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Guiding Patients Anytime Everywhere

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## 1. Executive Summary

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Deliverable D2.1 is about the description of the Shared Decision Model Framework developed for WP2 Task 2.3 of Mobiguide. The work done for task 2.3 is related to task 5.1 in WP5, which is described in the deliverable D5.1. D5.1 reports on the technical details of the design and implementation of the tools for shared patient-care provider decisions.

D2.1 is focused on the rationale for the development of such model, on the theoretical framework underlying the selected type of model and on the technical details of the solution implemented during the first year of the project. In particular, we will address the importance of considering patient preferences in the decision process and we will show the methods that can be used to perform such task. As a matter of fact, within MobiGuide, the personalization of the care delivery is not based on genetic distinction (that is another option to implement “personalized medicine”), but rather addressing patient’s attitudes, job-related requirements, free time exploitation, economic conditions, etc. We will introduce the main features of decision trees, a category of decision models particularly useful for healthcare analyses and we will explain how these models can be implemented using a specific software tool. We will report on a specific example of decision tree that has already been implemented for Mobiguide, and for which two web interfaces have been developed during this year.

This deliverable is organized as follows: Section 2 describes the main goals of the Decision Model Framework with respect to the Mobiguide project.

In Section 3, we present a background on decision analysis and decision trees. In particular, we will describe the main features of decision tree models applied to clinical decision support. We will introduce the theory of decision trees and describe the main concepts behind the decision tree construction, namely probabilities, pay-offs and utilities. Regarding utilities, the last part of Section 3 will be focused on the methods through which a physician can elicit utility coefficients and values from the patients. We

will describe the three most used methods, which are: the Rating Scale, the Time trade-off, and the Standard Gamble.

Section 4 introduces the tools we have selected to build and run our decision models. In particular, we will describe two products of the TreeAge suite: TreeAge Pro and its companion tool TreeAge Pro Interactive.

Section 5 will describe the part of the framework we have implemented during the first year of the project. We will provide a detailed description, including all the references to the literature, of the decision tree model we developed for evaluating the therapeutic choice between acetyl salicylic acid and oral anticoagulant therapy to prevent thromboembolism. The remaining of the section is devoted to the description of the tools we have implemented. First, we will introduce the web interface for running the decision tree and for changing selected variables according to the physician's and patient's preferences. Then, we will describe the utility coefficient elicitation web interface, focusing on the specific solutions adopted to present the three methods to the patient. Finally, we will introduce the cost model needed to run cost effectiveness analysis in the decision tree, in order to give the patient also an idea of the economical burden implied by each of the possible options.

In Section 6, we will discuss open issues and future developments we will address in the next years of the project. Section 7 contains some concluding remarks.

The result of the Shared Decision module will often be the decision, based on a combination of the patient's preferences and the current evidence, to follow one of several options for a protocol or a guideline, or to branch into some option within an existing guideline that is being applied to the patient. Support to the actual administration of the recommended protocol will then be handled by the Mobiguide guideline-application engine (a part of WP5).

## 2. Introduction

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Decision trees have been used for a long time in the medical decision making area. They have been mainly exploited for economic evaluation of healthcare programs, namely cost-effectiveness and cost-utility analyses. Pharmaco-economics is one of the applications. However, most of the applications have been targeted at the population (or sub-population) level, and are used to inform decision makers about healthcare policies. Unlike these common approaches, the target of the MobiGuide project's application of decision analysis is a specific patient. The goal is to integrate evidence-based and preference-based medicine, paying particular attention to avoid any conflict with scientific evidence. This may be accomplished by developing decision models for those situations, highlighted by the guidelines themselves, where lack of hard evidence makes it very important to *share* the decision with the patients and/or their relatives. Thus, our efforts have been (and will be) devoted to: (a) creation of decision trees related to those uncertain situations and (b) designing and developing a user interface to be used during the patient-physician face-to-face encounters. Through this interface, we collect as much data as possible that can lead to a personalization of the decision models. In fact, when building the trees, we quantify them with *default* probabilities and utilities, gathered from the literature, in such a way that, in the absence of more specific values, the tree may be used by the physician to reason about the general problem. But at the moment of face-to-face encounters, we want to assist the care providers in personalizing the patient's specific decision tree. Thus, the interface assists the physician, or the psychologist, in interviewing patients and eliciting their preferences. More precisely, concerning Task 2.3 of WP2, preferences are quantified through values and utility coefficients that a patient assigns to every possible health state that is included in the decision tree.

## 3. Background

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### 3.1. Decision trees for medical decision making

In the medical domain, the accuracy of the measurements, the comparison between different techniques and the diagnostic tests execution criteria, the so-called normal values determination, prognostic predictions, risk stratification, follow-up criteria, etc., are factors that require evaluation and are a source of variability in clinical practice.

