Application of Decisional Models to the Health-Economic Assessment of New Interactive Clinical Software

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***Abstract*—RT3S (Real Time Simulations for Safer vascular Stenting) is a partially EU-funded research project aiming to develop a software tool for supporting physicians during the preplanning of endovascular stenting procedures. The project is expected to improve the way limb-saving, minimally-invasive stenting procedures are currently performed, with positive clinical and economic impact. A hypothetical cohort of patients was modeled and used to simulate the patient's progression through the treatment of Peripheral Artery Disease (PAD). A Markov health state-based model was implemented, based on clinical and economic parameters derived from the literature and clinicians' feedback. The health-economic analysis allowed quantitative estimation of the economic and clinical advantages related to the implementation of the clinical software. A quantitative estimation of the potential health-economic impact was achieved. The model proved to accord well with observed predictions from endovascular experts in the field. It represents an important reference for future assessment of IT-related innovations in the healthcare sector.**

I. Introduction

The application of Information Technology to healthcare is increasingly driving change in the clinical sector, along with the medical industry as a whole [1; 2]. IT – related technologies can be used for the management of electronic clinical records as well as for software specifically developed for assisting physicians during interventions. Moreover, an increasing number of medical devices are incorporating software for performance enhancement. Endovascular procedures (i.e., those clinical procedures involving the usage of catheters and other percutaneous systems) are no exceptions. Endovascular techniques applied to the treatment of Peripheral Arterial Disease (PAD) commonly involve the implant of small metallic coils (stents) inside the native vessel, so to restore the physiological blood flow [3]. The mechanical reliability of such implanted devices is a major concern [4; 5].

RT3S (Real Time Simulations for Safer vascular Stenting) is a scientific project funded within the FP7 Framework programme. The aim of the project is to develop an interactive software tool to be used by physicians during the preplanning of stenting procedures (www.rt3s.eu). In particular, the software allows clinicians preliminary evaluation of the potential outcome of the procedure, investigating a broad range of device designs and locations of the implantation site. The software has the potential to revolutionize the way endovascular procedures are performed, so that stents can be implanted in a safer, more evidence-based way: in other words, RT3S-developed software is expected to consistently impact the endovascular sector, delivering both clinical and economic benefits [6].

It is therefore important to quantitatively estimate the potential improvements that the software suite developed by the project consortium will deliver. Analysis of health-economic impact is an essential component of the initial assessment for introduction of new clinical treatments or procedures [7; 8]. Clinical studies are commonly used for in-depth analysis of the outcomes of the procedure and are often sponsored by national healthcare systems and medical companies [9; 10]. These are usually coupled to costing assessment and expenditure estimates. The current tightening of healthcare budgets in European countries, due to shrinking government spending on healthcare, makes the need for such analyses, more urgent. The typical assessment of a newly-introduced clinical option takes into account both healthcare and cost-related factors [11]. The objective is to identify a sustainable working point in which any increase in costs due to the new procedure is counterbalanced by improvements in patients' quality of life. In the study described below, state-of-the-art tools have been applied to the specific RT3S case; the application of a health-state based Markov decision model is presented. A hypothetical cohort of patients undergoing endovascular treatment of femoral artery occlusions has been considered. The model was used to simulate the progress of a sample of PAD patients through the disease treatment. Clinical parameters and economics figures used to populate the model were taken from the literature and from interviews with experienced endovascular practitioners. The results obtained from the model were used to assess potential outcomes and impacts of the clinical software implementation.

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II. METHODS

A. Model Definition

The health-economic impact analysis was performed through the implementation of a Markov model [12] for the simulation of health and economic indicators of a hypothetical cohort of patients going through peripheral angioplasty and stenting.

The aim was to quantitatively estimate the impact delivered by the software implementation (i.e., the "RT3S scenario"), with respect to the standard, software-free treatment (standard, "baseline scenario").

A hypothetical cohort of patients referred for endovascular treatment of PAD was used as a reference for modeling the clinical and economic outcomes of the patients' treatment through the course of the disease. The reference scenario was defined as the most common treatment strategy for the cohort of patients included in the model. It was chosen to focus on Intermittent Claudication (IC) patients, rather than Critical Limb Ischemic (CLI). This was agreed so to focus on isolated SFA stenosis or occlusion, which more commonly presents as IC, whilst CLI patients are a heterogeneous group with a more variable disease course. Specifically, patients considered in the model were over-60, symptomatic IC subjects needing angioplasty and stenting of the SFA, due to a clinical history of PAD.

The reference treatment strategy encompasses a traditional angioplasty of the diseased artery, followed by stenting. The patients are typically undergoing angioplasty followed by selective stent placement. As discussed below, the decision problem addressed by the model relates to patients treated by means of the implant of one or more stents in the SFA.

The model implemented for the current analysis is shown schematically in figure 1. State 1 represents diseased patients as they are treated with stenting of the SFA due to a history of PAD. All the subjects enter the model at state 1. The other health states of the model correspond to typical health conditions of patients treated for PAD. For each time cycle of the model, a clinical "score" (utility) is assigned to each patient, reflecting the subject's clinical health (1 = healthy; 0 = dead). Utilities and costs associated to each patient, for each of the model time cycles, are then added on and used to quantitatively analyze the treatment scenario efficacy / efficiency [7].

After consulting with endovascular experts and clinicians, the major distinction with regards to the outcome of the subjects was agreed to be the one between "asymptomatic" and "symptomatic" patients. Symptomatic claudicant patients are considered to be those reporting discomfort or pain at rest, or while performing short-distance walking. The use of a pragmatic health state of "symptomatic" rather than a definition based upon walking distance or clinical parameters such as ABPI is more in keeping with clinical practice, where quality of life and therefore the probability of intervention will depend upon many factors such as patient age, mobility, co-morbidities and occupation or leisure activities.

Asymptomatic patients are referred to as "well" in figure 2, where "symptoms" identifies the health state associated to those patients classified as symptomatic or believed to share an equivalent clinical follow-up, during routine examination. Symptomatic patients experience the same decrease in the adjusted quality of life index, even though their progression to the "revision" state is not automatic. As reported in almost every publication on the matter, symptomatic patients are typically treated with additional endovascular procedure (i.e., revision of the first intervention), only when both the patient's reported symptoms, and the clinical state, as revealed by the clinical examination, meet inclusion criteria for re-intervention of the patient's limb to be performed.

It was decided not to run the simulation until all the patients included in the simulation are dead; instead, a shorter time – horizon was considered due to the lack of evidence relating to the long term outcomes of repeat endovascular procedures. A time horizon of 5 years was deemed to be appropriate, being in keeping with clinical views about the known duration of outcomes for such procedures. Death remains the only absorbing state of the model, although not all the patients will be found in that state at the end of the simulation.

As transition probabilities typically found in the literature are commonly expressed as yearly probabilities, these were converted to monthly values so to be compliant to the model 1-month cycle duration. The conversion was performed according to [7]:

$$yearly\ rate = -\frac{\ln(1-Prob_{yearly})}{t} \quad (1)$$

Where $Prob_{yearly}$ stands for yearly probability. The monthly probability can then be computed as:

$$monthly\ probability = 1 - e^{-(\frac{Rate_{yearly}}{months})} \quad (2)$$

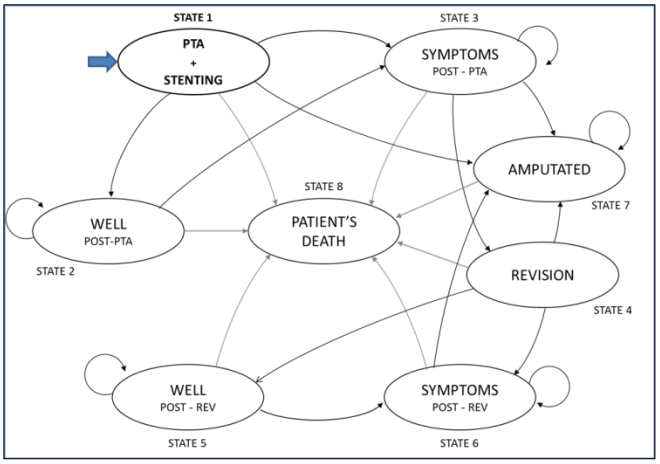

Figure 1. Scheme of the Markov model used; eight different health states have been included in the model. Each time cycle, patients can either transit to a different state or re-cycle internally to their current health state (except the procedures, states 1 and 4, which are assumed to last for a single time cycle). The only absorbing state of the model is represented by the patient's death. Amputation rates, as well as the occurrence of revisions to the previously-performed procedure, are also taken into account.

