

# hesim: Health Economic Simulation Modeling and Decision Analysis

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## Abstract

To do.

*Keywords:* health economic evaluation, cost-effectiveness analysis, simulation, modeling, R.

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## 1. Introduction

Health technology assessment (HTA) is a systematic approach for comparing competing health technologies to inform the efficient use of health care resources. Publicly funded health systems such as those in Australia, Canada, and the United Kingdom, among others, use HTA to help maximize health gains for the population given a fixed budget. HTA is also commonly used by private payers to guide coverage decisions and the adoption of new technologies (Trosman, Van Bebbber, and Phillips 2011). Such assessments usually rely heavily on cost-effectiveness analysis (CEA) so that decisions can be made on the basis of a formal evaluation of costs and effects (Dakin, Devlin, Feng, Rice, O'Neill, and Parkin 2015). CEA is made feasible by development of health economic models that simulate costs and effects over relevant time horizons using the totality of available evidence.

The most commonly used economic models are Markov state transition models (STMs) that simulate transitions between mutually exclusive health states. When the Markov assumption holds so that transition probabilities are either constant over time or depend only on model time, a cohort-level model can be used (Briggs and Sculpher 1998). If the Markov assumption is relaxed—e.g., with a semi-Markov model so that transition probabilities depend on time in an intermediate health state—then individual-level models are required in most cases (Brennan, Chick, and Davies 2006; Fiocco, Putter, and van Houwelingen 2008). Individual-level models afford considerably more flexibility and allow patient history to be tracked over time.

Decisions informed by economic models and CEA are subject to uncertainty. One source of decision uncertainty stems from uncertainty in the underlying model parameters. Parameter uncertainty is typically quantified using probabilistic sensitivity analysis (PSA), which involves randomly sampling the model parameters from suitable probability distribution and simulating the model for each sampled parameter set (Claxton, Sculpher, McCabe, Briggs, Akehurst, Buxton, Brazier, and O'Hagan 2005). When combined with individual-level simulation, PSA can take an appreciable amount of time to run (O'Hagan, Stevenson, and Madan 2007).

Estimation of model parameters should ideally be performed using statistical models that are

aligned with the structure of the economic model. For instance, when patient-level data is available, a multi-state model can be used to parameterize all possible transitions in a STM while accounting for censoring and competing risks (Williams, Lewsey, Briggs, and Mackay 2017). Similarly, in oncology, partitioned survival models (PSMs) can be parameterized from estimates of progression-free survival (PFS) and overall survival (OS). In other cases, parameters might be combined from disparate sources, such as within a single Bayesian model (Baio 2012). When the clinical evidence base is not limited to a single study, a formal evidence synthesis, such as a network-meta analysis (NMA), might even be performed (Dias, Ades, Welton, Jansen, and Sutton 2018).

Despite their computational demands and foundations in statistics, health economic models have historically been developed with specialized commercial software (e.g., TreeAge) or more commonly with a spreadsheet (almost always Microsoft Excel). The limitations of such software relative to programming languages like R have been increasingly emphasized in the literature (Baio and Heath 2017; Incerti, Thom, Baio, and Jansen 2019; Jalal, Pechlivanoglou, Krijkamp, Alarid-Escudero, Enns, and Hunink 2017). It is therefore no surprise that a number of related R packages have recently been developed, such as **BCEA** (Baio, Berardi, and Heath 2017), **SAVI** (Strong, Oakley, and Brennan 2014), **survHE** (Baio 2020), and **heemod** (Filipović-Pierucci, Zarca, and Durand-Zaleski 2017). Still, of the available packages, only **heemod** provides a general purpose framework for developing simulation models and it is limited to cohort Markov models.

**hesim** is an R package that advances the functionality and performance of the existing software. Multiple model types are supported including cohort discrete time state transition models (DTSTMs), N-state PSMs, and individual-level continuous time state transition models (CTSTMs), encompassing both Markov (time-homogeneous and time-inhomogeneous) and semi-Markov processes. To maximize flexibility and facilitate integration of the statistical methods and economic model, parameters can be estimated either by fitting a model in R or by inputting parameters obtained from external sources. So that individual-level simulation and PSA can be run quickly, **Rcpp** and **data.table** are heavily utilized. After simulating costs and quality-adjusted life-years (QALYs) from a PSA, decision analysis can be performed within a cost-effectiveness framework.

## 2. Framework

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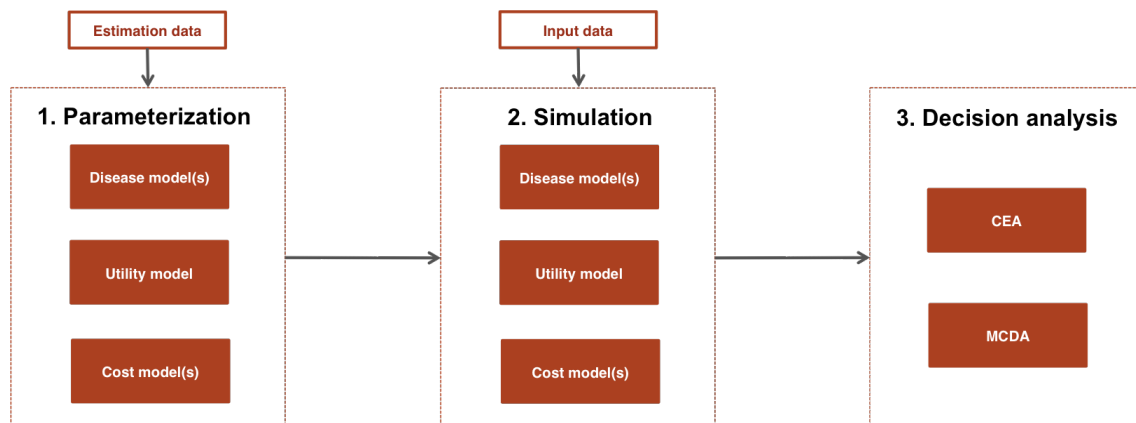


Figure 1: Economic modeling process

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