Decision analysis is a process that allows expressing and formalizing the problems of clinical decision in a structured way, in order to choose the optimal strategy among those possible in the interests of a patient or of a population of patients. It is characterized by being explicit because it analyzes and breaks down the decision problem into its logical components. These components will be individually examined and then reassembled in a systematic way. It is also a quantitative analysis, because the available scientific evidence has to be checked about the assumptions made and specific values have to be assigned to different outcomes.

Finally, decision analysis is prescriptive, and not descriptive, in the sense that it is a formal decision-making framework (with available computational tools) and not a cognitive model of medical thought.

There are basically two computational formalisms for implementing decision analysis: influence diagrams (ID) [2] and decision trees (DT) [22]. IDs are known as a very intuitive and compact tool for presentation to domain experts and even patients, because they display dependency and independency relations very clearly, by the existence or nonexistence of dependency arcs between the represented variables. However, we decided to use DTs because (i) their expressive power is equivalent to IDs, and (ii) the temporal order of decisions of IDs is much less clear and intuitive than that of DTs. A detailed description of DTs is given in the next section.

### 3.1.1. Decision Trees

Decision trees (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 effect and the final outcomes of each possible scenario. This is done following a precise formalism given by the combination of nodes and branches.

In the construction of a decision tree, the following conventions are used:

1. Each branch of the tree is associated with a node, located at the end of the branch. Each node represents a certain type of event: a decision, an uncertain event or a final result. They are called respectively decision nodes, chance nodes and terminal nodes.
2. A *decision node* is represented by a square. Decision nodes are the starting points for the alternatives options that the study must consider. The branch ending in the initial decision node is labeled with some context information about the target of the analysis (i.e. male population aged 45-55).
3. A *chance node*, represented by a circle, symbolizes 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. Thus, the total sum of the probabilities of the outcomes starting from the same node must be equal to 1.
4. A *terminal node*, usually represented by a triangle or a diamond, is used to identify the end of a path. These nodes are associated with a payoff value, characteristic of that path. A payoff is an outcome that the decision maker wants to maximize (e.g. years of life) or minimize (e.g. cost). All nodes at the end of a path must be terminal nodes.
5. Time flows from left to right. The trees have a horizontal structure, ordered from left to right, in which each subsequent set of branches is the result of an event or a decision. Thanks to the temporal sequence of events, decisions are made taking into account the knowledge gained up to that moment.

*Running* or *solving* a decision tree refers to 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 will be the one optimizing the utility of 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 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.

#### 3.1.1.1. Probabilities

Traditional decision tree structures do not allow representing transitions between health states that can occur over time, especially when a long time horizon has to be evaluated. To overcome this situation, Markov models (MM) [19] can be integrated into the tree model. MM are mathematical models allowing to follow a cohort of individuals over time and to determine how the intervention affects costs and benefits. MM are models used to describe systems evolving in a probabilistic manner and in which the state of the system at step  $i + 1$  depends only on the state at step  $i$ .

In decision analysis, discrete MM are used to describe the evolution of the health state of a cohort of patients. These states must be mutually exclusive. The transitions from one state to another are referred to a particular time range, called the Markov cycle.

A set of initial probabilities specifies the distribution of the cohort in the possible states at the beginning of the process. A transition probability matrix specifies the transitions between states in the following cycles.

In the graphical representation of a standard MM, each state is denoted by a circle. Transitions are represented by directed edges. An edge that returns to the same state from which it originates indicates that it is possible to stay in the same state for more than one cycle. The numbers above each edge identify the probability to move from one state to another; and the probabilities outgoing from each node must sum up to 1.

### 3.1.1.2. The QALY Payoff

A very important aspect of decision analysis is the evaluation of the impact the different decision options have on the quality of life. There are several methods to quantify this aspect, that are based on reliable estimates.

*Quality-Adjusted Life Years (QALYs)* [18], also referred to as *Quality Adjusted Life Expectancy (QALEs)* [17] are one of the most known and used indicator that combines duration and quality of life. In fact QALYs allow the analyst to combine into a single value the life expectancy and a qualitative description of the health states considering physical, mental and social aspects.

To define QALYs each health state is characterized by a coefficient ranging from 0 (death) to 1 (perfect health). This coefficient is defined as *utility coefficient*. More formally, given a time span  $T$  divided into  $n$  time intervals  $t_i$ ,  $i=1, \dots, n$  each spent in a particular health state  $s_i$ , QALYs are defined as  $\sum_{i=1,n} (t_i \times u_i)$ , where  $u_i$  is the utility coefficient for  $s_i$ .