It was agreed that the most suitable way to perform a quantitative assessment of the RT3S health-economic impact

was to exploit the model defined above and perform a sensitivity analysis on the parameters identified for the definition of the cohort simulation. This gave a clearer idea about the potential influence that a variation of the key variables of the model could have on the clinical and economic outcomes.

Sensitivity analyses such as those aforementioned have been extensively used to study Markov model variability and the dependence of simulations outcomes on each of the driving parameters. They were also applied to our case.

This method of evaluation was deemed to be the most appropriate way to evaluate the impact of the RT3S tools due to the data gaps related to the real implementation of the project software in a clinical setting

B. Parameter Setting

The Markov model implemented was populated using data from the literature and the clinical setting. Endovascular experts were contacted and their feedback collected in order to validate the model clinical parameters. The transition probabilities used in the model to define the treatment patients' history are listed in Table I.

TABLE I
TRANSITION PROBABILITIES OF THE MODEL

INDEX	VALUE	NOTES	SOURCE
Primary procedure outcomes	See Appendix 1	Confirmed by endovascular expert; constant over the model time horizon	[12] and expert feedback
Post-primary procedure	See Appendix 1	Related to the development of new symptoms post procedure.	Various. Mainly [13]; confirmed by endovascular expert
Secondary procedure outcomes	See Appendix 1	Confirmed by endovascular expert; dependent on outcomes of primary procedure	[12] expert feedback on assumptions to be used.
Mortality for claudicants	2.2% yearly mortality rate	Considered independent of the specific evolution of the disease for each patient.	Office for national statistics [14]
Amputation rate	0.7% yearly amputation rate	Values qualitatively confirmed by endovascular expert.	[15]

Economic figures were also obtained from real-life data, as well as from health-economic publications. Ref. Appendix 1 for a full list of all the economic and clinical parameters used within the model implementation.

III. RESULTS

A. Baseline Model Outcomes

The model developed retrieves the health and economics variables from a dedicated database defined according to the data reported above in the document. Fig. 2 shows how the hypothetical cohort of patients is distributed among the health states defined, for each virtual year of the model. There are 60 time cycles in the model, simulating a total duration of 5 years. These correspond to a hypothetical 5 year follow-up of the PAD patients composing the cohort.

As defined, the model provides a picture of the population of patients as the subjects are tracked through the whole duration of the simulation. In this way it is possible to retrieve the distribution of patients with respect to the eight health states defined, from month 1 until month 60. A decrease in the number of asymptomatic ("well post primary") patients is associated with an increase of symptomatic subjects ("symptomatic post-primary"), as well as that of patients going through secondary procedures, amputated, or dead. A full display of the health states evolution through the model time horizon can be found in Table II.

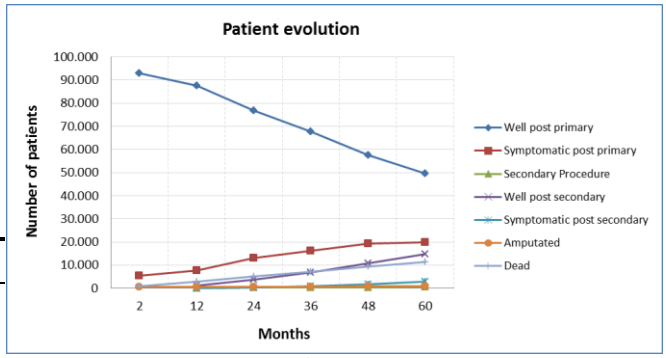

Figure 2. Graph showing results of the model related to patient distribution among health states over the course of the time horizon.

TABLE II[1]
PATIENTS DISTRIBUTION AMONG HEALTH STATES

Health state	Month 1	Month 12	Month 24	Month 36	Month 48	Month 60
Well post primary	SFA stenting	87,4%	76,9%	67,7%	57,5%	49,5%
Symptomatic post primary		7,6%	13,1%	16,1%	19,2%	19,9%
Secondary Procedures (each month)		0,2%	0,3%	0,4%	0,5%	0,5%
Well post secondary		1,2%	3,7%	7,0%	10,7%	14,7%
Symptomatic post secondary		0,1%	0,4%	1,0%	1,9%	3,0%
Amputated		0,5%	0,6%	0,7%	0,9%	1,0%
Dead		2,9%	5,0%	7,2%	9,4%	11,4%

[1]Values might not add up to 100% due to rounding.

B. Comparing the Scenarios Implemented

In the present analysis, the potential benefits RT3S-software could provide were evaluated for the hypothetical clinical scenarios based upon other technologies used in this situation, starting from analysis of the literature. Typical values reported, with regards to potential clinical improvements brought by the introduction of new

interventional technologies (e.g., drug-eluting stents), are in the order of a few percentage point decrease in the rate of occurrence of new symptomatic patients. In particular, [16] found that, overall, the introduction of the new technology might have resulted in a decrease in the yearly rate of patients becoming symptomatic ranging from -7%(-8%) to -3%. These figures were taken as reference and used for running a sensitivity analyses, under the assumption that results obtained from the RT3S software implementation, on the long term, could be comparable to clinical results from the introduction of similar innovation-driven medical device adds-on. The results obtained can then be used to obtain a rough estimate of the potential impact of software such as that under implementation by the RT3S consortium. Figure 3, for example, shows how the key clinical and economic drivers of the cohort of patients analyzed (i.e., the total cost per patient, the total number of secondary procedures, number of amputated patients, etc…) are sensitive to variations in the development of new symptomatic patients. The impact that a PC-aided, better planned stenting procedure could have, in terms of reducing the rate at which new symptoms are developed, is striking, accounting, for instance, for a -4.2% reduction in the total number of secondary procedures performed. Figures related to cost variation are even more significant when one considers that the primary stenting procedure accounts for most of the expenditure per patient, so the saving represents a high proportion of marginal costs related to recurrent symptoms and repeat interventions...

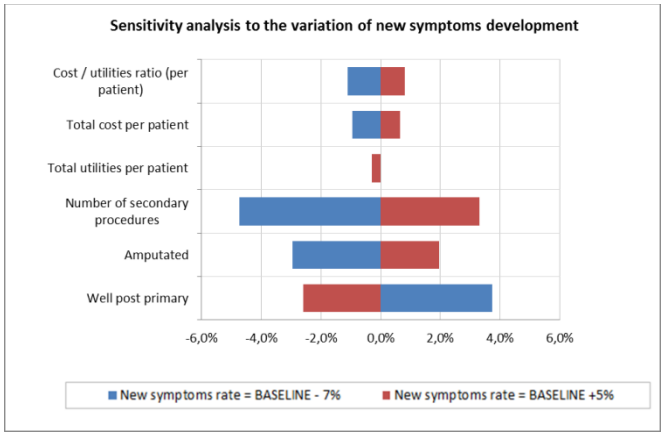

Figure 3. Tornado chart showing how selected health and economic indexes for the model (vertical axis) vary (with respect to their nominal baseline values) when applying a -7% (blue bars) and a +5% (red bars) variation in the rate of asymptomatic patients becoming symptomatic each month of the model horizon.

APPENDIX

TABLE III
COST FIGURES INCLUDED IN THE MODEL

INDEX	VALUE	NOTES	SOURCE
Cost of primary procedure for SFA stenting	3469 €	Values provided by European university hospital and including also pre-operation costs.	Expert feedback / data obtained from the field
Follow-up for symptomatic patients	See table IV	Mainly related to the cost and periodical occurrence of clinical examinations post-procedure.	Expert feedback / data obtained from the field
Follow-up for asymptomatic patients	See table IV		Expert feedback / data obtained from the field
Cost of revision procedures	5588 € (see below in the document)	Values provided by European university hospital and including also pre-operation costs.	Expert feedback / data obtained from the field
Amputation cost	9342 € (see below in the document)	Based on the data found in the literature, this cost was estimated starting from the cost of the stenting procedure	[17]
Follow-up for amputated patients	See table IV		[17]

TABLE IV
POST-PRIMARY AND POST-SECONDARY PROCEDURE FOLLOW-UP

	CLINICAL EVALUATION	COST [€]	EXAMS / YEAR
Asymptomatic patients	CTA	370	1
	US	126	2
	Personnel	40	2
Symptomatic patients	CTA	370	3
	US	126	3
	Personnel	40	3

TABLE V
HEALTH INDEXES (UTILITIES) INCLUDED IN THE MODEL

INDEX	VALUE	NOTES	SOURCE
Patient selected for stenting	0.6	Confirmed by expert opinion	[12]
Asymptomatic patient post-primary procedure	0.82	Confirmed by expert opinion	[12]
Symptomatic patient post-primary procedure	0.7	Confirmed by expert opinion	[12]
Asymptomatic patient post-secondary procedure	0.66	N/A	Expert opinion
Symptomatic patient post-secondary procedure	0.56	N/A	Expert opinion

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