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State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3

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A B S T R A C T

State-transition modeling is an intuitive, flexible, and transparent approach of computer-based decision-analytic modeling including both Markov model cohort simulation and individual-based (first-order Monte Carlo) microsimulation. Conceptualizing a decision problem in terms of a set of (health) states and transitions among these states, state-transition modeling is one of the most widespread modeling techniques in clinical decision analysis, health technology assessment, and health-economic evaluation. State-transition models have been used in many different populations and diseases, and their applications range from personalized health care strategies to public health programs. Most frequently, state-transition models are used in the evaluation of risk factor interventions, screening, diagnostic procedures, treatment strategies, and disease management programs. The goal of this article was to provide consensus-based guidelines for the application of state-transition models in the context of health care. We structured the best practice recommendations in the following sections: choice of model type (cohort vs. individual-level model), model structure, model parameters, analysis, reporting, and communication. In each of these sections, we give a brief description, address the issues that are of particular relevance to the application of state-transition models, give specific examples from the literature, and provide best practice recommendations for state-transition modeling. These recommendations are directed both to modelers and to users of modeling results such as clinicians, clinical guideline developers, manufacturers, or policymakers.

Keywords: decision-analytic modeling, guidelines, Markov models, state-transition modeling.

Background to the Task Force

A new Good Research Practices in Modeling Task Force was approved by the ISPOR Board of Directors in 2010, and the Society for Medical Decision Making was invited to join the effort. The Task Force cochairs and members are expert developers and experienced model users from academia, industry, and government, with representation from many countries. Several teleconferences and hosted information sessions during scientific meetings of the Societies culminated in an in-person meeting of the Task Force as a whole, held in Boston in March 2011. Draft recommendations were discussed and subsequently edited and circulated to the Task Force members in the form of a survey where each one was asked to agree or disagree with each recommendation, and if the latter, to provide the reasons. Each group received the results of the survey and endeavored to address all issues. The final drafts of the seven articles were available on the ISPOR and SMDM Web sites for general comment. A second group of experts was invited to formally review the articles. The comments received were addressed, and the final version of each article was prepared. (A copy of the original draft article, as well as the reviewer comments and author responses, is available at the ISPOR Web site: http://www.ispor.org/workpaper/State-Transition-Modeling.asp.) A summary of these articles was

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presented at a plenary session at the ISPOR 16th Annual International Meeting in Baltimore, MD, in May 2011, and again at the 33rd Annual Meeting of the Society for Medical Decision Making in Chicago, IL, in October 2011. These articles are jointly published in the Societies' respective journals, *Value in Health* and *Medical Decision Making*. Other articles in this series [1–6] describe best practices for conceptualizing models, building and applying particular types of models, and addressing uncertainty. This article addresses best practices for state-transition models (STMs) and considers both cohort ("Markov") and individual-level ("microsimulation") implementations. Examples are cited throughout, without implying endorsement or preeminence of the papers referenced and 4 appendices (in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2012.06.014) are provided detailing the terms used in this report; examples of individual-level state-transition models; some options for producing simplified graphical model representations; and additional figures displaying a Markov trace.

Use of State-Transition Models (STMs)

Many clinical situations can be described in terms of the conditions that individuals can be in ("states"), how they can move among such states ("transitions"), and how likely such moves are ("transition probabilities"). In these situations, STMs are often well suited to the decision problem, as they conceptualize it in terms of a set of states and transitions among these states. Several dimensions fall within this broad category. For example, some STMs allow for interactions among groups (i.e., the transition probabilities depend on the states of other individuals), while others assume no interactions. Some allow transitions to occur only at specified time intervals, while others use a continuous state-space process. STMs can be used to simulate a closed cohort over time or a dynamic population (e.g., the US adult population). They may simulate all individuals simultaneously or one at a time.

We focus on two common frameworks in health care: cohort, or "Markov," models [7,8] and individual-based models, commonly known as "first-order Monte Carlo" or "microsimulation" models [9–11]. These frameworks do not capture interactions, model a single (closed) cohort, and allow transitions to occur only at specified time intervals.

An STM should be used, rather than a simpler model with limited ability to reflect time (e.g., decision tree), if it requires time-dependent parameters (e.g., recurrence probability after cancer treatment), time to an event (e.g., disease-free survival), or repeated events (e.g., second myocardial infarction) [12]. Other modeling techniques are also suitable for these situations (e.g., discrete event simulation).

Key Concepts and Definitions

The formal elements of an STM are states, transitions, initial state vector, transition probabilities, cycle length, state values ("rewards"), logical tests performed at the beginning of each cycle to determine the transitions, and termination criteria.

Model Structure

STMs are structured around a set of mutually exclusive and collectively exhaustive health states. A modeled individual must be in only one state in any cycle. Events that occur within a cycle can be modeled with a Markov cycle tree—a series of chance nodes representing the events. The average number of cycles that individuals reside in each state can be used in conjunction with state values (e.g., life-years, health-related quality-of-life, and cost) to estimate life expectancy, quality-adjusted life expectancy, and expected costs.

An STM can capture many features present in the course of a disease or clinical process (e.g., disease risk over time, changing states, and episodic events), although this is not the only approach that can capture these features [13]. The principal advantage of cohort STMs is that they are relatively simple to develop, debug, communicate, and analyze using user-friendly software if the number of states is not too large. The primary disadvantage is the underlying assumption that transition probabilities do not depend on history—neither on past states nor on the time spent in the current state. This assumption (the "Markovian" property) can be very limiting for clinical applications where these aspects tend to be strong determinants of what happens next. A Markov model can handle memory by creating states that include history, but this can greatly increase the number of states, resulting in very large models that are difficult to manage (i.e., "state explosion").

Individual-level STMs (Table 1) are not limited by the Markovian property as they simulate one individual at a time. These microsimulations are evaluated by using first-order Monte Carlo simulation: whether an individual facing a certain transition probability makes this transition depends on a random number.

Whereas cohort models are analyzed as single cohorts progressing through the states simultaneously (which does not allow distinguishing one individual from another except by state descriptions), individual-level STMs keep track of each individual's history ("tracker variables"). This can greatly reduce the number of

Table 1 – Cohort versus individual-level state-transition models.

	Cohort state-transition models	Individual-level state-transition models
Ease of model development	Higher (if the number of states is limited)	Lower
Ease of model debugging	Higher (if the number of states is limited)	Lower
Ease of communication to nonexperts	Higher	Lower
Markov assumption, memoryless	Yes	No
Ease of modeling many different subgroups	Lower	Higher
Danger of explosion in number of states	Yes	No
Distribution of outcomes (as opposed to only means)	Possible, but technically more difficult	Yes
Report of individual patient histories	No	Yes
Decision-analytic software available	Yes	Yes (need advanced knowledge)