Deterministic Sensitivity Analysis for First-Order Monte Carlo Simulations: A Technical Note

Benjamin P. Geisler, MD,^{1,2,3,4} Uwe Siebert, MD, MPH, MSc, ScD,^{1,2} G. Scott Gazelle, MD, MPH, PhD,^{1,4} David J. Cohen, MD, MSc,⁵ Alexander Göhler, MD, MSc, PhD, MPH^{1,2}

¹Institute for Technology Assessment and Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ²Deptartment of Public Health, Medical Decision Making and Health Technology Assessment, UMIT—University for Health Sciences, Medical Informatics and Technology, Hallin Tyrol., Austria; ³Institute for Social Medicine, Epidemiology, and Health Economics, Charité—Universitätsmedizin Berlin, Berlin, Germany; ⁴Harvard School of Public Health, Boston, MA, USA; ⁵St. Luke's Mid America Heart Institute, Kansas City, MO, USA

ABSTRACT

Objectives: Monte Carlo microsimulations have gained increasing popularity in decision-analytic modeling because they can incorporate discrete events. Although deterministic sensitivity analyses are essential for interpretation of results, it remains difficult to combine these alongside Monte Carlo simulations in standard modeling packages without enormous time investment. Our purpose was to facilitate one-way deterministic sensitivity analysis of TreeAge Markov state-transition models requiring first-order Monte Carlo simulations.

Methods and Results: Using TreeAge Pro Suite 2007 and Microsoft Visual Basic for EXCEL, we constructed a generic script that enables one to

perform automated deterministic one-way sensitivity analyses in EXCEL employing microsimulation models. In addition, we constructed a generic EXCEL-worksheet that allows for use of the script with little programming knowledge.

Conclusions: Linking TreeAge Pro Suite 2007 and Visual Basic enables the performance of deterministic sensitivity analyses of first-order Monte Carlo simulations. There are other potentially interesting applications for automated analysis.

Keywords: decision analysis model, Markov model, methods, microsimulation, modeling.

Background

In recent years, Monte Carlo microsimulations have become increasingly common in decision-analytic modeling [1]. This is largely because of the fact that drastically increased computer power has made it possible to perform microsimulations in reasonable amounts of time. Although parameter-uncertainty ("second-order" uncertainty) can be assessed using probabilistic sensitivity analysis [2], stochastic uncertainty is only considered "random noise from a decision maker's point of view, and can be overcome by increasing the sample size of the microsimulation" [3]. First-order Monte Carlo simulations employing "tracker variables" enable one to overcome the "memory-less" nature of Markov transition-state models without increasing the number of health states, thus avoiding potential sources for errors. In this way, discrete events can be incorporated into Markov models. Nevertheless, with a standard modeling package such as TreeAge Pro (TreeAge Software, Inc. Williamstown, MA, USA), it can be difficult to perform multiple deterministic sensitivity analyses, because each single data point requires that a new Monte Carlo microsimulation be performed, and thus huge investments of time have to be spared by the researcher. We therefore sought ways to automate deterministic one-way sensitivity analysis of models requiring the use of first-order Monte Carlo simulations.

Methods and Results

Using TreeAge Pro Suite 2007 and Microsoft Visual Basic for EXCEL (Microsoft Corporation, Redmond, WA, USA), we con-

Address correspondence to: Benjamin P. Geisler, Institute for Technology Assessment, Massachusetts General Hospital, 101 Merrimac St., Floor 10, Boston, MA 02114, USA. E-mail: ben@mgh-ita.org

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structed a generic script that enables the performance of automated deterministic one-way sensitivity analyses in EXCEL employing microsimulation models. By using object-oriented programming, we accessed "TreeAgeProLib" objects of the TreeAge Pro EXCEL add-in to perform a specified number of first-order Monte Carlo simulations in EXCEL. Before the firstorder Monte Carlo simulation was run, a variable of interest was set. After the simulation had finished, we output the costs and effectiveness per strategy and then computed the incremental costs, effectiveness, and cost-effectiveness ratios. These three operations were repeated in a "FOR ... NEXT" loop to set the variable of interest to a value ranging from the lowest to the highest prespecified value of our deterministic one-way sensitivity analysis. The script that we used is included in the appendix. In addition, we constructed a generic worksheet in EXCEL (see Fig. 1) that allows for the use of the script without programming knowledge. The code and the spreadsheet are generic for all TreeAge models with two strategies and can be downloaded from our website, http://www.mgh-ita.org/index.php?option=com_ content&task=view&id=163&Itemid=84.

Conclusions

Linking TreeAge Pro Suite 2007 and Visual Basic allows the automatic performance of multiple deterministic sensitivity analysis in first-order Monte Carlo simulations. Generic code can be run in convenient EXCEL spreadsheets with no programming knowledge necessary. There are other potentially interesting applications, such as automated sensitivity analysis of cohort models, automated deterministic two or multiway-sensitivity analyses of models depending on first-order Monte Carlo simulations, automated model calibration, and automated secondorder Monte Carlo simulations, such as expected value of partial information analyses with varying sets of constant variables.

or	TreeAgee Pro Models Employing 1st Order Monte Carlo Simulations	
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This un ari: sim	s is an automated script written in Visual Basic for Excel and TreeAge Pro 2007 scripting language. The purpose of this script is automated one-way sensitivity analyses in models that employ first order Monte Carlo simulations (e.g. when using tracker ables). In these kinds of simulations, the built-in first-order sensitivity analyses cannot be carried out and thus the Monte Carlo ulation is not performed. This script runs a pre-defined number of trials for each value of the sensitivity analysis (e.g. you can ru lyses for a particular variable ranging from 0 to 200 and then display the results in a graph).	
ns	tructions:	F
1	Open the model you would like to analyze in TreeAge Pro. If you need to save the model, please do so now. Note that in your model the value of the variable of interest will have varied if your model has at least partially been run.	
2.	How many 1st order trials do you want do run per value of the sensitivity analysis? 50000 trials	
3.	Enter the variable of interest that you want to assess in this field: rr2	
4.	Please enter the starting value: 0.00	Γ
5.		
6		
7	Please enter the seed value: 1 (see below)	Г
8		
9.	If you're ready, please hit the start button: Start	
No	tes:	F
1.	The status of the simulation is displayed in the status bar (in total you'll be runnig 1050000 trials, so this might take a while)	-
	If the simluation is ready, please go to the analysis worksheet. There you can assess your data (e.g. graph it) or copy it to and worksheet/workbook.	
3.	Markov models employing 'tracker variables' enable one to overcome the 'memory-less' nature of Markov models. However, 1st order uncertainty is generally considered "random noise from a decision-maker's point of view and can be overcome by increas the sample size of the microsimulation." (Weinstein 2006). Thus, it is important to be certain the number of 1st order trials is latenough for your purposes.	ing
4.	If you specify a seed value in the random number generator, it allows a one to reproduce the same sample order subsequently when performing an identical query using identical data. The seed number you specify initially does not matter however it must remaing identical in subsequent runs. You can enter a random integer value between 1 and 64,000.	
5.	With respect to seeding behavior, you may choose between the following options (please also see TreeAge Pro manual):	_
	D : standard (constistent with DATA software)	Г
	1 : maintained distribution consistency	
-	2 : independently seed each other (unaffected by # of processors or addition of strategies/distributions)	-

 $\label{eq:Figure I} \mbox{ Figure I} \mbox{ Screenshot of the Generic EXCEL User interface}.$

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