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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)

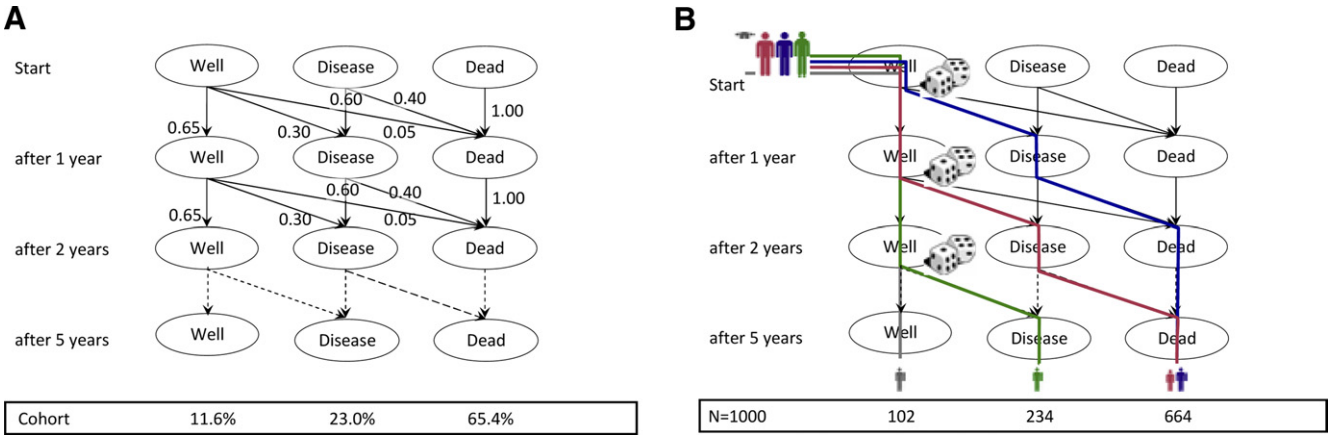

Fig. 1 – In a cohort simulation (A), the entire cohort is (re-)distributed across states after each cycle. In an individual-level microsimulation (B), a finite number of individuals are simulated by using first-order Monte Carlo microsimulation. In this simple example, all individuals start in the state 'Well' and the disease is chronic (i.e., there is no regression from "Disease" to "Well"). In principle, individuals can start in different states and they can regress to states they have already been in. (A) Cohort simulation in a state-transition model. (B) Monte Carlo simulation in a state-transition model.

states. The main disadvantages are that they are computationally intensive, often requiring simulation of millions of individuals to obtain stable values for the outcomes of interest, and they are more difficult to debug. Figure 1 displays the Markov trace of a cohort simulation and the possible paths of a microsimulation.

An STM must start with a decision node from which the intervention branches originate. Each branch leads either to a Markov node (followed by an STM) (Fig. 2A) or to a decision tree, which leads to multiple Markov nodes per intervention (Fig. 2B). An STM following one branch can have a different structure than one following another branch.

Types of interventions

STMs can be used to compare various types of interventions [14].

Primary prevention

STMs used to evaluate primary prevention strategies are concerned with reduction in the risk of developing a disease (e.g., [15]). Hence, their focus is on what happens prior to disease, such as the number and severity of risk factors. The starting cohort is individuals free of disease or complications being modeled.

Screening

STMs used to evaluate screening strategies [16,17] consider two types: one-time screening, (e.g., of newborns [18] or genetic screening [19–21]) or repeated (interval) screening (e.g., for cancer [22–25] or HIV [26,27]). The evaluated screening strategies can differ in many respects, such as the type and sequence of tests used, diagnostic workup modes, screening interval, and ages at which screening begins and ends.

Diagnosis

Diagnostic models are used to identify optimal diagnostic strategies among individuals who present with signs or symptoms of one or more suspected diseases [28]. Testing options may involve the use of one test versus another, one test versus multiple tests, different combinations or sequences, using one positivity criterion versus another (e.g., [29]) or a multiple-test diagnostic score, or focusing on the development of new diagnostic technologies [30].

