



ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

ISPOR TASK FORCE REPORT

Applying Dynamic Simulation Modeling Methods in Health Care Delivery Research—The SIMULATE Checklist: Report of the ISPOR Simulation Modeling Emerging Good Practices Task Force



Deborah A. Marshall, PhD^{1,2,3,*}, Lina Burgos-Liz, MSc, MPH, BSc Ind Eng¹, Maarten J. IJzerman, PhD⁴, Nathaniel D. Osgood, BS, MS, PhD^{5,6}, William V. Padula, PhD, MS⁷, Mitchell K. Higashi, PhD⁸, Peter K. Wong, PhD, MS, MBA, RPh⁹, Kalyan S. Pasupathy, PhD¹⁰, William Crown, PhD¹¹

¹Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; ²Division of Rheumatology, Department of Medicine, and the McCaig Institute for Bone and Joint Health, University of Calgary, Calgary, AB, Canada; ³Alberta Bone & Joint Health Institute, University of Calgary, Calgary, AB, Canada; ⁴Department of Health Technology & Services Research, University of Twente, Enschede, The Netherlands; ⁵Department of Computer Science, Health & Epidemiology and Bioengineering Division, University of Saskatchewan, Saskatoon, SK, Canada; ⁶Department of Community, Health & Epidemiology and Bioengineering Division, University of Saskatchewan, Saskatoon, SK, Canada; ⁷Section of Hospital Medicine, University of Chicago, Chicago, IL, USA; ⁸GE Health care, Barrington, IL, USA; ⁹SHS Illinois Divisions & Medical Group, Hospital Sisters Health System, Belleville, IL, USA; ¹⁰Health Care Systems Engineering Program, Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Rochester, MN, USA; ¹¹Health Care Policy & Research, Health Care Systems Engineering Program, Mayo Clinic, Rochester, MN, USA

ABSTRACT

Health care delivery systems are inherently complex, consisting of multiple tiers of interdependent subsystems and processes that are adaptive to changes in the environment and behave in a nonlinear fashion. Traditional health technology assessment and modeling methods often neglect the wider health system impacts that can be critical for achieving desired health system goals and are often of limited usefulness when applied to complex health systems. Researchers and health care decision makers can either underestimate or fail to consider the interactions among the people, processes, technology, and facility designs. Health care delivery system interventions need to incorporate the dynamics and complexities of the health care system context in which the intervention is delivered. This report provides an overview of common dynamic simulation modeling methods and examples of health care system interventions in which such methods could be useful. Three dynamic simulation modeling methods are presented to evaluate system interventions for health care delivery: system dynamics, discrete event simulation, and agent-based modeling. In contrast to conventional evaluations, a dynamic systems approach incorporates the complexity of the system

and anticipates the upstream and downstream consequences of changes in complex health care delivery systems. This report assists researchers and decision makers in deciding whether these simulation methods are appropriate to address specific health system problems through an eight-point checklist referred to as the SIMULATE (System, Interactions, Multi-level, Understanding, Loops, Agents, Time, Emergence) tool. It is a primer for researchers and decision makers working in health care delivery and implementation sciences who face complex challenges in delivering effective and efficient care that can be addressed with system interventions. On reviewing this report, the readers should be able to identify whether these simulation modeling methods are appropriate to answer the problem they are addressing and to recognize the differences of these methods from other modeling approaches used typically in health technology assessment applications.

Keywords: decision making, dynamic simulation modeling, health care delivery, methods.

Copyright © 2015, International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Published by Elsevier Inc.

* Address correspondence to: Deborah A. Marshall, Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, 3280 Hospital Drive NW, Room 3C56 Health Research Innovation Centre, Calgary, AB, Canada T2N 4Z6.

E-mail: damarsha@ucalgary.ca.

1098-3015/\$36.00 – see front matter Copyright © 2015, International Society for Pharmacoeconomics and Outcomes Research (ISPOR).

Published by Elsevier Inc.

<http://dx.doi.org/10.1016/j.jval.2014.12.001>

Background to the Task Force

In October 2013, the ISPOR Health Science Policy Council recommended to the ISPOR Board of Directors that an ISPOR Emerging Good Practices for Outcomes Research Task Force be established to focus on dynamic simulation modeling methods that can be applied in health care delivery research and recommendations on how these simulation techniques can assist health care decision makers to evaluate interventions to improve the effectiveness and efficiency of health care delivery. The Board of Directors approved the ISPOR Simulation Modeling Emerging Good Practices Task Force in November 2013.

The task force leadership group is composed of experts in modeling, epidemiology, research, systems and industrial engineering, economics, and health technology assessment. Task force members were selected to represent a diverse range of perspectives. They work in hospital health systems, research organizations, academia, and the pharmaceutical industry. In addition, the task force had international representation with members from Canada, The Netherlands, Colombia, and the United States.

The task force met approximately every five weeks by teleconference to develop an outline and discuss issues to be included in the report. In addition, task force members met in person at ISPOR International meetings and European congresses. All task force members reviewed many drafts of the report and provided frequent feedback in both oral and written comments.

Preliminary findings and recommendations were presented in forum and workshop presentations at the 2014 ISPOR Annual International Meeting in Montreal and ISPOR Annual European Congress in Amsterdam. In addition, written feedback was received from the first and final draft reports' circulation to the 190-member ISPOR Modeling Review Group.

Comments were discussed by the task force on a series of teleconferences and during a 1.5-day task force face-to-face consensus meeting. All comments were considered, and most were substantive and constructive. Comments were addressed as appropriate in subsequent versions of the report. All written comments are published at the ISPOR Web site on the task force's Webpage: <http://www.ispor.org/TaskForces/Simulation-ModelingApps-HCDelivery.asp>. The task force report and Webpage may also be accessed from the ISPOR homepage (www.ispor.org) via the purple Research Tools menu, ISPOR Good Practices for Outcomes Research, heading: Modeling Methods.

In the course of task force deliberations, in response to specific comments and suggestions from reviewers, and a growing concern about length, it became apparent that two task force reports would be needed to be thorough, covering the essential points, yet keep the report readable and digestible. With *Value in Health's* permission, the material has been split into two articles.

This first article is a primer on how dynamic simulation modeling methods can be applied to health system problems. It provides the fundamentals and definitions, and discusses why dynamic simulation modeling methods are different from typical models used in economic evaluation and relevant to health care delivery research. It includes a basic description of each method (system dynamics, discrete event simulation, agent-based modeling), and provides guidance on how to ascertain whether these simulation methods are appropriate for a specific problem via the SIMULATE checklist developed by the task force.

The second report will provide more depth, delving into the technical specifications related to the three dynamic simulation modeling methods. It will systematically compare each method across a number of features and provide a guide for good research practices for the conduct of dynamic simulation modeling. This report will appear in the March/April 2015 issue of *Value in Health*.

Introduction

Health care delivery systems are inherently complex and fragmented social systems consisting of governments, payers, and multiple providers responsible for delivering health care services to patients in defined regions [1–3]. Social systems are different from other systems in that people make decisions, interact among themselves, and also interact with other parts of the system in an interdependent nature. It is hard to plan health care services in these types of complex systems because decisions and choices by people are dynamic (i.e., can change over time and interactions between parts of the system and with other systems are adaptive). In the era of patient-centered care, customizing care to the needs of individual patients further escalates the complexity of health care delivery systems [4–9].

Complexity challenges decision makers to evaluate interventions that can improve the effectiveness and efficiency of health care delivery because of the emergent behavior of the system (i.e., the potential intended and unintended consequences). Although modeling approaches such as decision trees and Markov models have been standardized as methods to evaluate health care interventions, these approaches are not sufficient for analyzing complex health care delivery systems. Dynamic simulation modeling offers advantages with recent advances in accessible computing power and data analytics that make it possible to simulate the impact of system interventions on health care delivery systems without costly and time-consuming direct experimentation. The results of such simulation models can anticipate the

comparative effectiveness of a novel system intervention as well as its cost-effectiveness.

