Capacity Constraints and Cost-Effectiveness: A Discrete Event Simulation for Drug-Eluting Stents

Beate Jahn, Karl Peter Pfeiffer, Engelbert Theurl, Jean-Eric Tarride and Ron Goeree

Med Decis Making 2010 30: 16 originally published online 29 September 2009
DOI: 10.1177/0272989X09336075

Capacity Constraints and Cost-Effectiveness: A Discrete Event Simulation for Drug-Eluting Stents

Beate Jahn, PhD, Karl Peter Pfeiffer, PhD, Engelbert Theurl, PhD, Jean-Eric Tarride, PhD, Ron Goeree, MA

Background. *Waiting times for access to care, for example, for diagnostic imaging or surgery, are a highly relevant issue in health care. Waiting or deferred treatment caused by limited resource capacities can affect treatment success, quality of life, and costs. However, when treatment alternatives are compared in economic models, often unrestricted availability of resources is assumed, and dynamic changes in waiting lines remain unconsidered. The objective of this study was to evaluate the impact of potential real-world capacity restrictions and implied waiting lines on cost-effectiveness results and additional model outcomes.* ***Methods.*** *A case study of drug-eluting and bare-metal stent treatment illustrates the effect of hypothetical capacity limitations of daily stenting procedures. Therefore, a decision-analytic model which allows for explicitly defined resource capacities and dynamic waiting lines was built using discrete event simulation. Cost-effectiveness, utilization, waiting time, and budgetary impact of alternative treatment scenarios are analyzed under the assumption of limited and unlimited resource capacities.* ***Results.*** *The compared treatment allocation scenarios in the case study demonstrate that the additional cost for waiting increases the average treatment cost per patient. The different scenarios have different impacts on waiting lines because of the number of repeated interventions. Additionally, this effect leads to changes in cost-effectiveness results for the hypothetical capacity limit. Explicitly modeled capacities allow for further analysis of capacity utilization, waiting lines, and budgetary impact.* ***Conclusion.*** *Our model shows that neglected limited capacities can cause wrong cost-effectiveness results. Therefore, capacities should be explicitly included in decision-analytic models if there is evidence of scarcity.* ***Key words:*** *health economic evaluation; cost-effectiveness analysis; modeling technology; discrete event simulation; capacities; limited resources.* ***(Med Decis Making 2010;30:16–28)***

INTRODUCTION

Background

Economic analyses are increasingly used to assist health care decision makers.[1] A commonly applied type for these evaluations is the cost-effectiveness analysis (CEA). Within this analysis, costs and effectiveness of new health care technologies or treatments are estimated and compared to existing alternatives.[2,3] The goal of this analysis is to improve system efficiency in resource allocation decisions. However, the reliability of CEA results is hampered by a lack of information which is necessary for decision making. Furthermore, simplifications in decision models for CEA and other cost consequence analyses are questioned.[4,5]

Received 29 May 2007 from the Institute of Public Health, Medical Decision Making and Health Technology Assessment, Department of Public Health, Information Systems and Health Technology Assessment, UMIT-University for Health Sciences, Medical Informatics and Technology, Hall i.T., Austria and the Department of Medical Statistics Informatics and Health Economics, Innsbruck Medical University, Innsbruck, Austria (BJ); the Department of Medical Statistics Informatics and Health Economics, Medical University of Innsbruck, Innsbruck, Austria (KPP); the Department of Public Finance, Leopold-Franzens–University of Innsbruck, Innsbruck, Austria (ET); the Programs for Assessment of Technology in Health (PATH) Research Institute, the Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada (J-ET, RG). Revision accepted for publication 10 October 2008.

Address correspondence to Beate Jahn, Institute of Public Health, Medical Decision Making and Health Technology Assessment, Department of Public Health, Information Systems and Health Technology Assessment, UMIT-University for Health Sciences, Medical Informatics and Technology, Eduard-Wallnoefer-Center 1, A-6060 Hall in Tirol, Austria, Europe; e-mail: beate.jahn@umit.at.

DOI: 10.1177/0272989X09336075

Waiting times and rationing are becoming more relevant in real-life health service.[6,7] Resource capacities (e.g., number of occupied beds in an intensive care unit, number of interventions which require a specific device) can be a realistic constraint. In traditional decision-analytic models, capacities are not modeled explicitly. Usually, the CEA assumes unrestricted availability of resources at given prices; otherwise, capacity constraints are incorporated indirectly by using fixed waiting times. Therefore, in general, utilization is not reported, and the impact of limited capacities (waiting time, alternative treatment) on cost-effectiveness outcome remains either unconsidered or is taken into account in a very simplified manner. The different effects of treatment alternatives on waiting lines, for example, because of a reduced number of repeated interventions, also remain unconsidered. A main reason for these simplifications is the inability of commonly used decision-analytic models (Markov models, decision trees) to incorporate such constraints.

Discrete Event Simulation (DES)

Discrete event simulation is a well-established modeling technique for analyzing complex service, and it has been applied for simulation and planning of health clinics.[8–10] Recently, it has been proposed as a very flexible alternative modeling approach for the evaluation of competing health care interventions.[1,11–13]

Discrete event simulation has the ability to track patients and, therefore, to incorporate all kinds of characteristics such as baseline risk or patient history. It allows for modeling of patient pathways over extended time horizons. Patients move through the model, and they can experience events at any discrete point in time. Moreover, DES provides the flexibility to incorporate capacities explicitly and to account for interdependencies of patients due to limited capacities.[14] It is therefore a suitable tool for the modeling of waiting lines. This feature clearly distinguishes this simulation technique from commonly applied methods. A comprehensive overview of DES is given by Banks and others[15] or Fishman.[16]

Objectives

The primary research question is to evaluate the impact of potential real-world capacity restrictions and implied waiting lines on cost-effectiveness results. Drug-eluting stents and bare-metal stents are the 2 treatment alternatives which serve as a modeling example. They show differences in the number of repeated interventions. Therefore, they are assumed to have different impacts on waiting lines. Cost and effectiveness are analyzed assuming unlimited and limited numbers of daily stenting interventions. Additional health care system information (e.g., utilization, waiting time, budgetary impact) illustrates further advantages of explicitly modeled capacities.

The article is structured as follows: First, the modeling example (case study) is introduced. Secondly, the details on the DES model are given, the input data are presented, and the performed analysis is explained. The results of the modeling example in the base case (unlimited capacities) and the results in the case of limited capacities are compared and discussed.