Treatment

Treatment is defined as any intervention available for someone who already has a clinical condition that affects health consequences or prognosis. An STM disease process should reflect the

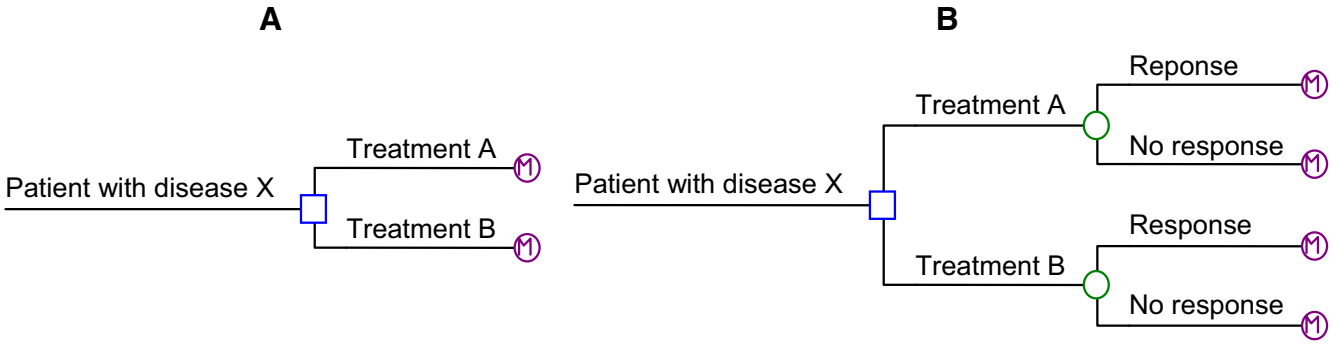

Fig. 2 – In model (A), decision branches lead directly to one Markov node per intervention strategy and the first events are modeled within the Markov cycle tree. Model (B) contains an up-front decision tree modeling the first events and leading to multiple Markov nodes per intervention strategy.

disease's natural history, expected prognostic pathways in the absence of intervention, and treatment effects [31–33].

Recommendations

An STM is a reasonable choice when the decision problem can be framed in terms of states, the interactions between individuals are not relevant, and the population of interest is a closed cohort. Multipurpose disease-specific models (e.g., [34]) are not addressed here.

Choice of model type

Before choosing between cohort or individual-level simulation, the characteristics of the population that must be carried through the model (i.e., state descriptors or tracker variables) must be specified. These must include all relevant states pertaining to the disease or clinical process and intervention(s) and all relevant histories (e.g., past states, risk factors, time in state, and time since last event) that are determinants of transition probabilities (e.g., determinants of disease incidence, progression, and mortality) or state values (e.g., determinants of utilities and costs). An advantage of using an individual-level STM is the ability to model individual characteristics as continuous variables and to evaluate dynamic intervention strategies—ones in which future decisions depend on current and past patient characteristics. In cohort STMs, continuous variables (e.g., blood pressure) have to be categorized; some guidance exists for determining how many states to create [35]. Individual-level STMs [36,37], however, require more computation time, which may be important if probabilistic sensitivity analyses or value-of-information analyses are performed.

Two examples of STMs that required microsimulation include one comparing intermediate and long-term clinical outcomes of different imaging screening strategies for breast cancer in women with *BRCA1* gene mutations [36] and one developed to estimate the long-term impact of interventions for people with type 2 diabetes [37].

Best practices

III-1. If the decision problem can be represented with a manageable number of health states that incorporate all characteristics relevant to the decision problem, including the relevant history, a cohort simulation should be chosen because of its transparency, efficiency, ease of debugging, and ability to conduct specific value of information analyses. If, however, a valid representation of any aspect of the decision problem would lead to an unmanageable number of states, then an individual-level state-transition model is recommended. Validity should not be sacrificed for simplicity.

Model structure

Problem statement

Interventions may be single time (e.g., one-time vaccination or surgery); static over time (i.e., not depending on intervention outcomes or other events); or dynamic (consisting of decision rules for how to start, stop, or change interventions over time [38]). Examples of dynamic strategies are 1) the start of a preventive behavioral intervention if the body mass index increases, 2) increase in the screening interval for cervical cancer if a woman has repeatedly tested negative, 3) repetition of a diagnostic test after an equivocal result, and 4) change to another drug after first-line treatment failure.

This recommendation refers to standard STMs. Other methods such as Markov decision processes generalize STMs by allowing embedding of sequential decisions, and thus, multiple decisions can be made in multiple time periods [39,40].

Best practices

III-2. The strategies being evaluated should be clearly defined. In particular, sequential decisions should not be modeled within the Markov cycle tree but rather be part of the specification of the alternative intervention strategies that precede the Markov tree.

Starting Cohort

The model outputs for a single cohort allow for the comparison of alternative strategies for that cohort. If the optimal decision varies by subgroup (e.g., defined by age, sex, and risk factors known to the decision maker at the time of the decision), the comparison can be reported for different cohorts. If outputs are desired for a population-based starting cohort, the model must be run multiple times, one for each stratum, and then aggregated across strata (e.g., [41]).

Best practice

III-3. The starting cohort should be defined by the demographic and clinical characteristics that affect the transition probabilities or state values (e.g., quality of life and cost).

Defining States

Conceptualization of an STM should begin by identifying states that reflect the disease/health process, with transitions among the states that would be expected in the absence of intervention, and the interventions' effects on these. The states should be specified as mutually exclusive (any individual can be in only one state during each cycle) and collectively exhaustive (every individual in the initial cohort must be in a state during each cycle) and should adequately capture the benefits or harms of any interventions. These effects can characterize the state values (e.g., differences in symptoms and quality of life) or reflect changes in transition probabilities.

At the start of a cohort simulation, the modeled population is allocated among the states. Each state is homogeneous—every individual in that state has the same transition probabilities—implying that any characteristics that determine those probabilities must not differ within the state. If history (prior states or time spent in a current state) is important in determining transition probabilities, the relevant states should carry that history in their definition (e.g., if the risk of myocardial infarction depends on prior myocardial infarction, then the states would need to include this historical element by using states such as "disease-free, no prior MI" and "disease-free, prior MI"). In an individual-level STM, these characteristics and other parameters can be heterogeneous within a state but must be tracked throughout and transition probabilities must be defined as a function of these characteristics.

When there are alternatives for modeling natural history (e.g., defining states with biological but often unobservable disease measures such as spirometry in asthma or with symptomatic descriptions such as "on treatment" stages for Parkinson's disease), the analyst should justify the approach used or compare alternatives in sensitivity analysis. Although it may be possible to describe natural history solely on the basis of health care utilization, this does not provide direct insight into health outcomes at the biological level and its value is limited for most decision problems. If the cause of death is an important outcome, or different causes have different costs, competing causes should be modeled in an unbiased way (e.g., probability of death modeled first, followed by a conditional distribution of cause-specific deaths).

Another important consideration in structuring an STM is initial immediate or short-term events. An efficient and transparent way to model such events is as a decision tree preceding the STM, unless there are justified reasons for representing them within the states. When events are modeled preceding an STM, the time spent before entering the STM should be captured appropriately

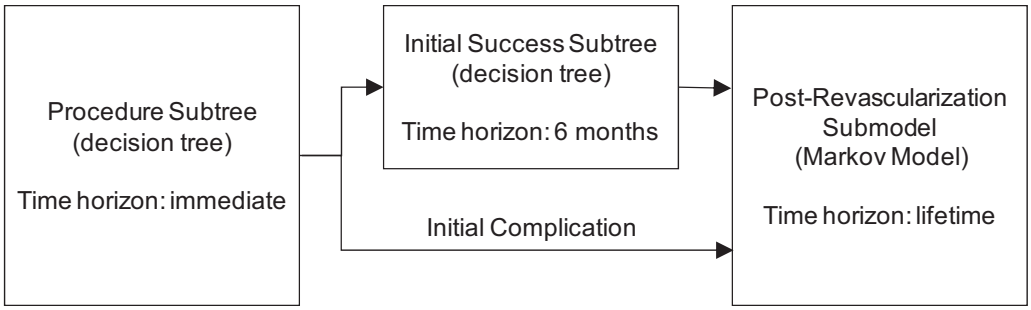

Fig. 3 – The model consists of two decision trees and one Markov model. Source: Siebert U. based on Cohen et al. (1994). With kind permission from Springer Science+Business Media: Z Kardiol, The role of decision-analytic models in the prevention, diagnosis and treatment of coronary heart disease, 3, 2002, III/148, U. Siebert, Fig. 2.

by giving credit to the starting cohorts for the time elapsed (e.g., an up-front decision tree could be used to represent results and subsequent outcomes from diagnostic test strategies [29], or treatments with limited duration [33], or initial coronary interventions [31]; Fig. 3).

Best practices

III-4. Specification of states and transitions should generally reflect the biological/theoretical understanding of the disease or condition being modeled.

Intervention effects

For models evaluating primary prevention, possible risk factor levels in the target population should be represented as predisease states or tracker variables. As current risk factors are often predictors of future ones, the state descriptions or tracker variables should capture their course and changes in sufficient detail. These models may not require as much detail postdisease as would those evaluating interventions for the disease, but they should sufficiently capture the relevant disease elements. One useful approach is to collaborate with investigators with well-developed disease-specific treatment models to derive relevant eventual outcomes (e.g., lifetime costs or survival) that can be used in the prevention model [42,43].

Models evaluating screening should define states reflecting the underlying disease process, especially for interval screening programs. It is not appropriate to take an empirical estimate of the probability of a positive screen from a study because this does not explicitly incorporate the underlying disease probability. For cancer screening, states should distinguish between cases detected by screening and incidental findings (e.g., through other diagnostic tests) or cases detected by symptoms. Modelers should describe how they have controlled for lead time and length bias [44]. Dynamic interval screening strategies ("individualized screening") may depend on screening history (e.g., some algorithms for cervical cancer screening recommend extension of the interval after repeated negative tests). As capturing screening history in the Markov states can lead to state explosion, it may be necessary to use an individual-level STM, with screening history included as tracker variables [22].

In models evaluating diagnostic strategies, it is typical to represent the testing pathways and their outcomes (e.g., true positive, false positive) in a pre-STM decision tree. If multiple tests are performed in combination or sequence, and some results are prognostic factors that can change over time, their history must be incorporated in the states or implemented as tracker variables.

In models evaluating therapeutic strategies, the mechanism by which the treatment alters the disease course should be explicit (e.g., reduction in event risk or mortality, slowing disease progression). In addition, how harms of the intervention(s) affect prognosis should be specified. STMs should incorporate realistic assumptions about adherence over time. Long-term treatment effectiveness and costs often depend on time-varying heterogeneous patient characteristics, and many treatments are "personalized" and follow dynamic rules (e.g., dose and second-line treatments, and compliance and treatment success depend on current treatment response and side effects). These dynamic characteristics should be considered in the states or tracker variables.

Best practices

III-5. States should adequately capture the type of intervention (i.e., prevention, screening, diagnostics, treatment) as well as the intervention's benefits and harms.

Heterogeneity

In a cohort STM, all individuals in a given state are indistinguishable in terms of their transition probabilities. Many characteristics that affect transition probabilities (e.g., age, sex, comorbidities, and disease stage) are known at the time of the decision and can be used to define the starting cohorts. These characteristics do not need to be incorporated into state definitions or tracker variables unless they are expected to change over time in a meaningful way. For example, a cohort starting with few comorbidities may develop more over time, and to capture this requires incorporating this attribute in the states. Variables that affect transition probabilities but are not known at decision time (e.g., genetic mutation and undiagnosed infection) can create "heterogeneity bias" [45,46], and inclusion of such variables should be considered.

Best practices

III-6. States need to be homogeneous with respect to both observed and unobserved (i.e., not known by the decision maker) characteristics that affect transition probabilities.

Time horizon

The time horizon relates to the number of cycles or the duration for which the cohort is tracked. Common approaches include modeling to an age of 120 years or tracking the cohort until more than 99.9% of the individuals are dead. If the intervention affects mortality, the time horizon should be lifetime to capture (quality-adjusted) life-years gained from delayed deaths.

Best practices

III-7. The time horizon for the model should be sufficiently large to capture all health effects and costs relevant to the decision problem.

Cycle length

Choice of cycle length should be based on the clinical problem, remaining life expectancy, and computational efficiency. It should allow transitions to occur consistent with the clinical problem and intervention effects (e.g., a model assessing monthly screening requires cycles no longer than 1 month). Cycle length should be short enough that an event occurs at most once per cycle. Shorter cycle lengths provide better approximations of life expectancy. If life expectancy is relatively short (e.g., with an acute disease or at older ages), a shorter cycle length should be considered, even if the clinical problem does not warrant it. Although shorter cycles will always yield more precise estimates, the error gets very small when the number of cycles required increases.

Best practices

III-8. Cycle length should be short enough to represent the frequency of clinical events and interventions.

Model symmetry

Symmetric models ensure that the disease process is represented consistently across strategies. For example, STMs used to compare cardiac catheterization and subsequent treatment dictated by its results versus initial medical therapy should specify true underlying disease status even though it is not observed in the medical therapy strategy [47]. Otherwise, errors result when conducting sensitivity analysis on the underlying probability of any particular anatomy (e.g., left main disease).

Best practices

III-9. Components of state-transition models that reflect similar clinical courses should not be recreated but rather should be incorporated once and linked to that structure throughout the model.

Data

STMs should provide clear justification for estimates of transition probabilities and state values and their ranges for sensitivity analysis.

Data sources

Ideally, transition probabilities pertaining to natural history are derived from population-based epidemiological studies, as these are most likely to be representative. Transition probabilities may be derived from the control arms of trials, recognizing that these may be less generalizable because of selection criteria for participants. If multiple sources are available, summarized data from a systematic review or meta-analysis are best for informing transition probabilities or state values. Methods assessing the quality of a body of evidence rather than the quality of individual studies are available [48–50]. In the absence of good systematic reviews, a detailed evidence table should be provided in an appendix with a description and justification of how key parameters—including the ranges used for sensitivity analyses—were derived.

Best practices

III-10. Transition probabilities and intervention effects should be derived from the most representative data sources for the decision problem.

Parameter derivation

Transition probabilities and rates should be used appropriately [51]. The conversion of transition probabilities from one time unit to another should be done through rates, which should never be presented as percentages. To avoid confusion, probabilities should never be called rates.

The assumed functional relationship between disease-specific and background mortality should be stated. Because an assumption of additive rates can give very different results than a multiplicative one [52], the impact of this assumption should be assessed.

Best practices

III-11. All methods and assumptions used to derive transition probabilities and intervention effects should be described.

Intervention effects

Efficacy derived from randomized clinical trials may have to be adjusted for compliance to reflect real-world effectiveness [53]. Effectiveness derived from observational studies must be adjusted for confounding (e.g., using multivariate regression techniques or propensity scoring). Adjustment for time-varying confounding (i.e., confounders that simultaneously act as intermediate steps in the pathway between intervention and outcome) require special methods such as marginal structural analysis or g-estimation [38,54]. When results from observational studies are used in the model, causal graphs can be used to explicitly state causal assumptions [53].

When extrapolating beyond a trial's duration, reductions in all-cause mortality should not be applied directly since background mortality (from other causes) increases with age. If disease-specific mortality is not available, a relative reduction can be applied to disease-specific mortality, providing a conservative estimate of treatment benefit. Alternatively, life-table mortality could be subtracted from total mortality to estimate the reduction in disease-specific mortality [55].

For preventive and therapeutic interventions, if evidence is available for reduction in disease incidence, events, or progression and also for mortality, using both may double count. If this is a concern, the consistency of the model-generated reductions should be validated with estimates from clinical studies.

Best practices

III-12. All parameters relating to the effectiveness of interventions derived from observational studies should be correctly controlled for confounding. Time-varying confounding is of particular concern in estimating intervention effects.

State valuation

Expected outcomes depend on values assigned to each state (e.g., quality-adjusted life-years can be derived if utilities are assigned). State values should be justified, preferably on the basis of theory.

Best practices

III-13. The valuation of intermediate outcomes/states should be justified.

