it simultaneously provides information on quality of life and on survival.

Instruments for measurement of preferences for health states are classified into two broad groups: direct or indirect.[7] Using direct measures, investigators can calculate a health utility value directly from assessment of a specific health state, without having to convert patient responses. Conversely, indirect methods are questionnaires whereby patient responses are converted into a utility value using a standardized, instrument-specific scoring system. Direct measures include the standard gamble, which is based on choosing between health states depending on the probability of their occurrence, and the time trade-off, where the respondent is asked how many years of life in a specified health state they would give up in exchange for recovering full health.[8] As these methods are more complex, they may not be applicable to all populations. In this context, indirect methods may be a useful alternative. Indirect utility measures include the EQ-5D,[9] the Health Utility Index (HUI),[10] and the SF-6D,[11,12] which is a derivative of the generic SF-36 instrument. All have been translated into Brazilian Portuguese, but only the SF-6D has had its scoring system adapted to the Brazilian reality, on the basis of health preferences measured in a sample of the population of Porto Alegre, state of Rio Grande do Sul.

After ascertaining which unit best expresses the effectiveness of a given health intervention, investigators must then collect data to estimate the probability of the outcomes of interest. Probability estimation requires synthesis of information collected from a variety of literature sources, including systematic reviews, meta-analyses, and randomized clinical trials. Probabilities express the degree of certainty that a given event will in fact take place, such as the probability of developing a specific condition, the probability of responding to a certain treatment regimen or developing adverse effects, and the probability of dying due to a certain health state. Mathematical models are constructed to aggregate data obtained from a variety of epidemiological sources. These models enable pooling of available outcomes and provide parameters for estimation of missing values. Another relevant aspect of health economic evaluation is measurement of the costs involved in each intervention.

Cost estimation

In health economic evaluation, cost can be classified in a variety of ways. The most common methods are as follows.

Direct costs include all costs associated with development and operationalization of a health-related intervention or program. Direct cost variables can be regarded as the ingredients of the program, such as the number and duration of medical visits and the cost of medications or supplements. The cost generated by the adverse effects of an intervention or technology are also included in this category.[13,14]

Indirect costs (patient- and family-related) include all resources consumed during treatment, as well as any resource that contributes to treatment. Patients and their relatives may incur a variety of out-of-pocket costs, such as transportation to health facilities or a live-in caregiver. Variables associated with loss of productivity, such as time spent by patients or their relatives in the search for

treatment, time spent on taking part in a health program, work days lost, or reductions in workload should also be assessed as indirect costs.[13,14]

Capital costs are those involved in purchasing the capital assets required by programs. Equipment, buildings, and land are the most frequent capital costs.[13]

Intangibles are costs to which a market value cannot be assigned. These can include suffering, pain, death, and leisure time lost.[13]

Another important aspect to be considered in costs estimation is the cost perspective - that is, from whose viewpoint expenses are being measured (societal, Ministry of Health, employers, insurers, etc.). Different viewpoints will include or exclude different costs. For instance, cost of transportation to a health facility may be regarded as a major variable by patients and society, but not by the Ministry of Health.[13,15]

In estimating the costs of a health technology, the amount of each consumed resource should be measured and the total cost should be calculated by multiplying these amounts by the relevant cost or price unit.[13,16] Cost units are usually determined by sources that describe market prices. Therefore, one should take into account the optimal manner of including costs according to the context in which they are being used.

In summary, cost analysis is a three-step process: 1) identify all relevant resources that shall be used; 2) quantify the resources actually used; 3) determine the monetary value of each resource. To clarify the concepts presented in this paper, a cost-effectiveness study from the literature will be used by way of example. It is an effectiveness and cost-effectiveness study comparing 10 antidepressants (citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, mirtazapine, paroxetine, reboxetine, sertraline and venlafaxine) for treatment of patients with moderate to severe depression in the primary care setting. A multiple treatment comparison meta-analysis was employed to determine the relative efficacy in terms of remission. These rates were then applied in a decision-analytic model in order to estimate costs and quality of life with different treatments at 1 year. The data set included 87 studies with close to 20 000 patients.[17] Cost-effectiveness analysis is undertaken from a societal perspective. Mean costs and QALYs for all treatment strategies are presented as ICERs estimates. The ICER should be interpreted as the additional cost required to achieve an additional unit of health outcome (QALY) when providing one treatment over another.

The direct costs were €374 /month for patients with depression in primary care treatment. In patients achieving remission, these costs decreased to €273/month. Mirtazapine (daily dose) presented the lowest cost among antidepressants. Indirect expected costs, including the value of lost productivity, were €3448/month. Regarding effectiveness, the SSRI escitalopram was more likely to provide remission than amitriptyline, citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. The results of cost-effectiveness analysis showed that, despite a high acquisition cost, the SSRI escitalopram was associated with greater clinical effectiveness and lower total

cost compared with all other treatment strategies. Furthermore, escitalopram was associated with a larger health gain (QALYs) at 1 year, and therefore dominated the other treatment strategies, as more QALYs are achieved at a lower total cost.

In the cost-effectiveness analysis, escitalopram was the dominant alternative in most comparisons. However, in the comparison between escitalopram and venlafaxine, escitalopram was more effective, but venlafaxine was cheaper. In this situation, calculation of the ICER is indicated. Many statistical programs that can assist in creating a decision tree, as the example shown above in Figure 1, thus enabling cost-effectiveness analysis. In this example, the ICER is represented in the numerator by the difference between total costs of both treatments, i.e., the total costs of escitalopram treatment minus the costs of venlafaxine treatment. In the denominator, effectiveness is represented by the difference between the QALY of both treatments, i.e., QALY rates obtained by patients on escitalopram are subtracted from the QALY rates obtained by patients on venlafaxine, Therefore, the ICER between the treatments is calculated as follows: ICER = (€5,088 - €5,074) / (0.6978 - 0.6942) = 14 / 0.0036 = 3888.88.

This means that the additional cost per QALY gained with the use of escitalopram was €3888,88 compared with venlafaxine from the health care perspective (the difference between the result of ICER described in this example and the result described in the original article is due to decimal places). The results of a CER analysis can only be interpreted by reference to an external standard. This can be done through comparison with other independent interventions, or using a threshold ratio above which a program would no longer be considered cost-effective. For example, the threshold adopted in the Netherlands to decide if an intervention will be implemented in the public health system is €80,000/QALY. Therefore, escitalopram, when compared with venlafaxine, has a CER that is below the national threshold, being a candidate intervention for implementation. (For more information, the complete results are described in the original article.[17])

Mental health costs

Mental health costs can be the result of the behavioral characteristics of individuals with mental disorders, as well as of the response of others to these behaviors. Mental health problems are defined by their clinical symptoms, but have impact on a variety of dimensions in life. Individuals with mental disorders thus require support from several areas of society, not only the healthcare system. Therefore, mental health costs involve not only the healthcare system but also the systems responsible for social care, housing, employment, criminal justice, and financial support.[18]

Expenses associated with health service utilization, inpatient care, and antidepressants or other medications are the main components that cause an economic impact on individuals with mental disorders. The productivity

losses usually associated with mental disorders and the costs of social care by family members or other caregivers also account for a major portion of expenditure on mental health problems. In addition to these variables, there is also the added challenge of taking into account other factors that may be involved, such as the stigma of mental disorders and societal discrimination of individuals with these conditions; certain inherent features of mental disorders, such as self-destructive or dangerous behaviors, suicide, and social exclusion.[18]

For better understanding of the cost dimensions of mental health, these can be divided into two groups. The first group concerns the morbidity costs of mental disorders, and the second, the response costs of mental health problems, that is the costs associated with the responses of others to mental disorders[19]:

1) Morbidity costs are those caused by the effects of the symptoms of mental disorders on the productivity of patients and their family members, such as unemployment, absenteeism, impaired work performance, reduced income for the individual, and reduced productivity for the economy; behaviors that result in damage (accidents or crime); and suicide and other premature mortality.[19]

2) Response costs are those associated with how others respond or react to the symptoms and characteristics of mental disorders[19]: services provided by others (social care, criminal justice, education, leisure, transportation, and security) in response to current needs; out-of-pocket expenses incurred by the individual or his or her family (for treatments, services, health-related travel, etc.); and the behavior of employers in response to people with recognized mental disorders, including discrimination, income losses, and impaired productivity.

Applicability of cost-effectiveness analyses

As described above, cost-effectiveness analyses are increasingly common in the literature as decision support tools. These analyses are broadly applicable and can be used in a variety of contexts.

Searching for treatment efficacy or effectiveness results alone does not suffice for an efficient decision-making process when the demand and cost of mental health programs is involved, whether in publicly or privately funded health systems. Most studies focus on pharmacotherapy and use simple methods; little is invested on economic assessment of psychosocial interventions and cost-effectiveness and cost-benefit analysis.[20] Furthermore, development of recommendations to support prioritization of investments in the prevention or treatment of mental illness is challenging not only due to the dearth of studies, but also to the distinctive characteristics inherent to each population.[21] In this context, several organizations have endeavored to bridge this gap by conducting economic evaluation research. At the international level, these organizations include the World Health Organization and its CHOosing Interventions that are Cost Effective program (WHO-CHOICE), the UK National

Institute for Health Research (NIHR) Health Technology Assessment program (HTA), and the Canadian Agency for Drugs and Technologies in Health (CADTH).

Based on the assumption that the results of cost-effectiveness studies are not equally applicable to all countries and that pooling these results at a single clearinghouse would be useful to researchers and health administrators alike, in 1998, WHO-CHOICE created a database of cost-effectiveness results divided into 14 WHO sub-regions that have similar epidemiological, infrastructure, and economic characteristics.[22] The program has published results for several mental health topics in the AMR B sub-region, which includes Brazil. These topics have included measures for reduction of hazardous alcohol use,[23] cost-effectiveness of schizophrenia treatment,[24] and clinical interventions for reducing the consequences of bipolar disorder,[25] and depression.[24]

The HTA program, operated by the UK NICE, was created in 1993 and is charged with providing reports on the efficacy, cost, and impact of health technologies. The results of these assessments are used by decision makers in the UK, including NICE itself and the National Screening Committee (NSC), to improve the quality of clinical practice within the National Health System (NHS). The HTA has conducted several economic evaluations in the field of mental health, including assessment of the effectiveness and cost-effectiveness of counseling in patients with chronic depression,[26] new drugs for bipolar disorder,[27] Alzheimer's disease,[28] and treatment of ADHD in children and adolescents.[29]

Using principles and methods similar to those of the UK program, the CADTH aims to deliver the information required by health managers for decision making in an efficient and timely manner.[30] Several of the agency's published studies were designed to answer questions relevant to the mental health field, such as reviews on the cost-effectiveness of cognitive-behavioral therapy (CBT) for patients with addictions,[31] programs to manage aggressive behavior,[32] self-directed CBT for adults with diagnosis of major depressive disorder,[33] and CBT for post-traumatic stress disorder.[34]

Currently, most investment on cost-effectiveness studies in the field of mental health is still focused in developed countries. It is abundantly clear that investing in these studies provides countrywide benefits and constitutes an intelligent and effective way of guiding government efforts and public resource expenditure.

Health technology assessment (HTA) in mental health in Brazil

Health economics in mental health in Brazil is a new area, and economic evaluations are still scarce. According to REBRATS (Rede Brasileira de Avaliação de Tecnologias em Saúde), economic studies in psychiatry represent only 5% of studies funded by the Ministry of Health.[35] However, the Brazilian government has been encouraging studies in the field, and in the last four years has

funded economic analyses in the psychosis, mood disorders and ADHD areas.

A search of the major databases available (PubMed, Cochrane Central, LILACS, CRD NHS, REBRATS) including articles published from January 1995 to January 2012 yielded a total of 334 studies using the MeSH terms mental health AND economic, medical and the filters Brazil AND humans for economics and mental disorders in Brazil. However, only five studies were Brazilian economic evaluations. Pharmacological interventions were the most common technology to be assessed, mainly in schizophrenia, alcohol/substance disorder, and major depressive disorders.[36-40] This scarcity shows the need for development of the mental health economics field in Brazil, mainly regarding human resources, to conduct methodologically adequate research.

Limitations of cost-effectiveness methods in general can also be applied to the mental health area. Despite being a valuable tool to support decision-making in health policy, cost-effectiveness analysis does not address the ethical issues of allocation of scarce resources. There is no absolute criterion that can be used to recommend an intervention based solely on a cost-effectiveness analysis. Opinions on whether any health intervention is worth a certain amount of money are subject to variations depending on the perspective and values of those who make the value judgment. Hence, cost-effectiveness analysis is most useful when it is used as one of many inputs to support resource allocation decisions.[41] Economic evaluations in particular are often expensive, time-consuming, and demanding in terms of trained human resources. Consequently, it would be impossible to conduct an economic analysis for every health care intervention. Geographical transferability of economic data can represent a way of making more efficient use of existing studies and may be the only alternative for some countries where information is scarce.[42] However, the potential applicability of such results to Brazil must be considered carefully. International clinical trials are frequently carried out in populations with different genetic, demographic, and cultural characteristics when compared to the majority of the Brazilian population. Such differences can significantly change parameters such as efficacy, effectiveness, and preferences. Therefore, the lack of data can represent an important limitation to conduction of robust cost-effectiveness analyses in Brazil.

Particularly in the area of psychiatry, some additional challenges are met. The paucity of epidemiological data on mental health makes it difficult to prioritize which health technologies need to be evaluated initially to define a research agenda; many studies are planned based on pressure from the pharmaceutical industry. Moreover, there is a knowledge gap concerning the effectiveness of different treatments in mental health - investigators must use data from other countries to support their economic studies.

Conclusions

Economic evaluation studies are growing exponentially in the medical literature. Health economics analyses aid the decision-making process, particularly by quantifying the extent to which the cost difference of a given intervention is acceptable in view of the additional benefit it may provide as compared to a standard intervention. Although these studies use complex methods to reach their results, clinicians should understand the key elements of economic analyses so as to enable critical judgment of the applicability of these results to different realities. Health economics is growing in the field of psychiatry, but Brazilian data are still incipient at best. In a country where financial resources are so scarce, there is a pressing need for economic analyses in major focus areas of psychiatry such as mood and anxiety disorders, psychosis, use of psychoactive substances, ADHD, and child and adolescent mental health, so as to ensure better use of public resources and wider population access to effective health technologies.

Authors Disclosure

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