This task force report presents dynamic simulation modeling methods to evaluate system interventions for health care delivery. It is a primer for researchers and decision makers who face complex challenges to deliver effective and efficient care. Based on experience from the fields of industrial engineering and operations research, three dynamic simulation modeling methods are well suited for and commonly applied to these types of problems: system dynamics (SD), discrete event simulation (DES), and agent-based modeling (ABM) [9–13].

This report provides an overview of these dynamic simulation modeling methods and examples of health care system interventions in which such methods could be useful. It is intended to assist researchers and decision makers in deciding whether these simulation methods are appropriate to address specific health system problems. An eight-point checklist referred to as the SIMULATE (System, Interactions, Multilevel, Understanding, Loops, Agents, Time, Emergence) tool is included to assist in determining whether these dynamic simulation modeling methods are suitable to address the problem of interest. The report also directs readers to other resources for further education on the topic of modeling system interventions in the emerging field of health care delivery science and implementation. On reviewing this report, readers should be able to identify whether these dynamic simulation modeling methods are appropriate to answer the problem they are addressing and to recognize the differences of these methods from other modeling approaches.

Definitions of Concepts and Terminology

Behaviors and interactions of systems are governed by their level of complexity. Likewise, complexity is considered a property of a system, not of an intervention [14]. *Complex systems* consist of tasks that are relationally dependent events with unpredictable outcomes [15]. A complex system is one that is adaptive to changes in its local environment, is composed of other complex systems (e.g., the human body), and behaves in a nonlinear fashion (i.e., change in outcome is not proportional to change in input) [16]. Moreover, the behavior of the system as a whole is different from that of its parts or components. Understanding this emergent behavior is part of understanding a complex system. In contrast to these complex systems, *simple systems* consist of tasks that can be answered as “yes” or “no,” whereas *complicated systems* consist of tasks that are based on “if-then” algorithms.

Health care consists of multiple complex systems. For instance, complex systems in health care delivery include primary care, specialists, outpatient facilities, hospitals, and long-term chronic care facilities. This framework of complexity can be useful for delineating simulation modeling applications to systems depending on the level of complexity (Table 1).

Overview of dynamic simulation modeling methods

Dynamic simulation modeling methods are used to design and develop mathematical representations (i.e., formal models) of the operation of processes and systems to experiment with and test interventions and scenarios and their consequences over time to advance the understanding of the system or process, communicate findings, and inform management and policy design [18–20]. The three dynamic modeling methods highlighted in this report—SD, DES, and ABM—are well suited for health care delivery problems.

System dynamics. SD is a simulation modeling method used for representing the structure of complex systems and understanding their behavior over time. It was developed in the 1950s by Jay

Forrester at the Massachusetts Institute of Technology with the goal of using science and engineering to identify the core issues that determine the success and failure of corporations. His involvement with General Electric (New York, NY) and the managerial problems faced by the company influenced his work greatly. From manual simulations of the stock-flow-feedback structure of the production plants, including the existing corporate decision-making structure for hiring and layoffs, Forrester [21] showed that the employment instability was due to the internal structure of the firm, not an external force such as the business cycle. Forrester and his team at the Massachusetts Institute of Technology developed the first computer SD simulator, DYNAMO. In 1961, Forrester [22] published the first book in the field, *Industrial Dynamics*.

The core elements of SD are feedback, accumulations (stocks), rates (flows), and time delays. Stocks are accumulations or aggregations of something (e.g., people, beds, and oxygen). Flows are rates; these feed in and out of stocks and have the same units of stocks per time unit (e.g., people per hour, beds per year, and oxygen per minute). An important concept in SD is nonlinearity. This concept is tied to the existence of feedback processes. It means that an effect is seldom proportional to the cause.

One of the core assumptions in SD is that the behavior of the system is due to its structure and not due to external forces or factors. Although SD models can be formulated at many different levels of detail, such models in health care are most traditionally *aggregate*, in the sense that they characterize the population in terms of sizes of subpopulations rather than at an individual level. Thus, rather than tracking specific persons on a longitudinal basis, such models provide a cross-sectional view of a system by *counting* over time the number of people exhibiting particular combinations of characteristics or in specific transitional health states.

In general terms, SD can produce patterns and trends, as well as mean values as outputs from the model. The patterns and trends resulting from simulation experimentation with different policies or strategies (“what-if” questions) can be analyzed by modelers and stakeholders to inform decision making.

Discrete event simulation. DES is a simulation method used to characterize and analyze queuing processes and networks of queues in which there is an emphasis on the use of resources [23] developed in the late 1950s by Tocher et al. for United Steel Companies (United Kingdom) for constructing a simulation model of one of the steel plants [24]. Most problems or questions that DES can help analyze are those regarding resource utilization and queues (i.e., wait times).

The core concepts in DES are events, entities, attributes, and resources. An *event* is something that happens at a certain time point in the environment that can affect resources and/or entities. *Entities* are objects that have attributes and consume resources while experiencing events, but consumption is not affected by individual-level behavior. *Attributes* are features or characteristics unique to an entity. They can change over time or not. *Resources* are objects that provide a service to an entity. Queues are another important concept in DES and occur when several entities compete for a specific resource for which there is a constraint. At a more technical level, time is discrete, and change happens when an “event” occurs.

In health care specifically, DES can be useful to analyze effects on health outcomes. DES is also useful for problems in which it is particularly relevant to be able to capture the changing attributes of entities (e.g., patients), and in which the processes to be characterized can be described by events [25].

The outputs of DES are generally mean values and distributions of values. Individual entities are followed through simulated processes, enabling event traceability. This methodology

Table 1 – Concepts and terminology definitions.

Term	Definition
Complex system	A system that is adaptive to changes in its local environment, is composed of other complex systems, behaves in a nonlinear fashion, and exhibits emergent behavior [14,15].
Emergent behavior	Also known as <i>emergence</i> , refers to the novel and coherent structures, patterns, and properties that arise from the interaction of the parts of a complex system and take place at the system scale rather than at the component’s scale [17].
Health care delivery systems	Health care delivery systems represent a continuum of providers in primary, secondary, and tertiary care as well as payers that grant patients access to affordable, quality care in defined regions; they are inherently complex entities, consisting of multiple tiers of interdependent subsystems and processes, as well as varying degrees of private and public elements throughout different regions [15].

generates high-level insight about the problem and system under study at logistic/operational levels. Outputs of DES can be interpreted or used for system performance indicators such as resource utilization, wait times, number of entities in queues, and throughput of services or products. Also, scenarios with different strategies and policies (“what-if” questions) can be tested. The mean values or distributions can be thought of as accurate; however, these are not necessarily optimal.

Agent-based modeling. ABM is a simulation method for modeling dynamic, adaptive, and autonomous systems [26]. It is used to discover systems by using “deductive” and “inductive” reasoning. At the core of an ABM model, there are “autonomous” and “interacting” objects called agents. Agents are social and interact with others and they live in an environment and their next actions are based on the current state of the environment. In addition, an agent senses its environment and behaves accordingly on the basis of defined decision rules. Agents may have explicit goals to maximize or minimize and may learn and adapt themselves on the basis of experience (i.e., agency).

In 1971, Schelling [27] used ABM to propose a theory to explain the persistence of racial segregation even though the legal and cultural environment was one of growing tolerance. Using a basic ABM model with if-then statements (e.g., individuals will tolerate racial diversity, but will not tolerate being in a minority in their locality), Schelling [27] showed via colored squares on a matrix that segregation will still be the equilibrium situation.