### 3.1.1.3. Utilities

Individual preferences for health outcomes can be measured through the use of three methods, which will be described in Section 3.1.2.

In addition to these methods, two alternatives can be considered. The first one exploits past efforts whose results are reported in literature: there are tables of utility coefficients for several specific diseases [4], derived by interviewing a large number of people.

The second one, which is very attractive and is being widely used, is to bypass the measurement task by using one of the pre-scored multi-attribute health status classification systems that exist.

Traditional utility theory was extended to cover multi-attribute outcomes [7] with one additional assumption to the three axioms of ordinality/transitivity, continuity and independence/invariance (see section 3.1.2.3). This assumption is that the utility independence among the attributes can be represented by at least first-order utility

independence, and perhaps by stronger utility independence (mutual utility independence, additive independence).

First-order utility independence implies that there is no interaction between preferences among levels on any one attribute and the fixed levels for the other attributes. Mutual utility independence is a stronger assumption. It requires that there is no interaction between preferences for levels on some attributes and the fixed levels for other attributes.

This characteristic must hold for all possible subsets of attributes. Additive utility independence implies that there is no interaction for preferences among attributes at all. That is, the overall preference depends only on the individual levels of the attributes and not on the way in which the levels of the different attributes are combined.

The three independence assumptions lead to three different multi-attribute functions. The simplest assumption, first-order utility independence, leads to the most complex mathematical function, the multi-linear function. The second possible assumption, mutual utility independence, leads to the multiplicative function; and the strongest assumption, additive independence, leads to the simplest function, the additive function.

In order to accomplish the project goals on personalization, we choose to follow a strategy that, starting from the literature coefficients, provides an opportunity to the caregiver (physician and/or psychologist) to elicit the patient's personal utility coefficients for each of the health states.

### **3.1.2. Utility coefficient elicitation methods**

The three most widely used techniques to directly measure the preferences of individuals for health outcomes are:

- The Rating scale and its variants (not suitable for QALY calculation, but useful for ranking states);
- The Time trade-off.
- The Standard gamble.

In the next paragraphs, a brief description of each method is given.

### 3.1.2.1. The Rating Scale

The simplest approach to measure preferences is to ask subjects first to rank health outcomes from the most preferred to the least preferred, and second, to place the outcomes on a scale such that the intervals or spacing between placements correspond to the differences in preference as perceived by the subject. That is, outcomes that are almost equally desirable would be placed close together while outcomes that are very different in desirability would be placed far apart.

There are a number of variations on the rating scale approach. The scale can have numbers (e.g. 0-100), categories, or just consist of a 10 cm line on a page. The different variations often have different names. A Rating Scale usually refers to a scale of numbers, often 0-100. Category rating is the variation that consists of a small number of categories, often 10, that the subject has to assume to be equally spaced. Visual analogue scaling consists of a line on a page, often 10 cm in length, with clearly defined endpoints and with or without other marks along the line. Sometimes several techniques are combined. The subject is asked to select the best health state, which presumably would be “normal health life” and the worst state, which may be “death”. He or she is then asked to locate the other states on the rating scale relative to each other such that the distances between the locations are proportional to his or her preference differences.

For measuring the utilities, the rating scale is always scaled between 0 at one end and 1 at the other end. If “death” is judged to be the worst state and placed at the 0 end of the rating scale, the preference value for each of the other states is simply the scale value of its placement. If “death” is not judged to be the worst health state but is placed at some intermediate point on the scale, say  $d$ , the preference values for the other states are given by the formula  $(x-d)/(1-d)$ , where  $x$  is the scale placement of the health state.

Rating scale methods are highly familiar to most people from a variety of everyday experiences in which they are asked to provide information on an array of experiences using this technique. However, an empirical work has shown that people have difficulty

directly assigning a number to feelings about health states [11] and this method does not provide utility coefficients for QALYs calculation but only values useful for ranking the considered health states.

### 3.1.2.2. Time trade-off

The time trade-off (TTO) method was specifically developed for use in health care [20]. To elicit utility for a state  $i$ , the subject is offered two alternatives:

- a) State  $i$  for a time  $t$  (life expectancy of an individual with that chronic condition) followed by death;
- b) Healthy for a time  $x < t$  followed by death.

Time  $x$  is varied until the respondent is indifferent between the two alternatives. At that point the required preference score (utility) for state  $i$  is calculated as  $x/t$ .