METHODS

Case Study: Drug-Eluting v. Bare-Metal Stent

This case study compares stent treatment alternatives for coronary artery disease. ''Coronary artery disease (CAD) is a condition caused by a narrowing or occlusion of coronary arteries that supply blood to the heart muscle.''[17] It may lead to symptoms such as angina and an increased risk of myocardial infarction. Percutaneous coronary intervention (PCI) with the use of stents has become an established treatment intervention. Percutaneous coronary intervention with bare-metal stents (*bms*) is considered to be effective, but renarrowing (restenosis) may require repeated interventions. Drug-eluting stents (*des*) aim to reduce the need for a repeated treatment. The results of recent randomized controlled trials have been summarized by Hill and others[18,19] Registry studies are beginning to address the effectiveness and cost-effectiveness of *des*.[19–22]

In this case study, an open cohort is evaluated assuming unlimited and limited number of daily stent placements. This scarcity can cause interdependencies between patients. Therefore, treatment allocation scenarios for all patients need to be defined. To account for the higher risks of revascularization, the patient cohort is split into 4 mutually exclusive subgroups: (S1) nondiabetics with long lesions or narrow vessels, (S2) nondiabetics with short lesions and wide vessels, (S3) diabetics with long lesions or narrow vessels, and (S4) diabetics with short lesions and wide vessels.

Treatment allocation scenarios. Treatment allocation scenarios describe the allocation of all 4 patient subgroups to the 2 treatment alternatives *des* or *bms*. For example, a scenario which reflects the time

Table 1 Example Treatment Scenario DBDD

Patient Cohort Consists of Subgroups (defined by baseline risk factors)			Treatment		
			First Line	Second Line[a]	Third Line
(S1)	Nondiabetes	Long lesion or narrow vessel	D	D	CABG
(S2)	Nondiabetes	Short lesion and wide vessel	B	B	CABG
(S3)	Diabetes	Long lesion or narrow vessel	D	D	CABG
(S4)	Diabetes	Short lesion and wide vessel	D	D	CABG

Note: D, drug-eluting stent; B, bare-metal stent; CABG, coronary artery bypass graft.
a. Type of stent for first line assumed to be type of stent for second-line treatment.

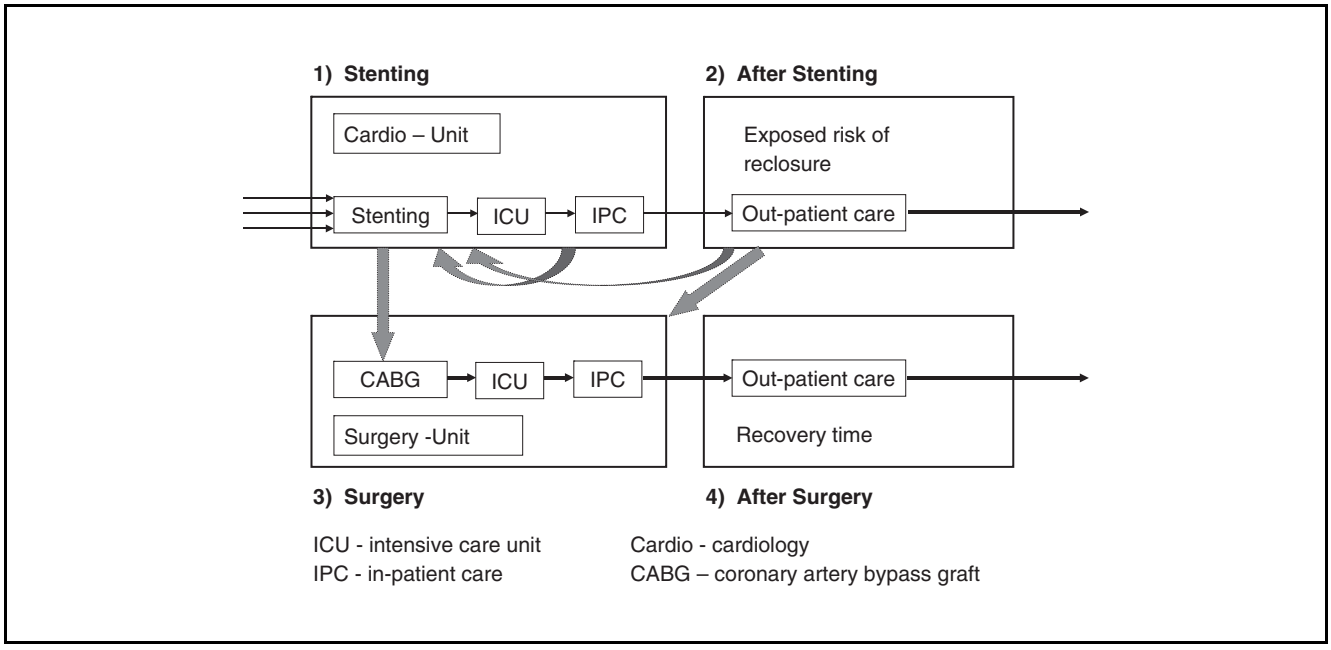

Figure 1 Structure of the model.

before the intervention of the *des* means that all patients are treated with *bms*. Another scenario would be that only the subgroup of patients who benefits the most with respect to decreased revascularization rates receives a *des*. The same type of stent is assumed for the first- and second-line treatment. In case the patient suffers renarrowing again, the CABG (coronary artery bypass graft) is considered to be the third-line and final intervention.

Therefore, each scenario considers the 4 subgroups (S1), (S2), (S3), and (S4). Different scenarios are conditioned depending on patient subgroups and the stent type they receive (*des* = "D" and *bms* = "B"). The complete allocation scenario is defined as scenario = {Stent type for subgroup (S1), subgroup (S2), (S3), (S4)}. For example, in scenario {DBDD}, subgroup (S2) received *bms* (B), and (S1), (S3), and (S4) received *des* (D) (Table 1).

Model

A DES model of the course (pathway) of individual patients with CAD has been built. The economic outcomes of treatment allocation scenarios for the 2 stent types (*des/bms*) are evaluated. The model allows for capacities of resources and impacts of scarcity (e.g., queues). It is built using the simulation software ARENA (version 10, Rockwell Software Inc., Milwaukee, WI). In the following, the modeling process is described in more detail for readers that are not familiar with DES.