The three core concepts that form the basis for ABM are agency, dynamics, and structure [28]. Dynamics means that both the agents and their environment can change, develop, or evolve over time. Structure is emergent from agent interaction. For example, how human populations will tend to aggregate in certain locations on the basis of predefined behaviors that have been coded into the agents. All the above factors can be modeled.

The widest use of ABM related to population health has been to model large-scale anthropogenic or natural disasters, such as a chemical spill, infectious disease outbreaks, forest fires, hurricanes, or flooding. The response of the affected population is driven by available information about the event, behaviors (e.g., evacuation), and containment strategies (e.g., vaccination or quarantine) [29].

ABM is a rapidly maturing health modeling technique well suited to addressing public health planning and policy needs, as well as health care infrastructure investment decisions. The attainment of specific population health goals can be simulated at the population level, and the specifics of investments needed to achieve these goals can be investigated in a more detailed fashion. Primary goals can be defined by disease outcomes, efficiency measures, return on investment, or costs [30,31].

The strength of interpretation of ABM results lies in the conduct of sensitivity analyses. ABMs can be a powerful tool to test assumptions, assist planning, and anticipate the effects of different health system scenarios on population health by varying the interventions applied to the health care system (e.g., introducing a new diabetes prevention program vs. lowering the co-pay for diabetes medications).

As applied to health care systems, ABM model outputs can include health outcomes (e.g., quality-adjusted life-years [QALYs] and mortality), disease patterns and trends (e.g., viral transmission and diabetes), costs, resource utilization, and labor productivity (e.g., patients treated per day and bed occupancy). ABM is well suited to generate insights into the health of large populations over time.

Why Is Dynamic Simulation Modeling Relevant to Health Care Delivery Research in Complex Systems? (See Box)

Health care delivery systems are inherently complex, characterized by nonlinearities, feedback loops, and a large number of

What is Dynamic Simulation Modeling Used for?

Health Care Delivery Research in Complex Systems

- Model building process and simulation are learning processes themselves
- Identify critical functional and relational aspects in complex systems.
- Understand why a system behaves the way it does as a function of its organization (structure).
- Shift paradigms and mental models

Design and Evaluation of Health Care Delivery System Interventions

- Evaluate intended and unintended consequences of an intervention using “what if...?” scenarios
- Tool for designers (e.g. policy design, system design and re-design) that is more prescriptive in nature by informing decision making.

variables that evolve dynamically over time. Simulation models can help identify the critical functional and relational aspects of a system. Thus, dynamic simulation modeling allows us to understand why a system behaves the way it does as a function of its organization and relationships among components of the system.

More recently, with the focus on patient-centered care, the complexity has increased in these systems. The Institute of Medicine’s seminal report, “Crossing the Quality Chasm: A New Health System for the 21st Century,” highlights patient-centered care as a necessary component of good practice, emphasizing the importance of continuous health relationships, knowledge sharing, and free information flow across segments of the health care system [5]. According to Berwick et al. [32], health care system improvement requires the simultaneous pursuit of three aims in iterative cycles: improving both the experience of care and the health of populations, and reducing per capita costs of health care.

A dynamic simulation model can help address these conflicting goals and complements the increased focus on patient centeredness as a research priority [33]. Providers are now challenged with implementing evidence-based practices, such as checklists, but lack guidance on incorporating patient preferences [34,35]. Dynamic simulation models of complex systems can capture patient preferences to simulate patient and provider behavior as well as anticipate the outcomes of behavioral interactions.

In the context of health care delivery, a patient-centered approach requires an understanding of the multiple and diverse determinants of health outcomes and patient experience. Modeling these relationships and interdependencies at the system level can provide a comprehensive view of the drivers that improve the quality of the patient visit experience, such as shortened waiting times, quality of information, and access to care. Care pathways can be designed to better reflect patient preferences for certain subgroups, such as risk tolerance for therapies [36], the avoidance of adverse effects [37], potential adherence to therapeutic regimens, or demographic characteristics and medical history [38]. In the complex interactions between doctors and patients, simulation modeling may also yield insights into revealed versus stated preferences.

Health care delivery systems are continually evolving as they strive to balance quality care against resource constraints. Classic

health economic models, however, do not account for the multiple constraints facing health care systems. Constraints are imposed on the health care system in many ways: provider budgets, patient out-of-pocket spending, physical space and facility designs, staff numbers, delivery processes, workflow productivity, access to technology, and time. Designing health care systems that deliver value will require these types of new methods [39].

What/How Can Dynamic Simulation Modeling Contribute to the Design and Evaluation of Health Care Delivery System Interventions? (See Box)

In the Medical Research Council's framework for the evaluation of interventions, an intervention is "built up from a number of components, which may act both independently and inter-dependently." Consequently, it can be challenging to determine what aspect(s) of the intervention effect change in the system [14].

When evaluating interventions, the report emphasizes that it is necessary to consider the wider ramifications of intervening and to be aware of the interaction that occurs between components of the intervention, as well as between the intervention and the context in which it is implemented. This includes the operations, structures, and relationships that exist in each setting and the implications that contextual effects have for designing and evaluating interventions.

Dynamic simulation modeling methods are useful in the design and evaluation of health care systems and the interventions needed to resolve their inherent problems. Many of the advances in disease diagnosis, treatment, and care are implemented without considering the unintended or unanticipated consequences of these interventions at the system level. In fact, interventions that are implemented to address difficult challenges in health care sometimes fail to solve persistent problems or create new problems. This phenomenon is known as *policy resistance*: the tendency for interventions to be defeated by the system's response to the intervention itself [40]. Dynamic simulation models enable evaluators and policymakers to account for and identify policy resistance in a system and design and test interventions that can overcome this phenomenon.

It is widely accepted in health care that generating reliable scientific evidence requires conducting experiments, comparing and differentiating hypotheses, and obtaining results that are replicable [40,41]. Generating reliable scientific evidence, however, becomes more difficult as complexity increases and is not always feasible because of ethical, physical, or technical reasons. Dynamic simulation models are virtual worlds that offer decision makers the capability of conducting experiments and evaluating system interventions [42]. Simulation models provide low-risk and low-cost laboratories to learn and gain understanding about health care systems and the effects that interventions may have on them.

Dynamic simulation modeling methods test "what-if" scenarios that can then be used to estimate the upstream and downstream outcomes associated with systems of care that are too complex to anticipate on the basis of piecemeal analyses of the system components. In the virtual world of the simulation model, decision makers can push the system to extreme conditions, extend the time of observation, and strengthen and relax assumptions, which is often impossible or infeasible in the real world [42]. Simulation models provide immediate feedback to decision makers, allowing them to gain years of simulated experience and knowledge about the system and interventions by revealing dynamics and mechanisms that are otherwise not obvious [40,42].

Traditional approaches and statistics provide *descriptive* ways of measuring and testing individual relationships. As massive amounts of data are collected and warehoused, the *descriptive* analyses are used by *predictive* models, which strive to forecast future scenarios. Dynamic simulation modeling takes it further

to anticipate the consequences of unforeseen interactions in the system (emergence) and become *prescriptive* in nature, such that the models prescribe what actions/interventions to take, on the basis of scenarios tested through experiments [43,44]. Through simulation modeling, decision makers can observe effects that interventions can have on different parts of the system concurrently; it engages decision makers into systems thinking and to focus on interdependencies, thus broadening their perspective on the problem and enhancing their understanding of interventions in the context of the overall system [3,45]. Hence, decision makers are forced to develop intuition about the system and how it really works, thereby informing the design of the system and interventions realistically and more accurately [44–48].

System redesign is an essential step to achieving sustainable implementation of evidence-based practice interventions across the care continuum, and dynamic simulation modeling can inform the adoption of evidence-based patient care practices. Suppose, for example, that policymakers are considering a new centralized system for the intake of patients with joint pain and disability because of long waiting times to access appropriate arthritis care. Redesigning the referral process can be informed by dynamic simulation modeling. Arthritis, most commonly osteoarthritis (OA) and rheumatoid arthritis, is a frequent cause of joint pain and disability, and is associated with a significant societal burden, in terms of both morbidity and costs. Early recognition and intervention prevents or minimizes permanent, irreparable joint damage, which results in functional impairment. Ensuring timely access to appropriate and effective care is the first step in preventing the deleterious, progressive effects of these diseases. A centralized intake referral system involves pooling of patients on waiting lists to create a single first-come, first-serve, but severity prioritized queue, from which patients are directed to an appropriate service provider [49]. In theory, pooling patient referrals for assessment and triage should help decrease the variability in the system and improve access to arthritis care [50]. But, a central intake system can be structured in various ways, and the impact of different structures on patient outcomes and costs is not obvious. Dynamic simulation modeling allows policymakers to evaluate these different structures and alternative scenarios [51]. This ability to evaluate system design and the intended and unintended consequences of implementing alternative interventions is a critical, but largely missing, tool in health services delivery research.

Nonetheless, there are challenges to using and implementing dynamic simulation models. Some of the challenges are the need of specialized skills in simulation modeling, for example, operations research, engineering, and computer science; data requirements for the models can be difficult to fulfill because of lack of access to certain data, costs associated with data acquisition, and data availability. Nevertheless, these models provide an advantage because their structure will not be limited by the available data and they can be used to do exploratory analyses until the additional data can be incorporated. It may be difficult at times to communicate how these models are built and the details of their mathematical structure. This can sometimes be interpreted by users (i.e., policymakers) as lack of transparency. These structures and sophisticated calculations, however, are necessary to adequately represent the problem and to obtain accurate results.

What Are the Differences between Health Economic Models in Health Technology Assessment and Dynamic Simulation Models in Health Care Delivery Systems?

Health technology assessment (HTA) is defined as "the systematic evaluation of the properties and effects of a health technology, addressing the direct and intended effects of this technology,

as well as its indirect and unintended consequences, and aimed mainly at informing decision making regarding health technologies” [52]. Traditionally, health economic models used in HTA are based on clinical evidence and perform analyses of economic consequences of that specific technology as an intervention compared with usual care. The standard approach used in HTA is cost-effectiveness analysis, in which the ratio of the incremental cost to the incremental benefit (often measured in terms of utility as QALYs) of a single or multiple interventions is most important.

Most HTA reports have a limited scope with regard to the consequences to the health care delivery system. For planning, design, and evaluation of health care delivery system interventions, dynamic simulation models can capture the feedback loops that reflect interactions among the operations, structures, and relationships in the health care system and evolve dynamically over time. Conventional evaluation of interventions in health care is often limited because it neglects these wider health system impacts that could be critical for achieving desired health goals.

For instance, a health economic model comparing tissue engineered and biodegradable gels for repair of small cartilage defects in patients with arthritis might evaluate the clinical effectiveness in terms of cost per QALY and economic consequences (budget impact) compared with physiotherapy, surgery, or watchful waiting. For health care planning and delivery, however, other questions may arise, such as the required health care facilities to deliver this minimally invasive therapy, and the change in hospital service due, for instance, to a delay in whole joint replacement in case of severe OA. In addition, the health system is likely to adopt minimally invasive interventions, but the diffusion may differ widely between regional health facilities, depending on interaction between health care payers, providers, and physicians. The impacts of such interactions are not typically accounted for in HTA.

A systems approach anticipates the upstream and downstream consequences of changes in health care delivery. This enables health service planners to identify upstream and downstream points of leverage through experimentation with various “what-if” scenarios without actually having to implement the policy first. Dynamic simulation modeling is used to model interventions before the cost-intensive design and development and implementation phases. Thus, effects on patient care, the health care system, as well as health economics aspects can be estimated and anticipated [53].

Characteristics of dynamic simulation modeling methods relevant to health care delivery system problems

Now we describe applications in which dynamic simulation modeling is appropriate beyond traditional HTA evaluation of a specific health technology.

Dynamic simulation modeling can be applied to a range of health care delivery system problems:

- a. *Simulation modeling can estimate the consequences of health care delivery system interventions:* Many interventions in health care have impacts on the health care delivery system that are not typically considered in health economic models. Simulation modeling can better estimate the downstream and upstream consequences once a health policy or delivery intervention is implemented, accounting for feedback loops and interdependencies to characterize the adaptive nature of the health care delivery system. These models can also be used to dynamically estimate the consequences of demographic change, or, for instance, aging of the population [54].
- b. *Simulation modeling allows the incorporation of behavioral aspects and personalized health care decisions:* One of the advantages of

dynamic simulation models is that they are flexible in the definition of either “health states” or “events” [55,56]. This enables a more realistic representation of the unique pathways of individual patients through the health care system as well as the health states they currently experience. Patients make decisions about when they will see a doctor, whether they will comply with their medication regimen, or whether they are willing to co-pay for expensive treatment. Dynamic simulation models in general, and ABM in particular, allow flexibility to incorporate the dynamics of people making decisions affecting population health outcomes, and thus efficient planning of health care interventions. Pombo-Romero et al. [57] developed an ABM to show social interaction to explain the use and diffusion of new drugs in a regional health care system. Such ABMs account for behavioral interactions between patients, physicians, and pharmacists regarding prescriptions.

- c. *Simulation models are flexible to consider consequences of comorbidities and health care utilization:* Most health economic models assume an underlying disease for which a treatment is evaluated. Many people with chronic diseases, however, suffer from multiple morbidities and experience multiple episodes of interactions with the health care system. Dynamic simulation models may also incorporate subroutines to model physiological interactions in the body that affect treatment outcomes and health care demand. For instance, Sabounchi et al. [58] created a system dynamics model specific to weight gain and obesity in women undergoing fertility treatment. The model includes several physiological subsystems that may affect body weight. The potential advantage is that networks of related diseases can be defined similar to networks of underlying genetic mutations and networks of social activities [59]. If such underlying physiological responses networks can be identified and modeled, the consequences of health care delivery interventions on the health system can be evaluated more precisely, taking into account time dependency.
- d. *Simulation models can consider the spatial consequences of a health care delivery intervention:* Many health care interventions also have a spatial component, such as infectious disease policies [60] or remote health services such as telemonitoring. If health services are delivered at home, or if general hospitals specialize into health care centers, this has a large impact on the number of patients traveling to health care facilities. At the least, it will impact the case-mix of patients in the hospital, and dynamic simulation modeling can be applied to estimate the consequences on hospital admissions and support further capacity planning [61]. One specific application is queuing and waiting list management in hospitals. Troy and Rosenberg [62] used a dynamic simulation model to determine the need for intensive care unit (ICU) beds for surgery patients. The background for the study was an increase in the number of patients admitted to the hospital for emergency care as the hospital developed into a tertiary care facility. The increase in acute patient admissions led to an increase in the need for ICU beds. Dynamic simulation modeling was used to estimate the required number of ICU beds on the basis of available surgeons and the expected number of patients admitted to the hospital.
- e. *Simulation modeling addresses system problems that are too complex to enable an analytic solution:* Health care consists of multiple complex systems. The inherent feedback loops that reflect interactions and interdependencies among the operations, structures, and relationships in the health care system evolve dynamically over time and cannot always be captured in an analytic solution. But simulation methods can be used to model such relationships.

Dynamic simulation methods for problems at different system levels (strategic, operational, and tactical)

The feasibility and relevance of dynamic simulation modeling methods to inform health system planning and decision making for improving system efficiency have been demonstrated [63]. The specific selection of the appropriate simulation modeling method depends on a number of factors, such as whether the problem is specific to individuals or groups, the level of the problem (strategic, tactical, or operational), and whether stochastic or deterministic solutions are sought [26] (Table 2). This will be the subject of a subsequent task force report.

The literature on the applications of dynamic simulation modeling in health care is large and growing rapidly, although most applications continue to be in the traditional operations research areas of scheduling, transportation, queuing theory, and allocation of resources [63,64]. The following examples illustrate how these dynamic simulation modeling methods have been applied to health care delivery problems and interventions:

- The Mayo Clinic's Center for the Science of Health Care Delivery has applied health care delivery systems thinking to redesign its practices, particularly in the domains of cardiac surgery [65] and outpatient practice [66]. The center used DES to predict the minimum number of beds needed to meet Mayo Clinic quality standards of care. The model incorporated assumptions about surgery growth and new patient recovery protocols, as well as smoothing surgery schedules and

transferring long-stay patients from the ICU. The model predicted 30% lower bed supply requirements than did the traditional bed planning approach. System dynamics modeling was used for high-level planning of primary care staffing that incorporated new care delivery modes. The model allowed for “what-if” scenarios to be evaluated, showing projected access performance for measures such as time to appointment and corresponding staffing requirements.

- Another example is the ReThink Health model. This system dynamics model simulates the behavior of a health system, tracking changes in health status, utilization, and costs. It has been used to analyze various health policy strategies (e.g., expanding health insurance coverage, delivering better preventive and chronic care, and improving environmental conditions) to reduce deaths and improve the cost-effectiveness of interventions [9,67]. For example, Milstein et al. [67] report on the use of the model to evaluate five different health reform policy proposals. The results demonstrated that expanding health insurance and improving the quality of health care delivery would improve health status but would do so at higher cost and health care inequality. In contrast, policies focused on strengthening primary care would improve health status, reduce inequalities, and lower costs. Such divergent outcomes would be extremely difficult to anticipate (not to mention quantify) without the aid of a simulation model [9].
- In Ontario, the median waiting time for total hip and knee joint replacements was more than 6 months, longer than clinically appropriate. To inform decisions to reduce waiting times and improve waiting list management, the team developed a DES model of the Ontario total joint replacement system to evaluate the effects of four management strategies on waiting times: 1) reductions in surgical demand, 2) formal clinical prioritization, 3) waiting time guarantees, and 4) common waiting list management. Using the DES model, they concluded that if the number of surgeries provided (supply) increased by less than 10% per year, demand would need to be reduced by at least 15% to reduce waiting times to clinically acceptable levels within 10 years. Clinical prioritization was found to improve the number of patients receiving surgery in severity-specific wait periods. Implementing general wait time guarantees, however, would only shuffle wait times among patients [68].
- GE Healthcare has applied ABM, combining demographic, economics, and epidemiological data, to support resource allocation decisions about the optimal delivery of care [30]. For example, in India, two government censuses and a socio-economic survey were integrated and used to simulate the expansion of India's health care infrastructure. Initially, the simulations had been limited to cardiovascular disease diagnosis and treatment within the state of Andhra Pradesh. Cardiovascular disease is an increasing health issue in India and a priority for the Indian Ministry of Health, with 2.58 million Indians predicted to die from the disease each year by 2020. Data visualization methods were used to detail the highest concentration of disease, which could then be overlapped over the existing or potential future health care infrastructure. Such visualizations allow health care scenarios over time to be compared, allowing for better future planning. In the future, the model will be expanded to cover other disease areas and adapted for use in other markets outside India.
- The Alberta Health Services Bone and Joint Strategic Clinical Network was seeking a sustainable solution to balancing access, effectiveness, and efficiency in delivering health services to patients with OA across the continuum of care. A system dynamics model was used to inform systemwide

Table 2 – Examples of problems addressed with dynamic simulation modeling methods to evaluate complex health care delivery interventions.

System level	Types of problems	Problem example
Strategic level	Policy	Informing regional or national policy regarding the implementation of a centralized intake system for referral to an appropriate provider for assessment and specialist consultation, if needed, for patients with musculoskeletal pain
Tactical level	Management	Wait time management for referral for a specific service, e.g., consultation with orthopedic surgeon or rheumatologist
Operational level	Logistics	Scheduling surgical dates for joint replacement in the operating room Evaluating the introduction of a new service using tissue engineered and biodegradable gels for repair of small cartilage defects with respect to the change in required health care facilities and hospital services Evaluating the change in hospital services due to a delay in total joint replacement in cases of severe osteoarthritis

Table 3 – Comparison between dynamic simulation models and other types of models.

Criteria	Dynamic simulation models	Markov models	Analytic models
Mode of description	Implicitly (via rules or state equations)	Implicitly (via transition matrices)	Closed-form expressions
Indexing	Time and space	Time	Varies
Linearity	Generally nonlinear	Linear	Generally derivable only for linear systems
Solution procedure	Simulation	Closed-form solution or simulation	Direct evaluation
Population character	Generally open population	Cohorts	Varies

planning for OA of the hip and knee [69,70]. This model contained a complex set of interactions among system components including initial OA diagnosis and care, specialist assessment, medical management, surgical management, and postsurgery rehabilitation characterized by various feedback loops. Other important variables included funding levels and the supply of orthopedic surgeons.

Comparison and Contrast of Key Simulation Modeling Methods (SD, DES, ABM) with Other Modeling Methods (e.g., Optimization and Markov Models)—Differences and Complementarities

There are a large variety of simulation models, some of which share similar capabilities. The International Society of Pharmacoeconomics and Outcomes Research and the Society for Medical Decision Making published seven ISPOR-Society for Medical Decision Making Modeling Good Research Practices Task Force reports providing guidance on state-transition models, such as Markov models [71–77]. Methods focused on in this report (SD, DES, and ABM) were selected on the basis of their suitability to address problems in health care delivery systems and ability to simulate dynamically the interactions between operations, structures, and relationships in the health care system (Table 3).

Simulation models in the sense that we are discussing here (dynamic simulation) are distinguished by their explicit representation of system states and the mechanisms of their evolution over time. Such states might, for example, include the health status and risk behaviors of population members, cumulative societal cost, and QALYs. In contrast to the situation for analytic models—in which the trajectories associated with system evolution are specified as an explicit function of time—for simulation models, this evolution is implicitly characterized by specification of the rules governing that system evolution. Such rules aspire to characterize the posited “physics” of the system, describing causal drivers hypothesized to characterize “how the system works.”

The resulting simulation models—like the systems that they characterize—are often nonlinear in character, a feature with several implications. First, the nonlinearity of the models and systems characterized implies that understanding the behavior of the system to a portfolio of interventions requires simulating those interventions together, so as to capture situations in which such interventions work synergistically and compete with one another. In contrast to Markov models, which are commonly used to characterize the evolution of isolated cohorts, nonlinearity in simulation models generally implies that individuals or cohorts cannot be simulated as solitudes, but must instead be simulated in a population context.

Second, the nonlinearity leads such models to exhibit emergence, in which the behavior of the whole can be very distinct from—and cannot be reduced to—that of its parts. Such emergent behavior is often surprising and counterintuitive and often differs strikingly across temporal and spatial scales. Third, although Markov models and linear systems models can be solved to provide a “closed-form” (analytic) description of the system’s evolution *a priori*, to understand simulation models, analytic solutions are in general not possible, and to derive dynamics of the system requires executing the rules governing the system over time in a mechanistic fashion accounting for the dynamics in the system.

Individual-based simulation modeling—modeling formulated at the level of individual agents or actors—is associated with two major traditions: 1) microsimulation, originating in economics and emphasizing evolution based on empirically grounded, statistical relationships, and 2) ABM, originating in computer science and traditionally depending on algorithmic and rule-based formulations in richer, dynamic, environments. Although their origins, emphases, and preferred patterns of practice differ, these methods overlap in content and underlying concepts, and we consider them here together. In accordance with growing practice, we refer to both below as “agent-based models.”

There are many other types of related simulation modeling methods. Reflecting the important role networks have come to play in many ABMs, we further consider aspects of dynamic social network analysis as specializations of ABMs. Similarly, we consider diverse compartmental modeling techniques such as those prevalent in mathematical epidemiology since its inception in the 1920s under the rubric of system dynamics. Furthermore, simulation models can be used to evaluate and optimize a health care intervention given constrained resources. For example, optimization models can consider the demand for imaging in the context of the limited availability of imaging capacity and scanning time to optimize the use of imaging services. Likewise, these modeling studies can be applied to improve scheduling and hence, to minimize waiting time for patients [78].

The SIMULATE Checklist

The SIMULATE checklist developed by this task force guides researchers in determining whether dynamic simulation modeling is appropriate to address the problem. The checklist identifies eight elements that characterize simulation modeling methods and differentiate them from other modeling approaches such as Markov models and decision trees.

SIMULATE	Does your problem require:
System	Modeling multiple <i>events, relationships, and stakeholders</i> representing health care delivery processes?
Interactions	Including <i>nonlinear or spatial</i> relationships among stakeholders and their context that influence behaviors and make <i>outcomes</i> in the system difficult to anticipate?
Multilevel	Modeling a health care delivery problem from strategic, tactical, or operational <i>perspectives</i> ?
Understanding	Modeling a <i>complex</i> problem to improve patient-centered care that cannot be solved <i>analytically</i> ?
Loops	Modeling <i>feedback</i> loops that change the behavior of <i>future interactions</i> and the consequences for the delivery system?
Agents	Modeling multiple stakeholders with <i>behavioral</i> properties that <i>interact and change</i> the performance of the system?
Time	<i>Time-dependent</i> and <i>dynamic transitions</i> in a health care delivery system, either between or within health care system levels or in health status change?
Emergence	Considering the <i>intended and unintended</i> consequences of health system interventions to address <i>policy resistance</i> and achieve target outcomes?

Applied Example of the SIMULATE Checklist

Now we provide an example of a problem with key characteristics that warrant the use of dynamic simulation modeling methods to illustrate the use of the SIMULATE checklist. We continue with the example of OA care delivery that was introduced earlier: seeking a sustainable solution to delivering health care services to patients with OA while balancing access (i.e., delivering care at the right time to address the problem of long waiting times to see care providers), effectiveness (i.e., delivering the right care to address the problem of inappropriate services), as well as efficiency and cost-effective care (i.e., address the problem of increasing costs and constrained health care resources). This problem can be studied using dynamic simulation modeling methods. The more elements of the SIMULATE checklist that are indicated, the more likely that dynamic simulation modeling is required or will be a more efficient approach to inform the problem.

System

The decision problem in the checklist includes the entire health care delivery system. This includes different health care entities

and patients moving through the system. For example, in OA care delivery, events and relationships to be modeled include elements throughout the care continuum: primary care visits for joint pain and disability, referral from primary care to specialist care, and in cases of end-stage disease, joint replacement performed by an orthopedic surgeon followed by subacute care (i.e., postsurgical care such as homecare). Stakeholders involved include patients, family doctors, orthopedic surgeons, and allied health providers.

Interactions

Patient characteristics and behaviors, such as obesity, socioeconomic status, and comorbidities combined with medication adherence and diet and exercise behaviors, may have a nonlinear relationship with their OA progression and their associated health care expenditures. As a result, the aggregate implications of patient characteristics and health behaviors for the health care system are difficult to anticipate. Similarly, the patient's geographic location (i.e., spatial relationships) may have strong influences on access to services for the patient with OA (e.g., orthopedic surgeon visit).

Multilevel

The management and treatment of OA is important at several levels of the health care system. At an operational level, patients' behaviors have an impact on their disease progression, as does their interaction with the health care system itself (their family doctor, allied health providers, local emergency room, etc.). Accumulating the experience of many patients can help to inform the development of decision rules to maximize the effectiveness and efficiency of care provided subject to the characteristics of a particular patient's case, spatial proximity to different types of health care providers, and so forth. This is the tactical level. Finally, at a strategic level, attempts to maximize the cost-effectiveness of OA care must account for patient characteristics, nonlinearity of health care expenditures, and interactions with health care providers. The data must be accumulated over the entire population with OA served by the health care system now and in the future to evaluate policies and plan for health services that are effective, efficient, and sustainable over the long term.

Understanding

The complexity of systems characterized by nonlinearities, interactions among system components, and behaviors and characteristics of agents (e.g., patients and doctors) makes it very difficult to anticipate outcomes associated with particular changes to the system such as the changes in OA incidence due to changes in obesity in the population, or the demographic and epidemiological shift of OA from the younger population to an older one. Traditional modeling approaches such as Markov models, decision trees, and multivariate methods can be helpful in understanding pieces of a system but are not generally adequate to understand outcomes at a system level because they cannot be solved analytically.

Loops

Systems of OA care have integrated loops that may feed forward or feed backward. For instance, presurgical care and modification of certain behaviors (i.e., exercise and diet) in patients who have been deemed surgical could lead to improvement in functionality, mobility, and reduced pain, which may, in turn, delay the need for surgery and associated health care utilization such as rehospitalizations.

The system may also integrate feedback loops, which actually implies that the system learns or adapts from experiences or from new policy interventions. For instance, physicians may change their referral patterns as new care paths are designed and tested within the system. Or, as waiting lists grow or lessen, the criteria for selecting patients as appropriate candidates for surgery may tighten or relax in response to a fixed surgical operating room capacity in the system.

Agents

Patients, doctors, and informal care providers are all examples of agents who interact with one another and other components of the health care system. Patients' behavior at any time is influenced by the consequences of their experiences in previous periods, their expectations for the future, and their interactions with their physician, the rehabilitation therapist, and the informal care provider who helps them maintain their independence when they return home. Similarly, the treatment choices of physicians are influenced by the outcomes of their previous patients, availability of alternative treatment options, expansion of evidence in the literature, and many other factors. Each of these behavioral responses is, in itself, complex, but their interaction makes it virtually impossible to anticipate outcomes without the use of dynamic simulation methods.

Time

Time is an inherent component of any health care system. A model of care for OA with specific waiting time benchmark performance targets can be implemented and temporarily decrease waiting times for joint replacement. Population characteristics and behaviors, however, change over time and as a consequence, the new model of care may no longer achieve the performance targets. Considering these dynamic changes is relevant to the management and design of a model of care for OA that allows for adaptation to new conditions in the population and the care delivery system and responds accordingly.

Emergence

Nonlinearities and interactions among agents over time and space can lead to such complexity that it is possible to understand the performance of the system only through dynamic simulation. Emergent behaviors can range from valuable innovations to unfortunate events. Policy resistance is related to emergence. Because of the complexity of the system, a particular policy intervention may fail because policymakers do not fully understand its mechanisms and cannot anticipate certain consequences or effects that may emerge. For instance, in an effort to encourage physical activity in the younger generations to reduce the risk of OA, sport-related injuries may increase, leading to an increase in the incidence of OA in a younger population as they age over time.

Summary and Conclusions

The translation of evidence into policy and clinical care through implementation in the health care system are core issues facing health care delivery system transformation around the world. Evidence-based practices can be implemented through simulation modeling to redesign health care delivery systems and improve patient outcomes and health system performance [6]. Traditional HTA and modeling methods are often of limited usefulness when applied to health systems. The hierarchical relationship between the health system, providers, and the

patients manifests a level of complexity that can be captured using dynamic simulation modeling methods.

Although dynamic simulation modeling methods are widely used in industrial and business operations to study processes and improve effectiveness and efficiency, they are still relatively new in health applications [42]. Recently, there has been a notable growth in studies applying simulation modeling methods in health sciences research and health systems management [64]. The feasibility and relevance of these methods to inform health care delivery system planning and decision making for improving system efficiency have been demonstrated [63].

In this report, we provided an overview of dynamic simulation modeling methods and examples of health care system problems for which such methods could be useful. We differentiate dynamic simulation modeling methods from other types of modeling approaches used typically in HTA applications. The SIMULATE checklist can be used to assist in determining whether dynamic simulation modeling methods are an appropriate modeling approach to address the specific health care delivery problems of interest. Key characteristics that necessitate simulation modeling or that take a more efficient approach to understand the system and inform decision making include a complex problem with nonlinear and/or spatial relationships among stakeholders in the context of a system characterized by emergent behavior.

In a subsequent report, we will describe each of the three dynamic simulation modeling methods (SD, DES, and ABMs) and present good research practice guidelines to support the application of dynamic simulation modeling methods in health care delivery.

Acknowledgments

We thank the following reviewers for valuable written feedback on earlier drafts of this report: Brian Denton, Beth Devine, Chris Jones, Jonathan Karnon, Nishkarsh Likhari, Andriy Moshyk, David C. Norris, Martin O'Leary, Luke Rudmik, and Amir Viyanchi. We also very much appreciate the comments, expertise, and insight of those who provided oral comments during presentations of our work to date. ISPOR member comments contribute to the high-quality consensus nature that characterizes ISPOR Good Practices for Outcomes Research reports. Finally, the steady and capable support of our ISPOR staff liaison, Elizabeth Molsen, is genuinely appreciated.

Source of financial support: The authors have no other financial relationships to disclose.

REFERENCES

- [1] Glouberman S, Zimmerman B. Complicated and Complex Systems: What Would Successful Reform of Medicare Look Like. Discussion paper number 8. Commission on the Future of Health Care in Canada, 2002.
- [2] Zimmerman B, Lindberg C, Plsek PE. A complexity science primer. In: Zimmerman B, Lindberg C, Plsek PE, eds. *Edgware, Insights from Complexity Science for Health Care Leaders*. Irving: VHA, Inc, 2001.
- [3] Ackoff RL. OR: After the post mortem. *System Dyn Rev* 2001;17: 341–6.
- [4] Padula WV, Breteler MJM. Sharing perspectives on HTA from both sides of the pond— lessons learned by graduate students at ISPOR's 15th Annual European Congress. *ISPOR CONNECTIONS* 2013;19:15.
- [5] Berwick DM. A user's manual for the IOM's 'Quality Chasm' report. *Health Aff (Millwood)* 2002;21:80–90.
- [6] Berwick DM. What 'patient-centered' should mean: confessions of an extremist. *Health Aff (Millwood)* 2009;28:w555–65.
- [7] Kravitz RL, Duan N, Braslow J. Evidence-based medicine, heterogeneity of treatment effects, and the trouble with averages. *Milbank Q* 2004;82:661–87.

- [8] Berwick DM. The science of improvement. *JAMA* 2008;299:1182–4.
- [9] Milstein B, Homer J, Hirsch G. Analyzing national health reform strategies with a dynamic simulation model. *Am J Public Health* 2010;100:811–9.
- [10] Homer JB, Hirsch GB. System dynamics modeling for public health: background and opportunities. *Am J Public Health* 2006;96:452–8.
- [11] Seila AF, Brailsford S. Opportunities and challenges in health care simulation. In: Alexopoulos C, Goldsman D, Wilson JR, eds. *Advancing the Frontiers of Simulation*. New York, NY: Springer, 2009.
- [12] Liu P, Wu S. An agent-based simulation model to study accountable care organizations. *Health Care Manag Sci* 2014 Apr 9. [Epub ahead of print].
- [13] Crane GJ, Kymes SM, Hiller JE, et al. Accounting for costs, QALYs, and capacity constraints: using discrete-event simulation to evaluate alternative service delivery and organizational scenarios for hospital-based glaucoma services. *Med Decis Making* 2013;33:986–97.
- [14] Medical Research Council. *A Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health*. London: Medical Research Council, 2000.
- [15] Padula WV, Duffy MP, Yilmaz T, Mishra MK. Integrating systems engineering practice with health-care delivery. *Health Systems* 2014;3:159–64.
- [16] Plsek PE, Greenhalgh T. The challenge of complexity in health care. *BMJ* 2001;323:625–8.
- [17] Goldstein J. Emergence as a construct: history and issues. *Emergence* 1999;11:49–72.
- [18] Harrison JR, Lin Z, Carroll GR, Carley KM. Simulation modeling in organizational and management research. *Acad Manag Rev* 2007;32:1229–45.
- [19] Banks J. *Handbook of Simulation*. Wiley Online Library, 1998.
- [20] Sokolowski JA, Banks CM. *Principles of Modeling and Simulation: A Multidisciplinary Approach*. Hoboken, NJ: John Wiley & Sons, 2011.
- [21] Forrester J. System dynamics—a personal view of the first fifty years. *Syst Dyn Rev* 2007;23:345–58.
- [22] Forrester J. *Industrial Dynamics*. Cambridge, MA: The M.I.T. Press, 1961.
- [23] Siebers PO, Macal CM, Garnett J, et al. Discrete-event simulation is dead, long live agent-based simulation! *J Simul* 2010;4:204–10.
- [24] Hollocks B. Forty years of discrete-event simulation—a personal reflection. *J Oper Res Soc* 2006;57:1383–99.
- [25] Karnon J, Stahl J, Brennan A, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Modeling using discrete event simulation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-4. *Value Health* 2012;15:701–11.
- [26] Gunal MM. A guide for building hospital simulation models. *Health Systems* 2012;1:17–25.
- [27] Schelling TC. Dynamic models of segregation. *J Math Sociol* 1971;1:143–86.
- [28] Borshchev A, Filippov A. From system dynamics and discrete event to practical agent-based modeling: reasons, techniques, tools. Presented at: 22nd International Conference of the System Dynamics Society. Oxford, England, 2004.
- [29] IPLER. Information Products Lab for Emergency Response (IPLER). 2008. Available from: http://ipler.cis.rit.edu/node/1?_sm_au_=_iVV0HQk2ZV57r4kR. [Accessed January 10, 2014].
- [30] Kruzikas DT, Higashi MK, Edgar M et al. Using agent-based modeling to inform regional health care system investment and planning. In: International Conference on Computational Science and Computational Intelligence (CSCI) (Volume 2). March 10–13, 2014, Las Vegas, NV.
- [31] Sobolev B, Harel D, Vasilakis C, Levy A. Using the Statecharts paradigm for simulation of patient flow in surgical care. *Health Care Manag Sci* 2008;11:79–86.
- [32] Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood)* 2008;27:759–69.
- [33] Selby JV, Beal AC, Frank L. The Patient-Centered Outcomes Research Institute (PCORI) national priorities for research and initial research agenda. *JAMA* 2012;307:1583–4.
- [34] Gawande A. *The Checklist Manifesto—How to Get Things Right*. New York: Metropolitan Books, 2009.
- [35] Pronovost PJ, Vohr E. *Safe Patients, Smart Hospitals: How One Doctor's Checklist Can Help Us Change Health Care from the Inside Out*. New York: Penguin, 2010.
- [36] Bewtra M, Kilambi V, Fairchild AO, et al. Patient preferences for surgical versus medical therapy for ulcerative colitis. *Inflamm Bowel Dis* 2014;20:103–14.
- [37] Mohamed AF, Zhang J, Johnson FR, et al. Avoidance of weight gain is important for oral type 2 diabetes treatments in Sweden and Germany: patient preferences. *Diabetes Metab* 2013;39:397–403.
- [38] Schneider A, Kanagarajan N, Anjelly D, et al. Importance of gender, socioeconomic status, and history of abuse on patient preference for endoscopic. *Am J Gastroenterol* 2009;104:340–8.
- [39] Garber S, Gates SM, Keeler EB, et al. Redirecting Innovation in U.S. Health Care: Options to Decrease Spending and Increase Value. RAND Corporation, 2014.
- [40] Sterman JD. Learning from evidence in a complex world. *Am J Public Health* 2006;96:505–14.
- [41] Brownson RC, Fielding JE, Maylahn CM. Evidence-based public health: a fundamental concept for public health practice. *Ann Rev Pub Health* 2009;30:175–201.
- [42] Sterman JD. *Business Dynamics: Systems Thinking and Modeling for a Complex World*. New York: McGraw-Hill, 2000.
- [43] Pasupathy KS. Transforming healthcare: Leveraging the complementarities of health informatics and systems engineering. *Int J Healthc Delivery Reform Initiatives* 2010;2:35–55.
- [44] Brown GD, Patrick TB, Pasupathy KS. *Health Informatics: A Systems Perspective*. Chicago, IL: Health Administration Press, 2013.
- [45] Richmond B. Systems thinking: critical thinking skills for the 1990s and beyond. *Syst Dyn Rev* 1993;9:113–33.
- [46] Scholtes P, Joiner B, Streibel B. *The Team Handbook*. (3rd ed.). Madison, WI: Oriel, Inc, 2013.
- [47] Vennix JAM. Group model-building: tackling messy problems. *Syst Dyn Rev* 1999;15:379–401.
- [48] Axelrod R. Advancing the art of simulation in the social sciences. In: Conte R, Hegselmann R, Terna P, eds. *Simulating Social Phenomena*. Berlin: Springer, 1997.
- [49] Bungard TJ, Smigorsky MJ, Lalonde LD, et al. Cardiac EASE (Ensuring Access and Speedy Evaluation)—the impact of a single-point-of-entry multidisciplinary outpatient cardiology consultation program on wait times in Canada. *Can J Cardiol* 2012;25:697–702.
- [50] Cattani K, Schmidt GM. The pooling principle. *INFORMS Trans Educ* 2005;5:17–24.
- [51] Vasilakis C, Sobolev BG, Kuramoto L, Levy LR. A simulation study of scheduling clinic appointments in surgical care: individual surgeon versus pooled lists. *J Oper Res Soc* 2006;58:202–11.
- [52] The International Network of Agencies for Health Technology Assessment. What is health technology assessment (HTA)? 2014. Available from: <http://www.inahta.org/>. [Accessed November 27, 2014].
- [53] Gantner-Bär M, Djanatliev A, Prokosch HU, Sedlmayr M. Conceptual modeling for prospective health technology assessment. *Stud Health Technol Inform* 2012;180:33–7.
- [54] Ansah JP, Eberlein RL, Love SR, et al. Implications of long-term care capacity response policies for an aging population: a simulation analysis. *Health Policy* 2014;116:105–13.
- [55] Stahl JE. Modelling methods for pharmacoeconomics and health technology assessment: an overview and guide. *Pharmacoeconomics* 2008;26:131–48.
- [56] Caro J. Pharmacoeconomic analyses using discrete event simulation. *Pharmacoeconomics* 2005;23:323–32.
- [57] Pombo-Romero J, Varela LM, Ricoy CJ. Diffusion of innovations in social interaction systems: an agent-based model for the introduction of new drugs in markets. *Eur J Health Econ* 2013;14:443–55.
- [58] Sabouchi NS, Hovmand PS, Osgood ND, et al. A novel system dynamics model of female obesity and fertility. *Am J Public Health* 2014;104:1240–6.
- [59] Barabasi AL. Network medicine—from obesity to the “diseasome”. *N Engl J Med* 2007;357:404–7.
- [60] Davis GS, Sevdalis N, Drumright LN. Spatial and temporal analyses to investigate infectious disease transmission within healthcare settings. *J Hosp Infect* 2014;86:227–43.
- [61] Hulshof PJ, Boucherie RJ, Hans EW, Hurink JL. Tactical resource allocation and elective patient admission planning in care processes. *Health Care Manag Sci* 2013;16:152–66.
- [62] Troy PM, Rosenberg L. Using simulation to determine the need for ICU beds for surgery patients. *Surgery* 2009;146:608–17.
- [63] Brailsford SC, Harper PR, Patel B, Pitt M. An analysis of the academic literature on simulation and modelling in health care. *J Simul* 2009;3:130–40.
- [64] Katsaliaki K, Mustafee N. Applications of simulation within the healthcare context. *J Oper Res Soc* 2011;62:1431–51.
- [65] Marmor YN, Rohleder TR, Cook DJ, et al. Recovery bed planning in cardiovascular surgery: a simulation case study. *Health Care Manag Sci* 2013;16:314–27.
- [66] Kuchera D, Rohleder TR. Optimizing the patient transport function at Mayo Clinic. *Qual Manag Health Care* 2011;20:334–42.
- [67] Milstein B, Homer J, Briss P, et al. Why behavioral and environmental interventions are needed to improve health at lower cost. *Health Aff (Millwood)* 2011;30:823–32.
- [68] Cipriano LE, Chesworth BM, Anderson CK, Zaric GS. An evaluation of strategies to reduce waiting times for total joint replacement in Ontario. *Med Care* 2008;46:1177–83.
- [69] Marshall DA, Rogers P, Rohleder T, Vanderby S. System dynamics modeling: A decision support tool to improve care for hip and knee osteoarthritis. *Inst Health Econ* 2010;1–44.
- [70] Vanderby S, 2 more authors, et al. Modeling the complete continuum of care using system dynamics: the case of osteoarthritis in Alberta. *J Simul* 2014. In press.

-
- [71] Caro JJ, Briggs AH, Siebert U, Kuntz KM. ISPOR-SMDM Modeling Good Research Practices Task Force. Modeling good research practices—overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-1. *Med Decis Making* 2012;32:667–77.
- [72] Pitman R, Fisman D, Zaric GS, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Dynamic transmission modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group-5. *Med Decis Making* 2012;32:712–21.
- [73] Siebert U, Alagoz O, Bayoumi AM, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. State-transition modeling: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-3. *Value Health* 2012;15:812–20.
- [74] Karnon J, Stahl J, Brennan A, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Modeling using discrete event simulation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-4. *Value Health* 2012;15:821–7.
- [75] Briggs AH, Weinstein MC, Fenwick EA, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Model parameter estimation and uncertainty analysis: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force Working Group-6. *Med Decis Making* 2012;32:722–32.
- [76] Eddy DM, Hollingworth W, Caro JJ, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. *Med Decis Making* 2012;32:733–43.
- [77] Roberts M, Russell LB, Paltiel AD, et al. ISPOR-SMDM Modeling Good Research Practices Task Force. Conceptualizing a model: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-2. *Med Decis Making* 2012;32:678–89.
- [78] Vanberkel PT, Boucherie RJ, Hans EW, et al. Accounting for inpatient wards when developing master surgical schedules. *Anesth Analg* 2011;112:1472–9.