Analysis

Half-cycle correction

When it is not known when the transitions occur within the cycle, we expect that, on average, they will occur about half-way through the cycle. To account for this, a half-cycle correction is

made by assigning half of the reward in each state. Giving a full reward at the start (i.e., transitions occur at cycle end) overestimates expected values; assigning no reward (i.e., transitions occur at cycle start) underestimates them [8].

Best practices

III-14. A half-cycle correction should be applied to costs and effectiveness in the first cycle and in the final cycle if not using a lifetime horizon.

Analyzing distributions

It may be important for the decision maker (e.g., for equity reasons) to know whether a treatment with a 1-year life expectancy gain extends life by 1 year for each person or by 3 years in 50% but reduces life by 1 year in the other 50%. Distributions are derived easily from individual-level STMs, but they can also be derived from cohort models, either by analyzing the Markov trace or by running the model individually (but without tracker variables).

Best practices

III-15. For certain decision problems, it may be important to report not only the expected value but also the distribution of the outcomes of interest.

Performing microsimulation

To achieve stable results in an individual-based simulation, sufficient individuals must be modeled. Stability of model results is assessed by calculating variance from multiple runs with identical number of individuals [55], which should be much smaller than the smallest difference expected between strategies. Variance reduction techniques (e.g., using common random numbers) can decrease the required numbers [56].

Best practices

III-16. The number of individuals simulated should be large enough to generate stable estimates of the expected values.

Communicating results

Graphical representation of an STM helps communicate key structure and most important assumptions made regarding states and allowable transitions. Since rigorous studies evaluating alternative presentation methods are lacking, these recommendations represent best judgments based on experience.

Presenting the model

STMs are often represented by two types of diagrams: a state-transition diagram, also known as a "bubble diagram," and a Markov cycle tree (a set of probability nodes that describes the progression from one state to the next). State-transition diagrams represent states as discrete compartments ("bubbles") and transitions as arrows between them. While a relatively simple model with few states may be fully represented in a single diagram, complicated models consisting of multiple states cannot feasibly be represented by displaying all states and transitions. Such models are invariably cluttered, and the resultant tangle of arrows and states often impairs communication, rather than enhancing it. In such circumstances, simplified or partial diagrams are desirable. Markov cycle trees, often stylized, can display the transitions between states, and probabilities and transitions that are conditional upon other events or parameters.

Best practices

III-17. The report should use nontechnical language and clear figures and tables that enhance understanding of the STM to communicate its key structural elements, assumptions, and parameters.

Presenting results

Presenting intermediate results can be helpful for demonstrating face validity for clinical experts, epidemiologists, and decision makers. Useful measures include incidences related to a fixed time horizon (e.g., 10-year risks), average number of events per lifetime, percentage of initial cohort that experienced two or more events in their lifetime, or mean age at which the first event occurred. In addition, it can be useful to generate summary data from STMs to indicate how much time is spent in certain states (e.g., a model of stroke prevention in atrial fibrillation could report the average amount of time spent without a stroke and the average time from first stroke to death). Such measures can also be used for debugging the model or for validating model results with empirical data or for internal debugging. As STMs allow deriving the time at which particular transitions occur, the results can be represented as (modeled) probability or survival curves and directly compared with survival curves from empirical studies.

Best practices

III-18. In addition to final outcomes, intermediate outcomes that enhance the understanding and transparency of the model results should also be presented.

Validation and Consistency

Ensuring that the STM provides a sufficiently accurate representation of the real system is important. This is covered in detail elsewhere in this series [6]. A useful method of identifying programming errors in an STM is to check whether model-building rules such as the use of symmetric branches or states in STMs are followed. Inspection of the Markov trace can also help find errors, by setting parameters in such a way that how the trace will look can be predicted (e.g., so that no modeled individual will visit a given state during the simulation).

Conclusions

STMs can provide a comprehensive and powerful tool to guide decisions in health care. Best practices, for cohort and individual-based STMs, are recommended for the development, analysis, validation, and reporting of STMs. Although many more aspects than those described in this article may have to be considered for good modeling practice, and not all models may be able to comply with all the recommendations, following these recommendations should help to make STMs more valid, transparent, and useful in guiding health care decisions.

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Supplemental Materials

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