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## Introduction

In health economics, analytical model is the most common term used to designate the mathematical framework that represents reality with enough details in order to inform a clinical or political decision.<sup>1</sup> The use of economic evaluation modelling can be justified by the fact that information comes from various sources and results are extrapolated into the future.<sup>2</sup> For instance, randomized clinical trials usually analyze a restrict number of interventions, have a short follow-up period and rarely bring information on the costs and other relevant elements for decision making.<sup>3</sup>

The research field on analytical modelling has expanded in the past decades, as well as the offer of softwares to run these models. Consequently, complex mathematical and statistical procedures have become more accessible. In this paper, the main characteristics, advantages and limitations of four analytical models are presented. Figure 1 summarizes all the information.

### Decision tree

Decision tree is the simplest way of representing decision modelling.<sup>4</sup> Graphic resources are used to draw possible pathways that patients would follow in case they were under the strategies or interventions investigated. In these pathways, the events and their respective probabilities of occurrence are included. In the end, costs and health outcomes are assigned to each itinerary taken by the individuals.

Given the limited circumstances of this type of modelling, regarding its use, only acute short-term

diseases are considered here. For situations where it is necessary to represent recurring events and long time horizons – chronic diseases, for example –, there are other options of decision models, as follows.

### Markov model

The Markov model has three essential characteristics. The first one is about the restricted number of clinically and economically relevant events that a cohort of individuals may experience during the evolution of the disease. These events are called health states. The second element refers to the period of time in which individuals remain in each health state, called Markov cycle. The third element relies on the transition probabilities from one health state to others. For instance, when considering breast cancer, possible health state would be: (i) local cancer; (ii) metastasis; (iii) cure; and (iv) death. Each cycle would last six months, i.e., every six months there would be a change in the health state (from local cancer to metastasis) or remaining in the same stage (local cancer to local cancer). If the time horizon were ten years, 20 cycles would be repeated, and, at the end of each cycle costs and health outcomes would be determined – these topics were discussed in the two last articles of this series.<sup>5,6</sup>

These characteristics of Markov model are appealing for chronic diseases analyses,<sup>7</sup> since the recurring events and the explanation of time through cycles can be easily included. Usually, Markov models are calculated through hypothetical closed cohorts of individuals,<sup>8</sup> cases in which its use presents some limitations. The first one is about the strictness of cycles' definition by

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Models	Characteristics	Advantages	Limitations
Decision tree	Used mainly for representing acute diseases, based on hypothetical closed cohorts and reduced time horizon.	Simple and transparent.	Does not take into account the recurring events and time-span. Includes individuals with similar characteristics.
Markov model	Usually represents chronic diseases, based on hypothetical closed cohorts and long time horizon. Explains the time-span through cycles. Includes recurring events.	Are usually simple to develop, calculate and analyze.	Ignores the interaction between individuals or groups. The cycle duration is constant, throughout time. Usually considers few health states. In most of cases the individuals have similar characteristics.
Discrete event simulation	Represents chronic diseases based on microsimulation, through stochastic processes and long time horizon. Considers the time-span in a continuous form. The recurring events may be influenced by the characteristics of the patients, time-span, interactions between patients, and resource constraints.	Considers individuals with different characteristics, which tend to vary over time. Events may occur at any time. Resource constraint can be included in the model.	Needs the simulation of a great number of individuals so the model can be stable. Demands advanced knowledge in statistics and programming. Requires a great volume of parameters, not always available on literature. Needs to be calibrated.
Dynamic model	Focus on infectious diseases, with interactions between people and groups. Enables the inclusion of direct and indirect effects of an intervention, such as the reduction of susceptible individuals. Can be conducted through open or closed cohorts.	Externalities of the disease can be considered. The transition probabilities depend on the health situation of other individuals.	Demands advanced knowledge in statistics and programming. Time horizons tend to limit the attractiveness of this model.

**Figure 1 – Main characteristics, advantages and limitations of analytical modelling in economic evaluation studies**

Markov, which are always constant. In real life, the length of each cycle tends to vary with time, due to the natural history of the disease. The second limitation is about the memoryless between two cycles, that is, the past is not taken into consideration. For instance, there would be the same possibility of transition from metastasis to death, regardless of the individual has been with metastasis for one or four cycles, which is not supported by clinical data. An individual with metastasis for twenty-four months (a total of four cycles) has higher probability of evolving to death than an individual that has been with metastasis for only six months (only one cycle). The third limitation of Markov model is related to its interaction between

individuals and groups, a characteristic that appears in the next models presented.

#### **Discrete event simulation**

The model of discrete event simulation is adequate for cases in which interactions between individuals or groups should be considered, when time-to-event is best described stochastically, when individual pathways through the model are influenced by multiple characteristics of the individuals, and when there are resource constraints.<sup>9</sup> Different characteristics mean the possibility of including patients with different traits, such as several age groups, various family histories concerning diseases, comorbidities. The resource constraint represents a situation in which

there is no intervention enough for all the individuals who need it, in a certain moment. This occurs, for example, when the health system is not able to offer a satisfactory amount of elective surgeries to the population, resulting in waiting lists. Time, in turn, may influence both the characteristics of the individuals and the events. Keeping the example of elective surgery, the longer the individual waits, the worse his/her health situation will become, that is, the individual's characteristics will get worse. A long period waiting for care also increases the probability of occurrence of events, such as reaching a more advanced stage of the disease.

### Dynamic model

The dynamic model is especially appropriate to the analysis of strategies or interventions that aim to control infectious diseases.<sup>10</sup> In this models, the direct and indirect effects of transmissions between groups are introduced, also known as externalities of the disease. The transition probabilities depend on the health situation of other individuals. For instance, if a vaccination campaign reduces the number of cases in the population, then the risk of transmission to non-ill people will be lower. In the case of chronic diseases, such as those represented by Markov models, this

characteristic does not exist, because the reduction in the prevalence of cardiac diseases, for example, does not affect the individual risk of having heart problems.

For dynamic models, an important measure is the basic reproduction number, an indicator of the disease spread among the population. Values higher than one indicate an exponential growth in the number of infected cases among the susceptible population, that is, in a higher proportion. For instance, when the basic number reproduction is 3, it means that, on average, a new case generates new three cases, and each of them will generate three new cases, resulting in nine new cases, and those, in 27 new cases, and so on.

### Concluding remarks

This article discussed the main analytical models recommended for guiding the decisions on the inclusion or exclusion of technology in health systems or services. As these models have different degrees of complexity, the option for one or another should happen observing the characteristics of the disease under investigation and its essential elements, such as recurring events, time horizon, interaction between individuals or groups, resource constraints and direct and indirect effects of the disease.

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