From Decision to Shared-Decision: Introducing Patients' Preferences in Clinical Decision Analysis - A Case Study in Thromboembolic Risk Prevention

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Abstract. In the context of the EU project MobiGuide, the development of a patient-centric decision support system based on clinical guidelines is the main focus. The project is addressed to patients with chronic illnesses, including atrial fibrillation (AF). In this paper we describe a shared-decision model framework to address those situations, described in the guideline, where the lack of hard evidence makes it important for the care provider to share the decision with the patient and/or his relatives. To illustrate this subject we focus on an important subject tackled in the AF guideline: thromboembolic risk prevention. We introduce a utility model and a cost model to collect patient's preferences. On the basis of these preferences and of literature data, a decision model is implemented to compare different therapeutic options. The development of this framework increases the involvement of patients in the process of care focusing on the centrality of individual subjects.

Keywords: Decision Trees, Patient Preferences, QALYs, Atrial Fibrillation.

1 Introduction

Taking into account patients' preferences is nowadays an essential requirement in health decision-making [1,2]. As a matter of fact, patients increasingly want their personal perspectives to be considered in the process of care. Besides genetic-based personalized care, which is another way of viewing personalized medicine, our attention is focused on addressing individual attitudes, considering patient's perception of his health status, personal context, job-related requirements and economic conditions.

Clinical decision analysis refers to the process of exploiting a decision model to evaluate situations that imply the choice between two or more alternatives [3]. Such alternatives might regard for example choosing between two pharmacological treatments, between a surgical intervention and a drug, etc. As a matter of fact, even in an evidence-based setting where directions are summarized into a clinical practice

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guideline (CPG), there might exist situations, highlighted by the guideline itself, where it is important for the care provider to involve the patient in the decision. The process during which the patient and his care provider reach a clinical decision together is known as *shared decision* [4] and its main goal is to take into account both the available scientific evidence and the patient's perception of the consequences of different options [5].

The key point to turn a clinical decision into a shared decision is the introduction of patients' preferences in the analysis. In particular, we introduce a web-based framework that can be used by physicians to first elicit patient preferences and consequently run a decision model, using (also) values directly derived from the patient under observation. The concept of preference in this paper refers to both a patient's perception of the health states he is experiencing or he might experience as a consequence of the therapeutic choice, and to the economic impact such choices might have from his viewpoint. To take into account all this information, we have developed a utility model and a cost model. Such models are coupled to a theoretical decision model framework to solve the decision task. The final decision will thus account for patient-specific parameters, which might be different from population parameters derived from the literature.

The framework was developed in the context of the MobiGuide project (http://www.mobiguide-project.eu/). MobiGuide is a European funded project carried on by a consortium of 13 partners from several countries in Europe (Italy, Israel, The Netherlands, Spain, and Austria). It is aimed at developing a knowledge-based patient guidance system based on computer-interpretable guidelines (CIGs) and designed for the management of chronic illnesses, including Atrial Fibrillation (AF). The main components of the MobiGuide System are a Decision Support System (DSS), devoted to the representation and execution of CIGs, and a Body Area Network (BAN), including a network of sensors and a smartphone, to support telemonitoring of the patient. The data collected by the system are stored in a Patient Health Record (PHR). Among all the challenging objectives of the project, one involves the identification in the CPG of those recommendations where the lack of hard evidence requires a shared decision. Once those recommendations are identified, a suitable framework is set up to allow the physician managing the shared decision process. To illustrate the proposed framework, in this paper we focus on the AF Guideline [6] and in particular on a recommendation regarding the therapeutic management of antithrombotic risk for patients belonging to a specific risk category. In the following we will first introduce some theoretical bases and we will then present the proposed models and the implemented interfaces for thromboembolic risk prevention in AF.

2 Methods

Building the shared-decision framework involved using different methodologies and technologies for (i) dealing with the collection of patients' preferences and (ii) developing and running decision-theoretic models. The first issue included the design of a utility model and a cost model, and resulted into an interface that requires an active participation of the patient and the physician (or better the psychologist) to collect the most relevant patient-specific variables. The second issue is related to computational formalisms for decision making: even though other formalisms, such as influence diagrams or decision tables are available, we chose to use the decision tree formalism, because it allows easier knowledge elicitation from the doctors. Once fed with parameters suitably elicited from the patient and/or taken from the literature, the model automatically runs relying on a specific commercial software tool.

Moreover, we rely on a relational database to store both the tree characteristics necessary for the user interaction (i.e. the represented health states and some numerical parameters) and the tree results. Results are stored together with data about the interaction session, such as the identity of patient and physicians participating to the encounter, and their opinion on the usefulness of such interaction. All these data will be used for a future evaluation of the framework.

2.1 Collecting Patient's Preferences – Values, Utilities and Costs

The ultimate goal of a decision process is to select one out of several *decision options*, which are the possible treatment alternatives, object of the analysis. During the course of the analyzed disease, a patient may experience a set of different *health states*. Starting from a specific decision option and moving through the health states, the model leads to the determination of a specific *outcome*. The probability of occurrence of each health state and of transition between states is highly dependent on the treatment option selected. Intuitively, different subjects may perceive differently the quality of life related to health states. Moreover, one patient might consider the economic impact of a specific treatment more relevant for the choice with respect to another subject. For this reason, it is very important to tailor the decision process on the single patient, taking into account this variety of aspects. This moves the perspective of the clinical decision process towards a shared decision model, where the physician, during a face-to-face encounter with the patient, elicits his preferences related to different future scenarios.

From the observations above, it is clear that it is important to measure the quality of life the patient associates to specific conditions. Quality-Adjusted Life Years (QALYs) [7] is one of the most known and used indicators combining in a single value the life expectancy and the subjective perception of the health states considering physical, mental and social aspects. Given a time span T divided into n time intervals t_i, i=1 .. n, each one spent in a particular health state s_i, QALYs are defined as $\Sigma_{i=1,n}$ $(t_i u_i)$, where u_i is the *utility coefficient* (UC) for s_i. To define QALYs, we thus need to characterize each health state by a UC, ranging from 0 (death) to 1 (perfect health). Literature and web provide UCs for several health states (e.g. [8,9]). Such coefficients can be also conveniently elicited from the single patient, according to the physician/psychologist judgment about the patient's capability of understanding the elicitation methods that we will briefly describe below. Note that UCs are related to health states, so if different decision options lead to the same states, UCs are only elicited once. In addition, periodical reassessment of UCs may be necessary, as patients' perception of health states may change in time.

The Utility Model

The MobiGuide framework for shared decision is provided with the three classical methods for eliciting values and utilities: rating scale (RS), standard gamble (SG) and time trade-off (TTO). In the RS method, the patient is asked to rate all the states represented in the decision model on a scale ranging for example from 0 to 100. While not suitable for QALY calculation [10], these values, rescaled to 0-1, represent a patient-specific ranking of the states, useful for further consistency check.

The TTO method was specifically developed for use in health care [11]. To elicit utility for a specific health state, the subject is asked to compare two different scenarios: 1) to stay in that specific state for a time t (computed as the life expectancy of an individual with that chronic condition) until death or 2) to live an healthy life for a time $x<t$. During elicitation, time x is varied until the patient is indifferent between the two alternatives and the UC for the examined state is computed as the ratio x/t.

In the SG approach [12], the subject is offered two alternatives. Alternative 1 is a treatment that, if successful, might enable the patient to live in perfect health for the rest of his life. Such treatment, though, carries a certain risk of death r (think for example to a surgical intervention). Alternative 2 is that the subject lives all his life in the specific chronic state under analysis. During the face-to-face encounter the value for r is varied until the patient is indifferent between the two alternatives, and the UC is computed as 1-r.

The Cost Model

Besides quantifying the patient's perception of different health states, it is also useful to involve him in the quantification of a cost model. In this model we consider the so-called "out-of-pocket" costs, which are the costs directly burdening the patient and causing an economic impact on his activities. While in the utility model the patient gives his opinion about the health states, for the cost model the patient is asked to provide information needed for quantifying the costs related to the clinical paths that are generated as a consequence of the different decision options. We have considered three categories of costs: (a) Costs related to the visits the patient has to undergo during his treatment; (b) Costs related to domiciliary care the patient may be in need of and (c) Home adaptation costs. As regards point (a), the value for the costs of the visits directly imputed to a patient depends on the position of the patient with respect to the national healthcare service, as some patients in Italy can have the visits costs totally covered. Besides the specific visits costs, we also took into account non-healthcare resources that are:

- The cost of the travel to the medical center where the visit is performed: this is a patient-specific value that depends on the distance the patient has to travel, the transportation facility, etc.;
- The cost of the meals that the patient might have to pay for during the visit day;
- Patient's productivity loss, in case the patient is self-employed or retired;
- The cost related to an assistant possibly needed by the patient to reach the visit location: the model takes into account the cost for his/her travel and meals. In addition, it is possible to quantify the assistant's time in terms of productivity loss or salary.

The inclusion of costs related to domiciliary care is based on the fact that, after some specific events (such as for example a stroke) the patient might need domiciliary assistance. This is quantified by the salary given to the assistant in the case he/she is a professional employed by the patient. In case the assistant is a member of the patient's family, the cost is quantified in terms of productivity loss.

Assistance to the patient after a specific health event may also imply some home adaptation to manage the impairments the patients may experience after the event. These costs are assessed based on the results presented in [13], where the authors present an analysis of the overall social costs of stroke in Italy in terms of direct costs and productivity losses.

Since several cost components are related to the specific patient's context, the quantification holds as long as the context remains the same.

2.2 The Decision Models

As mentioned, in MobiGuide we have used Decision Trees (DT) [3]. DTs are one of the most used formalisms in the analysis of the logical structure and timing of clinical decision. They connect the alternative decision options to their expected effects and the final outcomes of each possible scenario. This is done following a formalism based on the combination of nodes and branches.

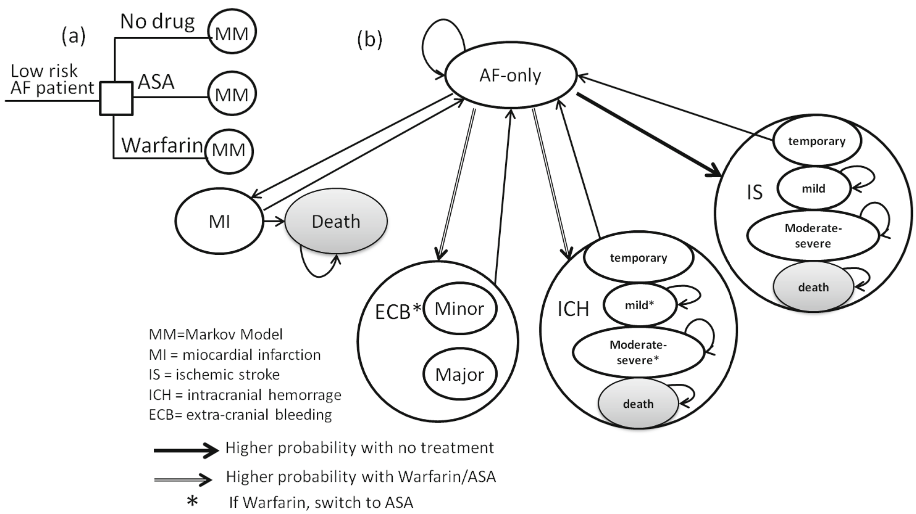


Fig. 1. (a) The initial part of the decision tree. Nodes labeled with "MM" are the starting point of the (simplified) Markov process represented in (b), where different line types indicate a trade-off between decreasing the risk of stroke and decreasing the risk of bleeding.

Figure 1 shows a scratch of a DT structure. It refers to the DT used for choosing the antithrombotic prophylaxis (note that, while the utility and the cost models presented so far are generic, i.e. they can be used for any type of shared decision, for every specific decision problem a specific decision-theoretic model must be implemented).

In a DT there are decision nodes, chance nodes and terminal nodes. Decision nodes are the starting points for the alternative options the study is considering. In the example shown in Figure 1, the decision node is the one labeled as "low risk AF patient", i.e. a patient eligible for that DT. Chance nodes symbolize an uncertain event, with a finite number of possible outcomes, which must be exhaustive and mutually exclusive. Each outcome is associated with its occurrence probability. A terminal node identifies the end of a path. It is associated with a *payoff* value, characteristic of that path, i.e. an outcome that the decision maker wants to maximize (e.g. QALYs) or minimize (e.g. cost). If events recur over time, and transitions among states must be represented, a Markov Model (MM) [14] is combined into the DT.

Running or solving a decision tree means calculating the expected values of the payoffs for all the possible decision options, by weighting the values at the end of the paths with their probability of occurrence. After a tree is run, the decision node shows, for each strategy, these expected values. The solution suggested by the model is the one optimizing the payoff. In case of multiple, competing payoffs, the results of the tree cannot be used as direct suggestions, but they just represent quantitative values useful to reason about. For example, suppose Option 1 gives better results in terms of QALYs than Option 2, which instead gives less out-of-pocket costs. In this case, the final choice could depend on the financial status of the patient.

In our framework, DTs are initially fed with probabilities and UCs found in the literature, and can be used as they are, when physicians judge that the patient is not able to provide additional, more personalized information. For the most frequent case, though, when the patient is able to provide his own preferences and context details, DTs can be personalized with patient's preferences and patient's profile features collected and stored through the above-illustrated generic models. As a result, decision-options are ranked on a personalized basis.

The MobiGuide trees are built using the commercial tool TreeAge (TreeAge Software Inc, www.treeage.com). Moreover, we have developed a web interface using the TreeAge Pro Interactive Tool, to make the models available also to the end users less familiar with the modeling technique. The physician will thus be able to browse probabilities, utilities, and costs, and to adjust values according to his knowledge if needed. Then he will run the decision tree and see the results.

3 Results

In this section we present the implementation of the proposed framework for shared decisions. To illustrate the specific developed decision model, we consider a recommendation included in the AF guideline on the management of thromboembolic risk:

For primary prevention of thromboembolism in patients with nonvalvular AF who have just 1 of the following validated risk factors, ***antithrombotic therapy with either aspirin or a vitamin K antagonist is reasonable****, based upon an assessment of the risk of bleeding complications, ability to safely sustain adjusted chronic anticoagulation,* *and* ***patient preferences****: age greater than or equal to 75 y (especially in female patients), hypertension, HF, impaired LV function, or diabetes mellitus*

This recommendation involves first of all the choice whether to treat or not, and in case of treatment, the choice between two drug options, namely acetyl salicylic acid (ASA) or oral anticoagulant therapy (OAT) with vitamin K antagonists such as warfarin. Thus, this is a case where the CPG recommendation itself suggests considering patient's preferences in the decision process.

3.1 The Decision Tree for Managing Antithrombotic Risk

In this paper we used an adapted version of a DT combined with MMs to compare the clinical pathways of an AF patient who may undergo the aforementioned treatment strategies for stroke prevention, or who takes no drug therapy at all [15]. During the Markov process, individuals move among health states that recur over time according to transition probabilities, which also may vary on time.

As shown in the diagram presented in Figure 1 (b), the health states implemented in the model are: AF-only, ischemic stroke (IS, which can be temporary, mild, moderate-severe, fatal), intracranial hemorrhage (ICH, which also can be temporary, mild, moderate-severe, fatal), myocardial infarction (MI), extra-cranial bleeding (minor and major), combined events and death. As outcomes, we have considered life years, QALYs, and costs. Figure 1 (b) shows a simplified representation of the implemented MM: the patient enters the process in the AF-only state. During the course of the disease, he can experience events such as MI, IS, ICH, and extra cranial bleedings. Temporary IS or ICH are events that cause only a transient disability and after which the patient recovers and goes back to the AF-only state. A patient experiencing more severe events, such as a mild/moderate-severe IS or ICH, is often subject to permanent impairment. The occurrence of these events depends on the different transition probabilities that are related both to the treatment and to the patient's risk for stroke, calculated on the basis of $CHADS_2$ score [16]. The administration of warfarin or ASA decreases the probability of occurrence of IS, but increases the probability of ICH and extra-cranial bleedings. On the other hand, the choice of not prescribing any therapy increases the probability of IS while limiting the occurrence of ICH and extra-cranial bleedings. If, while undergoing therapy with warfarin, a patient in the AF-only state experiences an ICH or a major extra-cranial bleeding, OAT therapy is interrupted and replaced by ASA, to decrease the probability of further bleedings.

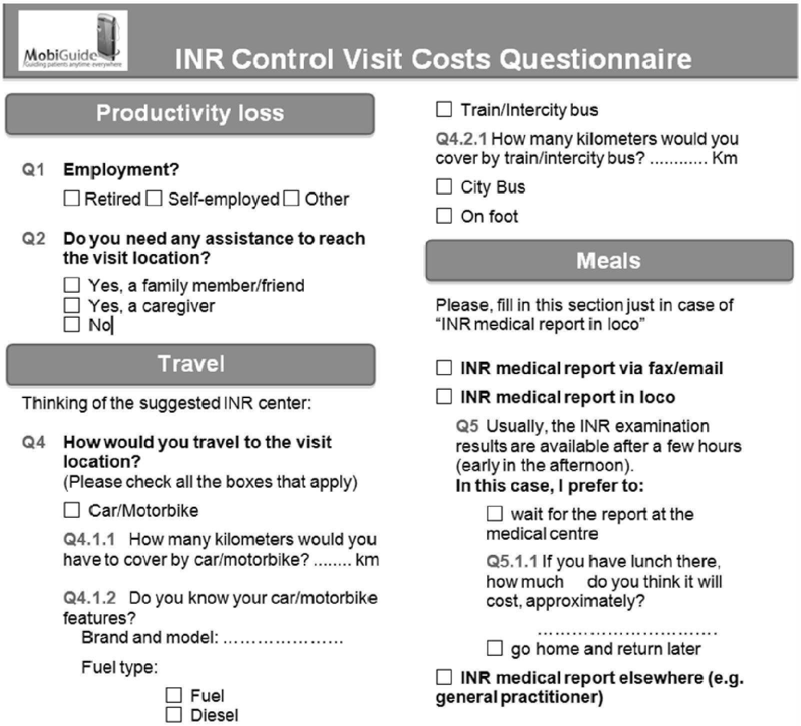
In order to make the decision analysis a *shared* decision, we have implemented a user interface to allow the doctor to elicit from the patient his UCs for each health state, as described in the following section.

3.2 The Utility Coefficients and Costs Elicitation Interface

The utility model is implemented through an interface to be used during face-to-face encounters between patients and physicians. Through this interface, the physician is able to interact with the patient to elicit values and UCs using all the methods presented in Section 2.1. The interface has been designed to give the patient the best possible understanding of the questions he has to answer. Consider for example the interface for the SG method. As previously explained, with this method the patient is asked to reason about a risky procedure potentially able to heal him. Since showing only the numeric value of the risk is not very intuitive for the patient, we have added a graphical representation that, for each value of the risk, turns into red a random set of yellow smileys corresponding to this percentage.

In the developed framework, we give the physician the possibility of evaluating UCs with both the described methods (SG and TTO). In this case, the final UC is calculated as the average value, which can also be a weighted average, according to the physician's confidence on one or the other method for that specific patient.

Besides utilities, costs are the other aspect that tailors the framework to the specific patient. On the basis of the cost model, a questionnaire has been designed to ask the patient the necessary personal data for cost calculation. The part of the questionnaire related to the cost for anticoagulant treatment monitoring is reported in Figure 2.


MobiGuide
INR Control Visit Costs Questionnaire

Productivity loss

Q1 **Employment?**
☐ Retired ☐ Self-employed ☐ Other

Q2 **Do you need any assistance to reach the visit location?**
☐ Yes, a family member/friend
☐ Yes, a caregiver
☐ No

Travel

Thinking of the suggested INR center:

Q4 **How would you travel to the visit location?**
(Please check all the boxes that apply)
☐ Car/Motorbike
Q4.1.1 How many kilometers would you have to cover by car/motorbike? .... km
Q4.1.2 Do you know your car/motorbike features?
Brand and model: ………………….
Fuel type:
☐ Fuel
☐ Diesel

☐ Train/Intercity bus
Q4.2.1 How many kilometers would you cover by train/intercity bus? .... Km
☐ City Bus
☐ On foot

Meals

Please, fill in this section just in case of "INR medical report in loco"

☐ **INR medical report via fax/email**
☐ **INR medical report in loco**
Q5 Usually, the INR examination results are available after a few hours (early in the afternoon).
In this case, I prefer to:
☐ wait for the report at the medical centre
Q5.1.1 If you have lunch there, how much do you think it will cost, approximately?
……………………………
☐ go home and return later
☐ **INR medical report elsewhere (e.g. general practitioner)**

Fig. 2. A portion of the questionnaire for valuing the cost model. INR is a laboratory test required to monitor anticoagulant therapy effects, and it must be done in general every 15 days.

3.3 Showing Decision Analysis Results

Results are presented in the interface as shown in Figure 3. The expected values for all the defined payoffs for each decision option are listed. The most common case is that the most expensive option is also the most effective from the health outcomes point of view. As well, it may happen that an option shows higher life expectancy but lower QALY than another one. These are the situations that require the patient to reason with his doctor about the best choice.

Expected Values			
Payoff	Warfarin	ASA	No therapy
Life Years	22 years 3 months	22 years 1 months	21 years 1 months
QALYs	15 years 12 months	15 years 10 months	15 years 0 months
Patient Costs	10154 €	3179 €	3041 €

Fig. 3. Example of the results provided by running the decision tree for a specific patient: expected values of the payoffs (rows) for the possible therapeutic options (columns)

4 Conclusions and Future Developments

In this paper we have presented the design and implementation choices underlying the definition of a shared decision framework to be used by physicians and patients to introduce patient preferences and run a patient-specific clinical decision model. We believe that such a framework might be of help to improve patients' empowerment, increasing their involvement in the process of care focusing on the centrality of the individual instead of considering populations or cohorts.

The novelty of our work relies in the possibility of fully personalizing and deploying decision trees on the web. This represents a possible future exploitation of the MobiGuide project results, putting the basis for a repository of web-interactive tools for medical decision making.

The very next step will include system usability tests. As a matter of fact, the current interface is the result of a set of iterations performed together with physicians involved in MobiGuide. Further usability tests with external users are thus required to check additional system characteristics.

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