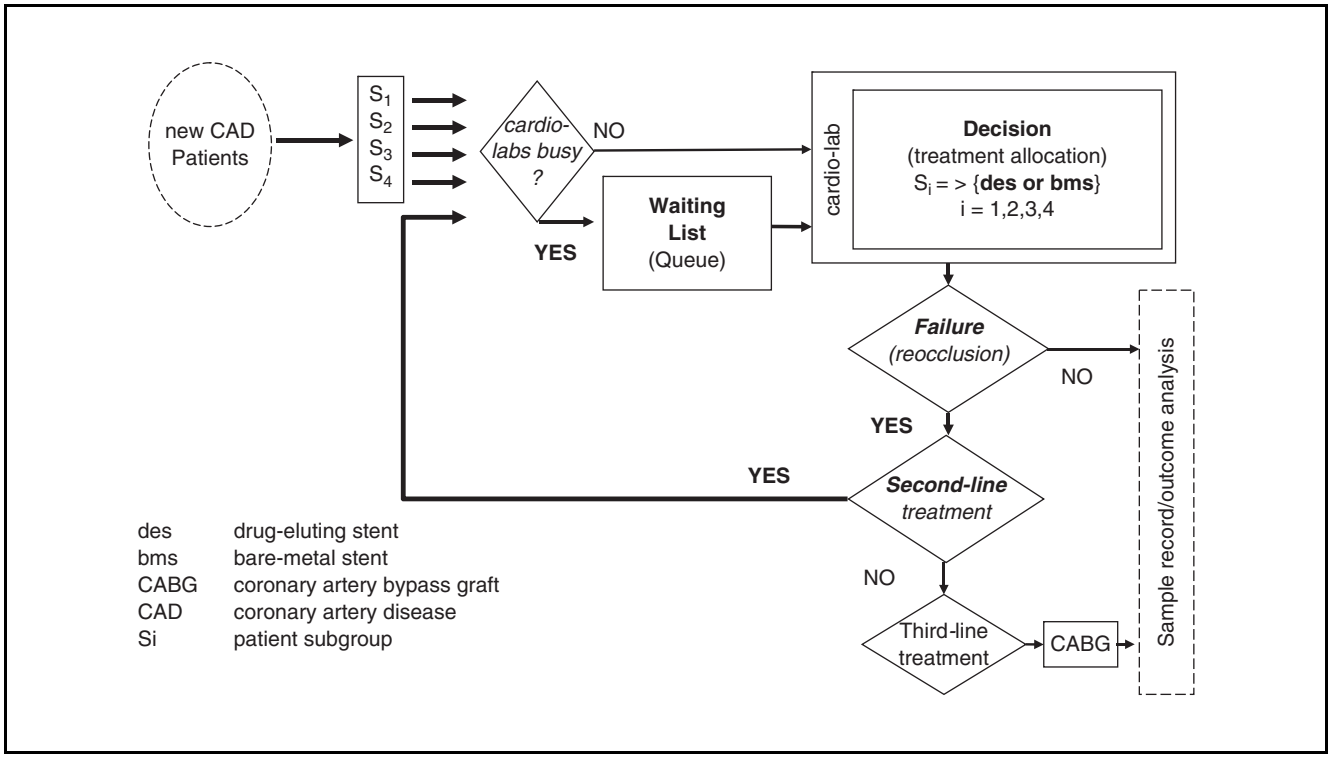

Figure 2 Patient arrival, queuing, and repeated interventions.

Structure of the model. The model is based on 4 main time intervals within the treatment process (Figure 1):

1. Stenting: hospitalization where the patient receives the stent
2. After stenting: time period after the hospital stay but still being at risk of reocclusion
3. Surgery: time in the hospital undergoing a CABG
4. After surgery: time after a CABG hospital stay but still receiving medication

Patient pathway. Each patient is modeled as an entity. Starting with initial stenting (when resources are available), patients proceed on to the in-patient care (IPC) and stay for a certain amount of time (Figure 1). ''Critical'' patients are assumed to be treated in the intensive care unit (ICU). If patients do not suffer from reocclusion, they leave the hospital and go through the period of ''after stenting'' and eventually leave the model afterwards. In case a reintervention is necessary, patients either return to the ''stenting'' submodule (for second-line treatment) or to the ''surgery'' submodule (third-line treatment). Bypass surgery (CABG) is considered to be the final reocclusion. Therefore, patients proceed from the ''surgery'' to the ''after surgery'' module and leave the model thereafter. The arrival process and treatment decisions are displayed in Figure 2.

For the arrival process of new patients, independent and exponentially distributed interarrival time is assumed. As new patient entities enter the model, each patient is randomly assigned to 1 of the 4 patient subgroups (S1), (S2), (S3), and (S4). The respective baseline characteristics (diabetes, lesion and vessel characteristics) are assigned to each entity. Patient-specific attributes are used in a DES model to store this information. These attributes determine the treatment success and the pathway of the patients.

Patients with repeated interventions are determined by relapse probabilities. New patients and patients who need repeated interventions are scheduled for stent placement. If not all of the scheduled patients can be treated due to daily capacity restrictions, they need to wait. In the model, they move into a queue until treatment is available.

Processes. The process-interaction approach[15] is adopted to model all potential pathways in detail. Main treatment processes in the ''stenting'' submodel are stenting (i.e., PCI with the use of *bms* or *des*),

Table 2 Input Parameter

Model Input				Source
Patient cohort				
Total number of new patients per year[a]		14,600		[23]
Subgroup defined by risk factors		Percentage	Abbr.	Source
Nondiabetes: long lesion or narrow vessel		38%	(S1)	[19]
Nondiabetes: short lesion and wide vessel		40%	(S2)	[19]
Diabetes: long lesion or narrow vessel		12%	(S3)	[19]
Nondiabetes: short lesion and wide vessel		10%	(S4)	[19]
Revascularization rate in subgroup (risk of repeated intervention in subgroups)				
	Treatment			
	des	***bms***	***CABG***	
(S1)	0.054	0.095	NA	[19]
(S2)	0.054	0.051	NA	[19]
(S3)	0.069	0.143	NA	[19]
(S4)	0.051	0.055	NA	[19]
Resource utilization (average per patient)				
Cost of intervention (EUR)	2648	1953	6560	[26]
Cost of hospital stay (EUR)	2808	2808	16,180	[26]
Time of hospital stay (days)	4.9	4.9	15.2	[26]
Cost while waiting (EUR per day)	15	15	NA	Expert opinion[b]
Waiting time	Depending on queue length		NA	
Number of stents per intervention	1.24	1.24	NA	[26]
Quality-of-life utility values (EQ-5D utilities)				
Baseline	0.69	0.69	0.68	[25]
1 month	0.84	0.84	0.78	[25]
6 months	0.86	0.86	0.86	[25]
12 months	0.86	0.86	0.87	[25]

Note: *des*, drug-eluting stent; *bms*, bare-metal stent; *CABG*, coronary artery bypass graft. During waiting time, QALY assumed to be equal to baseline.
a. Population of Austria is approximately 8.2 million.
b. Division of Cardiology, Medical University Innsbruck, Innsbruck, Austria.