### 3.1.2.3. Standard Gamble

The standard gamble is the classical method for measuring cardinal preferences. It is based on the fundamental axioms of utility theory, first presented in [21]. They are the following:

- Preferences exist and are transitive: for any pair of risky prospects  $y_1$  and  $y_2$  either  $y_1$  is preferred to  $y_2$ ,  $y_2$  is preferred to  $y_1$  or the individual is indifferent between  $y_1$  and  $y_2$ . In addition, for any three risky prospects,  $y_1$ ,  $y_2$  and  $y_3$ , if  $y_1$  is preferred to  $y_2$ , and  $y_2$  is preferred to  $y_3$ , then  $y_1$  is preferred to  $y_3$ ; similarly, if  $y_1$  is indifferent to  $y_2$ , and  $y_2$  is indifferent to  $y_3$ , then  $y_1$  is indifferent to  $y_3$ .
- Independence: an individual should be indifferent between a two-stage risky prospect and its probabilistically equivalent one-stage counterpart derived using the ordinary laws of probability. For example, consider two risky prospects  $y_1$  and  $y_2$ , where  $y_1$  is made up of outcome  $x_1$  with probability  $p_1$  and outcome  $x_2$  with probability  $(1-p_1)$ , indicated symbolically as  $y_1 = \{p_1, x_1, x_2\}$  and  $y_2 = \{p_2, x_1, x_2\}$ . This axiom implies that an individual would be indifferent between the two-

stage risky prospect  $\{p, y_1, y_2\}$  and its probabilistically equivalent one-stage counterpart  $\{pp_1, (1-p)p_2, x_1, x_2\}$ .

- Continuity of preferences: if there are three outcomes such that  $x_1$  is preferred to  $x_2$ , which is preferred to  $x_3$ , there is some probability  $p$  at which the individual is indifferent between outcome  $x_2$  with certainty (often referred to as the "*certain equivalent*") or receiving the risky prospect made up of outcome  $x_1$  with probability  $p$  and outcome  $x_3$  with probability  $(1-p)$ .

In the standard gamble approach, the subject is offered two alternatives. Alternative 1 is a treatment with two possible outcomes: either the patient is returned to perfect health and lives for an additional  $t$  years (probability  $p$ ), or the patient dies immediately (probability  $1-p$ ). Alternative 2 has the certain outcome of chronic state  $i$  for life ( $t$  years). Probability  $p$  is varied until the respondent is indifferent between the two alternatives. At this point, the required preference score for state  $i$  for  $t$  is simply  $p$ . In this case  $p$  is measured on a utility scale where perfect health for  $t$  years is 1 and immediate death is 0.

## 4. TreeAge: A tool to build decision trees

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For implementing Decision Tree models, we chose to exploit the commercial suite TreeAge (TreeAge Software Inc, [www.treeage.com](http://www.treeage.com)). Three main factors are at the basis of this choice. First of all, this is the only tool that embeds a module completely dedicated to health care (TreeAge Pro Healthcare). This module provides some very useful analysis tools, such as Markov processing, comparative effectiveness and cost-effectiveness analysis. Thanks to the presence of this module and to an extensive use of these tools, UNIPV had already gained great expertise in the use of the TreeAge suite, which has already brought to the development of other models, such as the ones described in [5, 9, 10, 13, 14, 10]. The availability of this expertise is the second motivation for our choice. The last reason underlying the selection of this software package relies on the availability of the TreeAge Pro Interactive module, which allows to create web interfaces to make the models available to remote users. This is one of the goals of Task 2.3 of Mobiguide, as stated in the DoW.

In the next two Sections we will give some more details about TreeAge Pro and TreeAge Pro Interactive.

### 4.1. TreeAge Pro

TreeAge Pro is a sophisticated yet highly user-friendly software package that facilitates decision making in complexity and uncertainty scenarios. TreeAge Pro provides a systematic methodology and a framework that breaks the problem into its components, identifying available decision options and their associated uncertainties.

Based on this methodology, TreeAge Pro allows implementing a model in the form of either a decision tree or an influence diagram. The developed model is graphically displayed on screen and the user can interact with it.

Unlike other software packages, TreeAge Pro imposes no constraints on the size or content of models, there are no built-in limitations on the number or location of variables, nodes, decision options, chance events, etc.

Through the models developed using TreeAge Pro, it is possible to envision the strategies that maximize the likelihood of success while minimizing unacceptable levels of risk.

The sensitivity analysis module allows identifying those uncertainties which, in light of the potential range of outcomes, are (or are not) critical to the decision at hand. Sensitivity analysis is used to test the sensitivity of a proposed course of action to changes in the projected value of one or more variables. If only a single variable is being tested the analysis is known as a 1-way sensitivity analysis. When the analysis is performed at a decision node, the expected value of each decision option will be plotted as a function of the range of values assigned to the selected variable.

Analytical features include: 1-, 2- and 3-way sensitivity analyses, tornado diagrams, threshold analysis, single and comparative probability distribution graphs, Bayes' revision, Monte Carlo simulation and multi-attribute analysis. