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# **Economic Evaluations in Health from the Perspective of the Costs Associated with Diabetes Mellitus Treatment**

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Additional information is available at the end of the chapter

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## **Abstract**

Diabetes mellitus (DM) is a morbidity that presents a wide range of difficulties for the patient to reach the control. This reality not only has impact on the clinical practice but also has serious financial and social consequences for both the patient and the health system. Health technologies that are capable of improving glycemic control have been tested in cost-effectiveness analysis to assess the efficiency of DM care. According to the Brazilian Society of Diabetes, patients with glycated hemoglobin (A1c) within the values considered adequate, less than 6.5%, present a relative risk of developing complications (neuropathy, retinopathy, diabetic foot, pressure ulcers, cardiovascular diseases and renal disease) equal to that of a nondiabetic patient. In highlight, health technologies have presented positive impact on reducing A1c and, consequently, on reducing diabetes complications. Thus, new health technologies have been capable saving of 72% of resources spent on DM care.

**Keywords:** diabetes mellitus, economics, pharmaceutical, technology assessment, biomedical

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## **1. Economic evaluation in health**

Historically, evaluation processes are part of the development of humanity as a society. After World War II, there was an increase in State activities in the control of services such as health and education in many countries. An economic current gained strength in the development of methodological processes to evaluate these State activities, assessing their

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costs and their advantages. These processes conformed themselves into economic health assessments [1].

In the course of time, economic evaluation in the area of health has been gaining more rigorous methodological contours, and nowadays, it is characterized as an important tool of public services, in the health economy sector. Health assessment has specific bodies in some developed countries such as the United States, Canada and France [1, 2]. In Latin America, Brazil is considered one of the pioneers in the implementation of economic health assessment methodologies, and countries such as Colombia, Mexico, Argentina and Chile have advanced a lot in the area's development [3].

The health area constantly goes through processes of technological innovation. Associated with the epidemiological changes of recent years, the incorporation of new health technologies has become a reality with which the management of health services has to deal constantly. This scenario has contributed to the increasing cost of maintaining health services and corroborated the increase in complexity in the administration and functioning of health services [2, 4]. It is noteworthy that health has limited and finite resources, which makes health evaluation a complex task, with criteria that go beyond the cost-related, ethical, safety and equity issues [2]. Given the complexity of the health scenario, economic evaluation in health aims to subsidize management in decision-making about the incorporation of new technologies, as well as its monitoring, with the standardization of criteria and practices that may facilitate the management of public health services [5, 6].

The researches of economic evaluation in the health area are constituted by some basic structural elements. Initially, it is necessary to define the costs that will be assessed during the study, which may be direct medical or nonmedical costs, which correspond to the costs directly applied to the provision of patient care, for example, the cost of medication (medical) or the cost of moving a patient to another municipality for care (nonmedical). There are also indirect costs that are related to the social losses of the individual or of society itself or of the State with the sick individual, such as, for example, days of work lost as a result of a disease. Another cost category is intangibles, which are considered difficult to measure monetarily, for example, pain. For any economic evaluation in health, it is necessary to define the perspective under which the costs will be analyzed, which will guide which costs will be included in the economic analysis, and how to carry out the costing. Costs can be assessed from the perspectives of the health system, the hospital service, the government or of the society as a service provider or buyer can be changed for payer [5, 7].

Another structural element of economic evaluation research is the identification of the outcome, that is, of the result that will be evaluated by the research. This outcome can be expressed as a monetary unit, a clinical outcome or quality of life. The use of primary outcomes (cure, eradication of infection, death) is preferable compared to intermediate outcomes (reduction of blood pressure or glucose levels). However, the measurement of primary resources is usually more difficult to perform and, consequently, little is used in research. According to the objective of the economic evaluation in health and the context in question, the type of economic evaluation to be performed must be defined [4, 7].

As evaluative surveys are still considered recent in the world scenario, it is important to highlight some concepts that may facilitate the understanding of terms that are given below, according to the Thematic Glossary – Health Economy [8]:

- Efficacy is the measurement of the results obtained from ideal or experimental situations.
- Effectiveness is the measurement of the results obtained in real situations, that is, as happens in the health service.
- Efficiency is the economic concept that relates the results obtained with the necessary financial resources to achieve these results.

In resume, economic evaluations in the health are structured through specific scientific areas that produce analyses with specific methods, which are preponderant for the rational process in decision-making; pharmacoeconomics is a science with multidisciplinary characteristics that has been standing out into this process [4].

## 2. Pharmacoeconomics

Pharmacoepidemiology is able to provide much information for routine health services. Pharmacoeconomics is one of the aspects of pharmacoepidemiology [9] and, following this logic of providing information for management, seeks to subsidize decisions regarding the economy and pharmaceutical services [10].

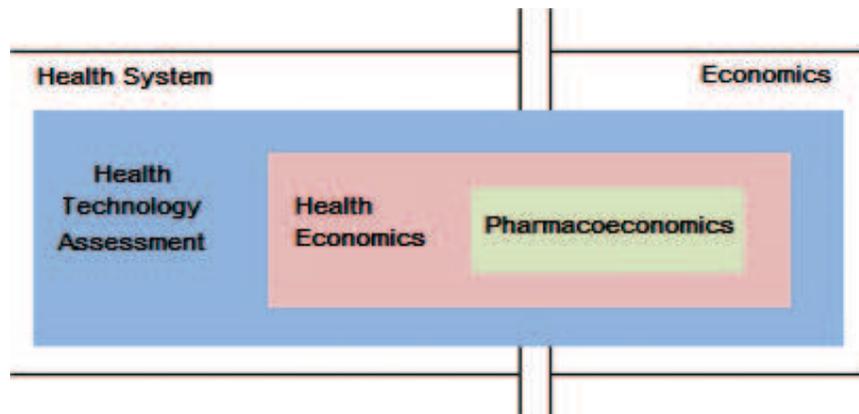
Currently, many medications are introduced into the market. The Ministry of Health and Regulatory Agencies (*ministério da saúde e as agências reguladoras*), the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and in Brazil, the National Agency of Sanitary Surveillance (*Agência Nacional de Vigilância Sanitária – ANVISA*), adopt measures with the aim of regulating this market. Among the strategies, we can mention the inclusion of medication in clinical protocols and the regulation of prices and public health financing. However, it can be seen that these measures are no longer sufficient to guide decision-making within public health services [11]. In this sense, pharmacoeconomic studies contribute to the degree of evidence subsidizing the discussion about the need to incorporate new pharmaceutical technologies [12].

Pharmacoeconomics is a component of the economic evaluation of health services, which assists decision-making and allocation of resources related to services, as well as products or health programs/strategies [13]. The products evaluated by pharmacoeconomics can be both tangibles such as medication and intangibles such as practices that promote the rational use of medication [14], in the case of pharmacotherapeutic empowerment and medication management treatment (MTM). **Figure 1** presents the interface between health and economy and how pharmacoeconomics fits into this scenario [15].

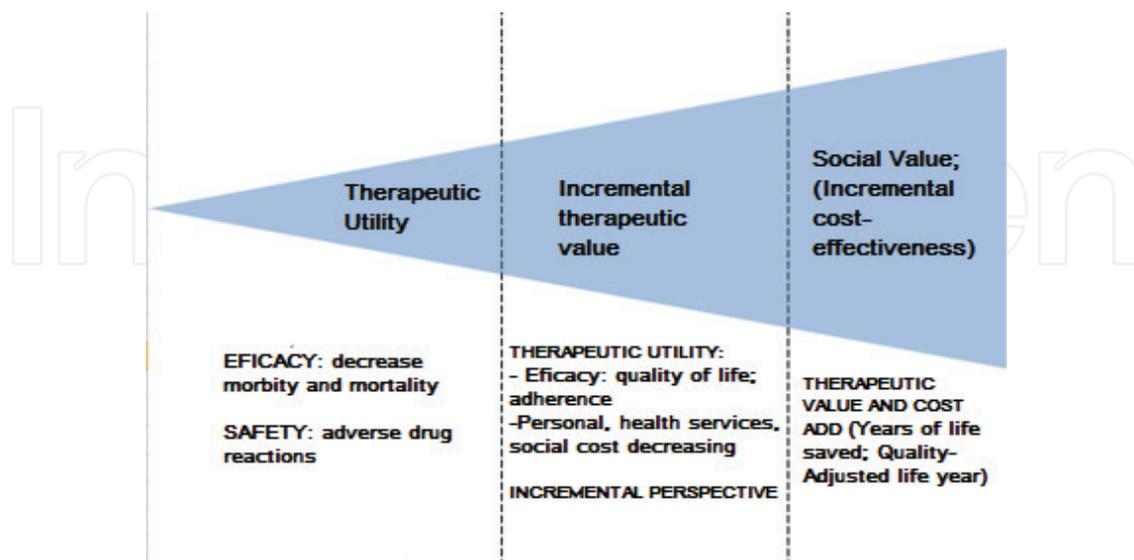
The analysis of the clinical-pharmacological viewpoint is usually limited to the binomial efficacy-safety; however, a discussion that considers other variables, such as secondary and final outcomes (death), adherence to treatment and social aspects, is necessary for the decisions

to achieve broader aspects such as the social value attributed to a medicinal product. Social value is understood as all the positive effects produced by medication such as welfare promotion, satisfaction with treatment and social production capacity (family life, work) [11]. **Figure 2** shows how the complexity of pharmacoeconomic works evolves starting from the binomial efficacy-safety to more complex analyses that evaluate the quality of life of the patients [11].

Pharmacoeconomics uses specific methodologies for the construction of evaluation models that produce comparisons that adjust all the variables involved in this complex process [15]. **Figure 3** presents the scenario into which the pharmacoeconomic assessments are introduced. For this purpose, it needs different sources of information such as clinical trials, systematic reviews, meta-analyses and health service databases [15]. All these are important sources of information in the construction of pharmacoeconomic studies [11, 15].



**Figure 1.** Pharmacoeconomics as one of the areas of evaluation of the technologies in health and its positioning within the health system scenario and economy. Source: Adapted from Bristol [15].



**Figure 2.** Evolution of pharmacoeconomic studies according to the complexity of the variables evaluated. Source: Adapted from Puig-Junoy et al. [11].

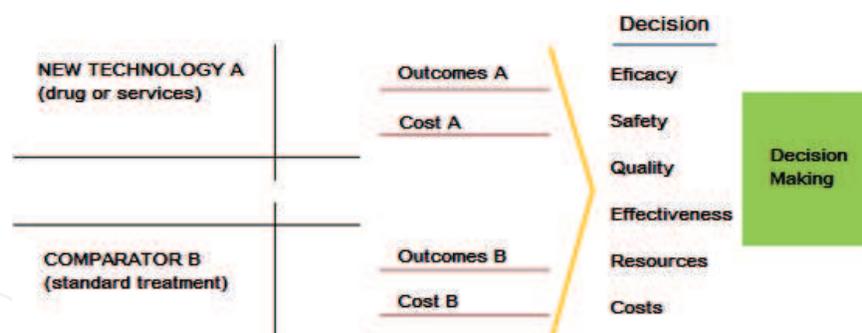


Figure 3. Scenario and variables involved in pharmacoeconomic studies. Source: Adapted from Bristol [15].

For a better understanding of the concepts worked in pharmacoeconomics, some definitions become relevant:

- Cost-minimization analysis: is performed by comparing two or more alternatives which assume the same safety profile and effectiveness; the comparison is between the costs of each alternative [7].
- Cost-benefit analysis: shows evidence of which alternative is most cost-effective, with benefits measured in monetary values [7].
- Cost-effectiveness analysis: allows comparison between alternatives as to their cost and their effect, measured in outcomes, and these outcomes are considered as a clinical parameter [7, 12].
- Cost-utility analysis: many authors defend this type of analysis as a variable of cost-effectiveness analysis. The great difference is in the measure of the outcome, which must measure quality of life and is usually a specific unit, quality-adjusted life year (QALY) or disability-adjusted life year (DALY), always comparing costs with these specific outcomes [7].
- Incremental cost-effectiveness ratio: predicts the cost increment for one more unit of outcome, and guides decision-making in relation to the threshold to be invested in health [7, 12].
- Markov modeling: a mathematical method that allows estimation of disease progression over the years, allocating patients a health status according to the probabilities, and predicting outcomes and costs [12].
- Sensitivity analysis: tests the oscillations of the variables involved in the study, improving the robustness of the study results [7].

### 3. Costs associated with the treatment of diabetes mellitus

Diabetes mellitus (DM) is a morbidity that is difficult for the patient to control, because it involves changes of habits with severe restrictions and a high demand of time for care. According to Stark et al. (2014), data between 2007 and 2010 from the National Health and Nutrition Examination Survey (2010) presented that 40% of Americans with DM failed to

achieve adequate glycemic control [16]. This high prevalence of uncontrolled patients increases the occurrence of complications associated with diabetes [17, 18]. These complications can be summarized as acute and chronic, which give rise to more complex clinical conditions for the treatment of DM [19, 20]. This reality not only has impact on the clinical practice but also has serious financial and social consequences for both the patient and the health system [21].

Acute complications include hyperglycemia (casual glycemia  $>250$  mg/dL), with or without ketoacidosis and hypoglycemia (casual glycemia  $<60$  mg/dL). Acute complications require immediate intervention, so it is very important that patients and caregivers know how to identify the symptoms and manage care to prevent the situation from worsening. This stage of care is directed mainly to the direct costs. The glycemic value can be considered an intermediate outcome, and thus, health technologies capable of reducing glycemia have been tested in cost-effectiveness analysis to verify the efficiency of DM care [4, 5, 22].

Chronic complications can be divided into microvascular complications related to the natural evolution of DM and macrovascular complications, which are not necessarily related to DM, but are commonly more severe in patients with this clinical condition. Microvascular complications include retinopathy, nephropathy and neuropathy [6]. Retinopathy is the leading cause of blindness in adults, and after having DM for 20 years, approximately 60% of patients will already have some visual impairment. DM remains the leading cause of chronic kidney disease (CKD). About one in five patients with DM have a decreased glomerular filtration rate (GFR), that is, they have some degree of diabetic nephropathy. Neuropathy also has a high prevalence among DM patients. In DM, some degree of neuropathy may normally be verified at the time of diagnosis. Neuropathy stands out as a complication that directly impacts the patient's quality of life [23–24].

Macrovascular complications are represented by cardiovascular diseases; the major diseases associated with DM are as follows: ischemic heart disease, cerebrovascular disease and peripheral vascular disease [6]. In these cases, prevention of risk factors and pharmacotherapy are the main tools in the fight against the onset of these complications, which in patients with diabetes tend to occur earlier and be more severe than in the rest of the population [23]. Chronic complications can be considered in a cost-effectiveness analysis to measure costs against the years of life saved (YLS), cost-utility in the cost measurement by QALY or DALY and also in a cost-benefit analysis, when monetary values saved by reducing the chronic complications of DM by some health technology are compared to the cost of this technology. The best way to develop such an analysis would be to carry out Markov modeling for the projection of the patient's health status over time [7, 25].

Alfradique et al. [26] establishes DM as a condition sensitive to primary health care, that is, if managed correctly in basic care, it is possible to obtain positive results in reducing the complications and hospitalizations resulting from this clinical condition. The DM management is a complex process, which requires continuous clinical follow-up, preferably by a multidisciplinary team, and considers education for self-care as one of the pillars in preventing the occurrence of complications in both short- and long-term. In this sense, the primary care system and new health technologies play an important role for the systematized monitoring of diabetic [6, 19].

During the routine of the DM patient in primary care, their choices are able to impact more on their health condition, and consequently, on the results achieved, than the clinical decisions made by a health professional [27]. The health professionals involved in patient care play an important role in the search for glycemic control; however, this is only achieved with the active participation of the patient in their daily care [28].

Empowerment is a concept that was introduced by Anderson et al. in 1991 [29]. Subsequently, the WHO [30], defined empowerment as a strategy in which the patient gains control over decisions that interfere with their health conditions. Later, Kleba and Wendausen [31] added to this concept, the idea that empowerment drives people or groups of people to achieve a better quality of life by changing their daily practices.

In this sense, patient empowerment proves to be an effective strategy for glycemic control. It aims to promote a direct involvement of the patient in self-care, allowing them to know about their real situation and thereby make the best decisions about the care of their health. The health professional plays a supporting role in the process of empowerment, since the whole educational process is developed in a patient-centered way and provides information and contributes to the development of ability, so that the patient has control over their health [29].

Empowerment activities, when developed in an individual way, allow the patient's habits and routines to be understood, narrowing the patient-professional relationship and also allowing the creation of individualized goals and objectives, which consider the patient's psychosocial needs [32].

Studies have shown that empowerment is an efficient strategy for improving glycemic control as well as emotional control of the patient [32]. Kraemer et al., showed a 0.5% reduction in glycated hemoglobin (A1c) through individual pharmaceutical counseling for the empowerment of DM patients. In this sense, such training of the DM patient for their care has shown to be an important alternative in the search for the improvement of quality of life of the diabetic patient, being able to become an economically and clinically viable tool for primary health care [33].

It is worth noting that A1c is the clinical parameter, considered a gold standard for the clinical follow-up of DM, since it allows estimating the patient's glycemic profile for a period of approximately 90–120 days. In a clinical trial that considered diabetic patients on treatment or not, it showed mean values for A1c of 10.2% (3.9–19.1%) [34]. When only diabetic patients under treatment were considered, the mean A1c decreased to 7.7% [35]. According to the Brazilian Society of Diabetes, patients with A1c within the values considered adequate, that is, less than 6.5%, present a relative risk of developing complications (neuropathy, retinopathy, diabetic foot, pressure ulcers, cardiovascular diseases and renal disease) equal to that of a nondiabetic patient [23]. Whereas, values close to 8% for A1c presents a relative risk approximately equal three. With an A1c value between 11 and 12%, type 2 diabetes mellitus (T2DM) patients are 20 times more likely to present these complications when compared to patients without diabetes. A reduction of 1% in A1c values reduces the risk of amputation by 43%, the risk of acute myocardial infarction by 14% and microvascular complications by 37% [23, 35].

The direct medical and nonmedical costs and indirect costs related to the diabetes patient increase over time, especially due to the consequences of the relative risk associated with A1c values, and consequently, to the presence of late complications [7, 36]. Thus, health services need to cope with rising costs in contrast to scarce resources [37]. This scenario becomes a challenge for the health system, considering the increase in the life expectancy of DM patients. Several studies are able to show that preventive measures have a positive benefit/cost ratio when considering the care of the diabetic individual [36, 38]. In addition, it is possible to have a 33% increase in expenses related to DM care in 2 years when glycemic levels are not at satisfactory levels and complications of the disease occur [39].

Expenditures on DM treatment consume up to 12% of the annual health expenditure in the world [40]. It is noteworthy that medications are responsible for 48.2% of the direct costs of a diabetic patient [41]. In a study performed by Marinho et al., in a medium-complexity institution for DM patients, direct costs related to type 2 diabetes mellitus (T2DM) totaled US \$ 2,066,081 and 250,000 procedures were performed in the same period. Of this total, 36.3% was consumed by medication, 20.5% was third-party services (administrative, courses, rent, etc.) and 20.1% was spent by paying highly educated professionals in health care and management, high school educated supporting professionals and trainees involved in health care [42].

In Brazil, for example, the prevalence of T2DM patients is approximately 15% and annual expenditures are approximately 3.9 billion dollars. The Public Health System (PHS) spends an average of US\$ 2108.00 per year for outpatient treatment with each diabetic patient. Of this, US\$ 1335.00 is considered a cost directly related to diabetes [41]. In a Pharmaceutical Care program for diabetic patients, Obreli-Neto et al. showed a mean reduction of 0.7% in A1c values for patients who had empowerment, along with medication treatment management (MTM) in the program. In addition, US\$ 660.80 of the total of US\$ 916.30 spent per patient on DM care was saved [23, 35].

It is noteworthy that many patients become incapacitated as a result of the severity of DM complications, which leads to an increase in indirect costs for the health system [21, 43]. The WHO estimates that the costs of loss of productivity of DM patients can exceed up to five times the direct costs of this disease [20, 36]. It is seen that empowerment of the diabetic patient improves glycemic control and, consequently, reduces the incidence of DM complications over time, which is the main aspect to reduce costs with the treatment of the disease; empowerment of the diabetic patient can be considered an efficient health technology for health systems.

Many studies have presented the theme of economic evaluation focused on the care provided by the pharmacist, such as pharmaceutical care, which uses methods such as MTM and patient empowerment [22, 44]. Pharmaceutical care in a program for the elderly with T2DM and systemic arterial hypertension followed in primary health care in a municipality in the interior of the state of São Paulo, showed that the implementation of pharmaceutical care does not add significant costs to the health service when compared to the results of the best outcomes achieved in patient care [35]. In other words, care strategies such as pharmaceutical care may be more effective and efficient alternatives for health systems.

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## Conflict of interest

The authors declare no conflict of interest.

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