IPC after the stent placement, and treatment in the ICU. The ''surgery'' submodel includes CABG and ICU as well as IPC treatment. The submodels ''after surgery'' and ''after stenting'' encompass out-patient care such as further drug medication or physiotherapy. However, the costs of the out-patient care are not included in the reported costs.

Time, capacities, and waiting lines. For each process, the duration and required capacities (resources) are defined. In addition, units of available capacities are explicitly defined. The number of daily stented patients and the number of surgery interventions are considered as capacities (defined in terms of number of interventions). Furthermore, the IPC and the ICU in the cardiology and the surgery unit are modeled by using capacities defined in terms of beds. While patients use a particular resource capacity, it becomes unavailable for others. In the simulation, all capacities are available without limitation, and only the number of daily stent placements is assumed to be limited. As a consequence, patients enter a waiting line until resources are available. Information on waiting lines for stenting is collected. Utilization is measured for all other defined resource capacities.

Patients in the waiting lines are assumed to be treated with alternative drug medication until stent placement is possible. This implies additional costs. Waiting time further changes utility values (QALYs) because of continuing anginal symptoms.

The simulated system operates on a first-come, first-served basis synonymous to a waiting list which is processed from the top to the bottom and in which newly arriving patients are included at its bottom.

Data

Model input parameters are summarized in Table 2.

Based on the Austrian Cardiac Care registry data report of 2004,[23] the annual number of first-line percutaneous coronary interventions, including stent placement, is assumed to be 14,600 per year. The patient cohort is split into 4 mutually exclusive subgroups: (S1) nondiabetics with long lesions or narrow vessels, (S2) nondiabetics with short lesions and wide vessels, (S3) diabetics with long lesions or narrow vessels, and (S4) diabetics with short lesions and wide vessels. The risk of restenosis and an implied repeated intervention in these subgroups is estimated on the base of a constant rate of revascularization over 1 year. The respective revascularization rates are derived from the CARDIACCESS (the cardiac care registry of Ontario, Canada) database and the interim report of 2005. In this report, a cohort of 9103 patients with at least 9 months of follow-up is analyzed.[19] The size of the representative subgroups is also derived from this database because the Austrian registry does not provide equal definitions.

Physician expert opinion is used to identify approved patient follow-ups for repeated revascularizations (first-, second-, and third-line treatment). Systematic literature reviews[18,19] indicate no apparent differences between *des* compared to *bms* with respect to mortality, acute myocardial infarction, or stent thrombosis. The results of stent thrombosis are also confirmed by Mauri and others, who have pooled 4 years of follow-up data of 4545 patients.[24] Therefore, the model does not account for differences in these events explicitly.

Utility values are derived from the Arterial Revascularization Therapies Study.[25] Only direct costs are included. Cost data and related durations are derived from the accounting database of the Innsbruck Medical University Hospital (2003–2005)[26] and expert opinion.

Simulation settings. The model is evaluated in the context of a fixed time horizon of 7 years (terminating simulation using a 7-year replication period). One hundred replications within this fixed time horizon were done for each simulation (in a run). Each replication is achieved by using different random numbers (e.g., for determining the time of repeated interventions). Subsequently, the independent output of these replications is averaged. Confidence intervals for 100 replications are reasonably narrow. Days are considered to be the underlying base time unit.

Analysis

The treatment allocation scenarios are evaluated for a limited (base case) and an unlimited number of daily stent placements.

Base case analysis. In the base case analysis, it is assumed that all patients who enter the model on a daily basis can be treated immediately. They make their way through the model, and all required resource capacities are available on time. This implies unlimited capacities.

All scenarios are simulated, and cost-effectiveness is analyzed based on average patient cost in these scenarios and the number of repeated interventions based on the annual revascularization rates. In this analysis, no dominant scenarios can be identified. Therefore, the exclusion of the dominated (nonoptimal) scenarios leads to a selection of scenarios (optimal) which involve a tradeoff between increased effects and higher cost. From these tradeoff treatment scenarios, 4 are chosen, and simulation results are presented.

Analysis assuming limited capacities. These 4 selected tradeoff treatment scenarios from the base case (assuming unlimited capacities) are afterwards evaluated under the assumption of a hypothetical fixed number of percutaneous interventions per day.

By changing the maximum intervention capacity (36, 38, . . . 44 per day), the absolute effect of limited capacities on the outcome compared to the base case analysis is studied. Whether the assumed fixed capacities influence the average patient costs and effects in the alternative treatment scenarios equally (relative effect) is of major interest. In fact, this would lead to similar results in the cost-effectiveness analysis (the comparison of scenarios). Whether the 4 selected scenarios still involve tradeoffs is therefore subsequently investigated.

RESULTS

Impact of Limited Capacities on Scenario Outcomes

Cost and effectiveness. Table 3 shows the average total long-term cost per patient and the number of reinterventions (based on 14,600 initial procedures) in 4 scenarios. Base case results (no capacity limitations, left) are presented and compared to the results

Table 3 Long-term Cost per Patient and Number of Reinterventions

			Long-term Cost per Patient (EUR)							
			Base Case: No Capacity Limits				Max. 36 Stented Patients per Day			
		Scenario	DBDD	DBDB	BBDB	BBBB	DBDD	DBDB	BBDB	BBBB
Nondiabetics (proportion total population)										
(S1)	Long or narrow	38%	5803	5805	5380	5379	7574	7577	7372	7442
(S2)	Short and wide	40%	5055	5054	5055	5054	6814	6820	6945	7011
Diabetics										
(S3)	Long or narrow	12%	5921	5916	5923	5797	7729	7731	7851	7967
(S4)	Short and wide	10%	5783	5083	5080	5083	7548	6856	6982	7045
Average patient cost			5516	5446	5285	5269	7286	7220	7220	7293
Reintervention for 14,600 initial stent placements			813	819	1060	1200	813	819	1060	1200

Table 4 Quality-of-Life Utility Values

			Quality-of-Life Utility Values (QALYs)							
			Base Case: No Capacity Limits				Max. 36 Stented Patients per Day			
		Scenario	DBDD	DBDB	BBDB	BBBB	DBDD	DBDB	BBDB	BBBB
Nondiabetics (proportion total population)										
(S1)	Long or narrow	38%	0.86312	0.86312	0.86286	0.86286	0.84373	0.84369	0.84101	0.84024
(S2)	Short and wide	40%	0.86313	0.86314	0.86313	0.86314	0.84383	0.84379	0.84242	0.84169
Diabetics										
(S3)	Long or narrow	12%	0.86303	0.86303	0.86303	0.86255	0.84327	0.84325	0.84186	0.83873
(S4)	Short and wide	10%	0.86313	0.86311	0.86311	0.86311	0.84381	0.84365	0.84227	0.84156
Average QALY			0.86312	0.86311	0.86302	0.86296	0.84372	0.84367	0.84180	0.84077

in which a maximum of 36 stent placements can be done daily (right). This limit only serves as an example. Waiting lists are built up because this number is much smaller than the average number of daily stented patients in the base case (average of 42–43 patients per day [Table 6]).

In the 4 selected tradeoff scenarios in the base case, the average patient cost decreases with the increase of subgroups of patients who receive *bms*. However, health benefits also decrease due to increasing reinterventions.

Costs increase when patients have to wait due to additional treatment while they are delayed. Average patient cost in scenario {DBDD} is 7286 EUR (95% CI, 7281–7305). This cost decreases to 7220 EUR (95% CI, 7207–7232) when *bms* is provided to (S2) and (S4) (scenario {DBDB}). Providing *bms* to (S2), (S4), and (S1) leads to further decreases (mean, 7220 EUR; 95% CI, 7209–7232). Treating all 4 subgroups with *bms* even leads to increased average patient cost of 7293 EUR per person (95% CI, 7275–7298). The number of reinterventions is independent of capacity scarcity. Therefore, the application of {BBBB} means choosing a treatment scenario which provides less benefits (more reinterventions) at higher costs compared to all other scenarios (dominated). Furthermore, the scenario {BBDB} leads to similar patient cost at a lower health benefit compared to {DBDB} (29% more revascularizations).

Interdependencies of patients caused by limited capacities are also illustrated in Table 3. Waiting time and thereby induced cost for one subgroup depends on the provided treatment for all other subgroups because the number of repeated interventions depends on the provided stent type. Subgroup (S2), for example, is treated with *bms* in every scenario. However, in the analysis with assumed

Table 5 Cost-effectiveness of Treatment Allocation Scenarios

Base Case: No Capacity Limits					
				Incremental Cost-Effectiveness[a]	
Scenario	Cost	QALY	Reintervention	EUR/QALY	EUR/Reintervention Avoided
DBDD	5516	0.86312	813	1,580,492	0.636
DBDB	5446	0.86311	819	1,143,679	0.462
BBDB	5285	0.86302	1060	275,939	0.113
BBBB	5269	0.86296	1200		
Max. 36 Stented Patients per Day					
				Incremental Cost-Effectiveness[b]	
Scenario	Cost	QALY	Reintervention[c]	EUR/QALY	EUR/Reintervention Avoided
DBDD	7286	0.84372	813	1,402,455	10.748
DBDB	7220	0.84367	819		
BBDB	7220	0.84180	1060	Dominated	Dominated
BBBB	7293	0.84077	1200	Dominated	Dominated

a. Compared to treatment allocation scenario BBBB.
b. Compared to treatment allocation scenario DBDB.
c. Calculated based on 14,600 initial stent placements.

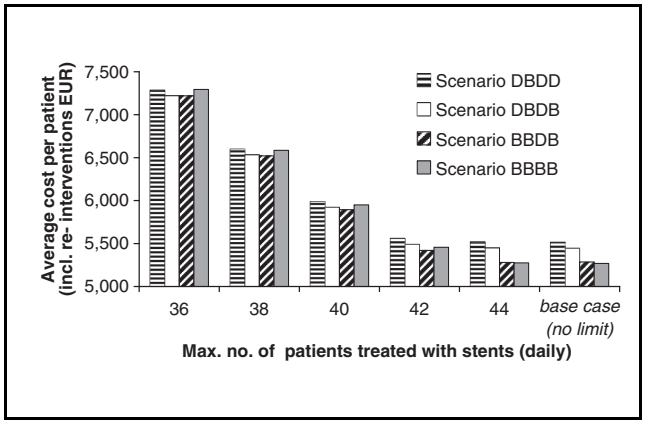

Figure 3 Effect of capacity limitation on average patient cost.

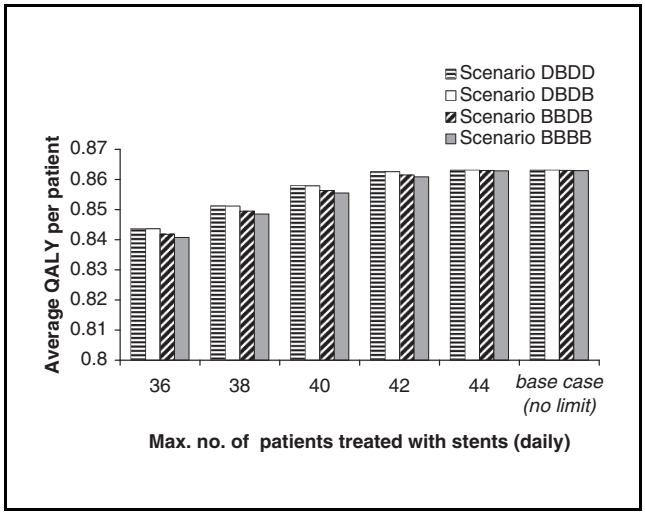

Figure 4 Effect of capacity limitation on quality-of-life utility values.

limited capacities, the estimated cost varies. Average cost per patient in subgroup (S2) is 7011 EUR when all patients are treated with *bms* {BBBB}. Providing *des* to all subgroups which benefit from the new stent device {DBDD} leads to a decrease in total reinterventions and subsequently to decreased average patient cost in (S2) (6814 EUR).

Quality-of-life utility outcomes in the base case and under the assumption of limited capacities are presented in Table 4 (Figure 4). The incremental cost-effectiveness is presented in Table 5.

If capacity constraints are accounted for in the analysis, the results are different with respect to the absolute cost. Moreover, the scenarios {BBDB} and {BBBB} become dominated. This means that the assumed capacity limit changes the relative cost-effectiveness results.

Impact of different capacity limits. The impact of a range of capacity limits on long-term patient costs,

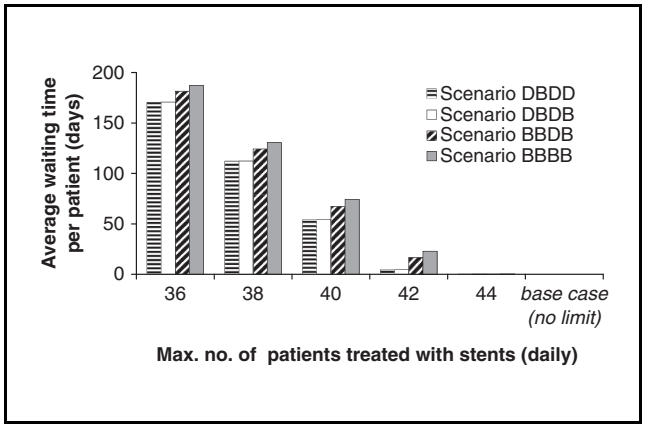

Figure 5 Effect of capacity limitation on average waiting time.

quality-adjusted life years (QALYs), and waiting time is shown in Figures 3, 4, and 5.

The *des* leads to a reduction of repeated interventions. Therefore, the results indicate different capacity utilization in the comparison of the scenarios. Consequently, equal capacity limitations have different impacts in each scenario. The waiting time is longer in the scenarios in which more patient subgroups received *bms*.

Utilization. Health care system utilization information (average daily number of patients treated with stents/bypass, number of beds occupied in hospital units) for the alternative scenarios is displayed in Table 6.

In the base case, scenario {BBBB} implies that on average 42.78 patients per day have a percutaneous coronary intervention with stent placement (Table 6). Because all patients are observed over long periods of time, this number includes initial interventions as well as repeated procedures. It could be reduced by 2% by providing *des* to all patients who benefit from the new coronary stent {DBDD}, which would result in an average of 41.95 patients daily. This reduction in average utilization is a result of reducing repeated interventions. Furthermore, scenario {DBDD} leads to a decrease in daily surgeries by 43% compared to {BBBB} (0.1 v. 0.2 patients on a daily average). Assuming limited capacities, the average number of daily stent placements is 35.99 due to the parameter setting of a maximum of 36 interventions.

The displayed estimates are means of time-averaged values. The impact of the stochastic patient arrival does not become apparent. Therefore, the value of 41.95 stent placements (scenario {DBDD} base case [Table 6]) should not lead to the inference that a fixed number of 42 interventions is sufficient to avoid waiting lists. In scenario {DBDD}, for example, patients would have to wait for on average 4.7 days (Figure 5).

Budgetary impact. As an example, annual budgetary impact information is displayed for 2 scenarios in Table 7 (scenario {BBBB}) and Table 8 (scenario {DBDD}). Expenditures in hospitals for percutaneous intervention with stent placement and surgery are accumulated. The system is assumed to be populated right from the first year. Therefore, expenditures for stenting and CABG increase in the first 2 years because of repeated interventions. Thereafter, they level off. Variations are only due to the stochastic arrival process and the time needed for reinterventions.

The restriction of the number of daily percutaneous interventions to 36 per day initially leads to reduced annual expenditures for stenting and bypass (less interventions compared to the base case). However, expenses for medication for patients on the waiting list burden a further budget. Queues are built up as time advances, and hence, expenditures caused by waiting patients increase. By year 7, more money will have been spent for people on waiting lists than for actual stent placements.

Base Case: Treatment Group Results

Table 9 presents the estimated base case long-term cost and QALYs for each of the 4 patient subgroups (assuming unlimited capacities). Results are presented for each treatment group (*bms* and *des*).

The treatment groups are no longer independent in the case of limited capacities. Treatment group results differ depending on the considered scenario because of different queue lengths. The results for the subgroups in the scenarios are displayed in Tables 3 and 4.

DISCUSSION

Traditional decision-analytic models for cost-effectiveness analysis do not account for capacities. With the analysis of *des* and *bms*, the present study illustrates the impact of a limited number of daily stented patients. In fact, 2 of 4 base case tradeoff scenarios prove to be dominated. Although the limit is arbitrary, the study demonstrates the potential effects of limited capacities. If capacity limits are ignored, the model provides wrong messages to decision makers with respect to the absolute outcomes and the relative cost-effectiveness results.

Table 6 Utilization of Hospital Units

	Utilization (average number of patients treated/used beds per day)							
	Base Case: No Capacity Limits				Max. 36 Stented Patients per Day			
Scenario	DBDD	DBDB	BBDB	BBBB	DBDD	DBDB	BBDB	BBBB
Clinical Unit								
Cardiostenting	41.95	41.96	42.49	42.78	35.99	35.99	35.99	35.99
ICU - Cardio	19.71	19.71	19.96	20.10	16.91	16.91	16.91	16.91
IPC - Cardio	143.70	143.71	145.51	146.49	123.29	123.29	123.27	123.27
Bypass surgery	0.10	0.10	0.17	0.22	0.07	0.07	0.12	0.16
ICU - BP	0.39	0.40	0.70	0.92	0.29	0.30	0.50	0.66
IPC - BP	1.06	1.08	1.88	2.47	0.79	0.81	1.35	1.77

Table 7 Annual Budgetary Impact of Scenario BBBB

	Annual Expenditure BBBB (Mio EUR)							
	Base Case: No Capacity Limits				Max. 36 Stented Patients per Day			
Year	Stenting[a]	CABG[a]	Delay	Total Cost	Stenting[a]	CABG[a]	Delay	Total Cost
1	71.51	0.34	0.00	71.85	62.10	0.24	4.20	66.55
2	74.75	1.78	0.00	76.54	62.55	1.28	14.57	78.40
3	74.70	2.16	0.00	76.86	62.55	1.54	25.66	89.75
4	74.76	2.20	0.00	76.95	62.55	1.53	36.75	100.84
5	74.66	2.18	0.00	76.83	62.55	1.55	47.89	111.99
6	74.73	2.17	0.00	76.90	62.55	1.58	58.99	123.13
7	74.73	2.13	0.00	76.86	62.55	1.54	70.08	134.17

a. Including intensive care unit and in-patient care.

Table 8 Annual Budgetary Impact of Scenario DBDD

	Annual Expenditure DBDD (Mio EUR)							
	Base Case: No Capacity Limits				Max. 36 Stented Patients per Day			
Year	Stenting[a]	CABG[a]	Delay	Total Cost	Stenting[a]	CABG[a]	Delay	Total Cost
1	77.13	0.15	0.00	77.29	67.57	0.11	4.02	71.69
2	79.63	0.74	0.00	80.37	68.03	0.56	13.48	82.07
3	79.56	0.93	0.00	80.49	68.04	0.71	23.48	92.23
4	79.62	0.96	0.00	80.57	68.03	0.69	33.50	102.23
5	79.56	0.93	0.00	80.49	68.04	0.71	43.57	112.31
6	79.57	0.91	0.00	80.47	68.04	0.68	53.58	122.30
7	79.58	0.95	0.00	80.52	68.04	0.70	63.59	132.32

a. Including intensive care unit and in-patient care.

In our model, we have not included monetary resource limitations explicitly. However, such limits are directly related to capacity constraints because annual expenditures are, amongst others, determined by the number of interventions and their cost.

However, the indicated small differences in the QALYs in our study are comparable to the results of Bowen and others[19] Their study is also based on the CARDIACCESS registry data. Therefore, the marginal differences could be the result of methodological difficulties of the QALY.[27]

Cost-effectiveness results in the base case show comparable results like Bowen and others[19] In their systematic review of published literature studies,

Table 9 Subgroups, Revascularization, Base Case Cost, and Quality-of-Life Utility Values

		Total Cost[a] (base case / EUR)			QALY (base case)			
		BMS	DES	Delta	BMS	DES	Delta	ICER[b]
Nondiabetes								
(S1)	Long or narrow[c]	5379	5807	428	0.86286	0.86312	0.00025	1,699,382
(S2)	Short and wide[d]	5054	5804	750	0.86314	0.86312	–0.00002	Dominated
Diabetes								
(S3)	Long or narrow	5797	5913	116	0.86255	0.86303	0.00048	240,757
(S4)	Short and wide	5083	5784	701	0.86311	0.86313	0.00002	28,697,050

a. Average cost per patient including repeated revascularization.
b. Incremental cost-effectiveness ratio (Cost DES–Cost BMS)/(QALY BMS–QALY DES).
c. Long lesion or narrow vessel.
d. Short lesion or wide vessel.

Hill and others summarize that *des* is more cost effective for higher risk groups. They have found a great disparity between studies with a variety of outcomes and a range of ICERs. They have built a model that uses average waiting times for PCI and CABG to explore the impact of limiting the PCI wait to 13 weeks on cost-effectiveness. They have discovered that this target wait of 13 weeks modestly increases all estimated ICERs but that this is not sufficient to cause any of them to exceed a level of 30,000 per gained QALY. The comparison of our results with other economic studies that account for average waiting times is difficult because we use a simplified treatment model but account for patient interdependencies in dynamic queues. In addition, most published economic studies have used clinical trial data, and they are based on different follow-up treatment assumptions.[17–19] However, the empirical results of our example should only illustrate our improved modeling approach without adding another study on drug-eluting stents.

Utilization is valuable additional information to identify demand, oversupply, or undersupply. Based on these results, resources/capacities can be planned, and reallocation can be tested and optimized for the evaluated treatment alternatives. In our example, the information gathered about the amount spent for waiting patients can be used to consider an expansion of cardiology units in order to meet the demand for stenting.

The incremental cost-effectiveness ratio (ICER) is a well-accepted approach to assess cost-effectiveness.[28] However, the ability of the ICER to lead to efficient resource allocation has lately been discussed.[29,30] In our study, the question has been raised whether incremental costs, effects, and utilization should be combined to present an ''adjusted'' ICER. We have decided to present the outcomes separately. Further research could provide more insights into these questions.

A limitation of the simulation model is that it begins with an empty idle system. However, the impact of initial conditions on the output is undoubted (e.g., existing waiting lists). Because all scenarios are evaluated with an empty system at the beginning, the absolute outcome values might change for an already populated model. Nevertheless, the comparative results remain valid. Starting with an already populated model would enable the testing of not only the build up of queues but also of the reduction of potentially existing queues due to, for example, more efficient treatment alternatives. This model provides the flexibility to start the simulation based on a populated system. Therefore, a so-called warm-up period is used. Data collection and methodological questions of these issues need to be addressed in further research.

Other limitations in our model are the simplified capacities. We have not taken weekdays and holidays into account. Capacity limits were chosen arbitrarily. Major events, which would lead to prioritized treatment (such as myocardial infarct or thrombosis), have been assumed to be similar in treatment groups. Therefore, we have not included prioritization of capacity usage for specific patients.

Furthermore, there are some important limitations to the clinical input data and to the assumptions underlying this model. First, we have combined clinical data from the CARDIACCESS database of Ontario (Canada) with cost data from the Innsbruck University Hospital (Austria). In addition, the model has only captured single de novo lesions and no multivessel diseases. The placement of different stent types or percutaneous interventions without stenting has not been considered for repeated procedures. Evidence from the ongoing debate of late

stent thrombosis remains unconsidered. However, our aim has been to illustrate important methodological developments in health economic modeling and not to provide an in depth cost-effectiveness study for CAD.

The DES approach for decision-analytic modeling has been discussed recently. For example, the outcomes of a Markov model and a DES have been compared by Karnon.[13] Similar outcomes have been observed because of the characteristics of the underlying data. However, our study illustrates that cost-effectiveness outcome can change when capacities are assumed to be limited. As a major drawback of individual modeling, Barton[1] points out long running time. We cannot confirm this statement with our model. We agree with Caro[11] that ARENA presents the model very transparently. Nevertheless, to familiarize people who are used to Markov models with our DES model might require some time.

Much recent research interest has focused on affordability and cost-effectiveness.[29,31,32] Therefore, Trueman and others suggest a budget impact analysis as a complement to economic evaluation.[4] Furthermore, an ISPOR (International Society for Pharmacoeconomics and Outcome Research) task force has lately been established, and ''Principles of Good Practice for Budgetary Impact Analysis'' was published online in winter 2006.[33] With our example, we have illustrated that a DES is very suitable to satisfy the proposed principles and to accommodate multiple perspectives within one model. Hence, budgetary information has been evaluated with a low effort. Because we have used the same underlying assumptions, this approach has led to consistent outcomes for the different analyses.

The feature of explicitly modeled capacities is supported by software such as ARENA to a broad extent.[15,16,34] Modelers can define prioritization rules (e.g., treatment of patients subject to severity of the disease) and alternative patient pathways in case of temporary shortage of capacities. The software controls the utilization and manages waiting lists subject to predefined characteristics and patient flow.

CONCLUSION

The DES model for alternative stent treatments shows that neglected limited capacities can lead to oversimplified models and wrong cost consequence results. Our conclusion is that capacities must be explicitly included in decision-analytic models if there is evidence for existing or upcoming scarcity that could affect the model outcomes. In any case, utilization estimates for capacities can support decision making in addition to CEA.

Discrete event simulation has proved to be an excellent technique for decision-analytic modeling that accounts for capacities and implied patient interdependencies. It allows multiperspective analysis that covers patient level and health care system outcome. Consistent cost-effectiveness and budgetary outcomes can therefore be derived within one simulation. Finally, this technique supports flexible modeling for real-world settings.

REFERENCES

1. Barton P, Bryan S, Robinson S. Modelling in the economic evaluation of health care: selecting the appropriate approach. J Health Serv Res Policy. 2004;9(2):110–8.

2. Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-effectiveness in Health and Medicine. New York: Oxford University Press; 1996.

3. Drummond MF, O'Brien B, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes. Oxford: Oxford University Press; 2004.

4. Trueman P, Drummond M, Hutton J. Developing guidance for budget impact analysis. Pharmacoeconomics. 2001;19(6): 609–21.

5. Adang E, Voordijk L, van der Wilt GJ, Ament A. Cost-effectiveness analysis in relation to budgetary constraints and reallocative restrictions. Health Policy. 2005;74(2):146–56.

6. Willcox S, Seddon M, Dunn S, Edwards RT, Pearse J, Tu JV. Measuring and reducing waiting times: a cross-national comparison of strategies. Health Aff (Millwood). 2007;26(4):1078–87.

7. Canadian Institute for Health Information. Waiting for health care in Canada: what we know and what we don't know. Available from: www.cihi.ca

8. Ball P. Introduction to discrete event simulation: 1996. In: Management and Control: Tools in 447 Action. Algarve, Portugal: European Community Copernicus Network; 1996. p 367–76.

9. Jun JB, Jacobson SH, Swisher JR. Application of discrete-event simulation in health care clinics: a survey. J Oper Res Soc. 1999; 50(2):109–23.

10. Cochran JK, Bharti A. Stochastic bed balancing of an obstetrics hospital. Health Care Manag Sci. 2006;9(1):31–45.

11. Caro JJ. Pharmacoeconomic analyses using discrete event simulation. Pharmacoeconomics. 2005;23(4):323–32.

12. Weinstein MC. Recent developments in decision-analytic modelling for economic evaluation. Pharmacoeconomics. 2006; 24(11):1043–53.

13. Karnon J. Alternative decision modelling techniques for the evaluation of health care technologies: Markov processes versus discrete event simulation. Health Econ. 2003;12(10):837–48.

14. Brennan A, Chick SE, Davies R. A taxonomy of model structures for economic evaluation of health technologies. Health Econ. 2006;15(12):1295–310.

15. Banks J, Carson J, Nelson BL, Nicol D. Discrete-Event System Simulation. 3rd ed. Upper Saddle River, NJ: Prentice Hall; 2005.

16. Fishman GS. Discrete-Event Simulation: Modeling, Programming, and Analysis. New York: Springer-Verlag; 2001.

17. Hill R, Bagust A, Bakhai A, et al. Coronary artery stents: a rapid systematic review and economic evaluation. Health Technol Assess. 2004;8(35):1–256.

18. Hill RA, Boland A, Dickson R, et al. Drug-eluting stents: a systematic review and economic evaluation. Health Technol Assess. 2007;11(46):1–242.

19. Bowen J, Hopkins R, He Y, et al. DES report systematic review and cost-effectiveness analysis of drug eluting stents compared to bare metal stents for percutaneous coronary interventions in Ontario. Report no. HTA002-0512. December 2005.

20. Zahn R, Hamm CW, Zeymer U, et al. "Real life" use of sirolimus-eluting coronary stents in Germany: results from the prospective multi-centre German Cypher Registry. Z Kardiol. 2004;93(4):287–94.

21. Hamon M, Petrescu V, Rossi P, et al. Initial and follow-up results of the European Seaquence coronary stent registry. J Interv Cardiol. 2004;17(1):9–15.

22. Williams DO, Kereiakes DJ. Safety and efficacy of drug-eluting stents. Rev Cardiovasc Med. 2005;6 Suppl 1:S22–30.

23. Mühlberger V, Leisch F, Probst P. Reports of the Working Group Interventional Cardiology of the Austrian Society of Cardiology. 2004; Available from http://iik.i-med.ac.at/files/2004/countrysum_04.pdf

24. Mauri L, Hsieh W-h, Massaro JM, Ho KKL, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. N Engl J Med. 2007;356(10):1020–9.

25. Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med. 2001;344(15):1117–24.

26. Accounting System, Innsbruck Medical University Hospital. Unpublished report 10.2005. Innsbruck, Austria.

27. McGregor M. Cost-utility analysis: use QALYs only with great caution. CMAJ. 2003;168(4):433–4.

28. Berger ML, Bingefors K, Hedblom EC, Pashos CL, Torrance GW, ed. Health Care Cost, Quality, and Outcomes: ISPOR Book of Terms. Lawrenceville, NJ: ISPOR; 2003.

29. Birch S, Gafni A. The biggest bang for the buck or bigger bucks for the bang: the fallacy of the cost-effectiveness threshold. J Health Serv Res Policy. 2006;11(1):46–51.

30. Gafni A, Birch S. Incremental cost-effectiveness ratios (ICERs): the silence of the lambda. Soc Sci Med. 2006;62(9):2091–100.

31. Nuijten MJC, Rutten F. Combining a budgetary-impact analysis and a cost-effectiveness analysis using decision-analytic modelling techniques. Pharmacoeconomics. 2002;20(12):855–67.

32. Sendi PP, Briggs AH. Affordability and cost-effectiveness: decision-making on the cost-effectiveness plane. Health Econ. 2001;10(7):675–80.

33. Mauskopf JA, Sullivan SD, Annemans L, et al. Principles of good practice for budget impact analysis: report of the ISPOR task force on good research practices–budget impact analysis. Value Health. 2006;10(5).

34. Kelton WD, Sadowski RP, Sturrock DT. Simulation with Arena. 3rd ed. New York: McGraw-Hill; 2004.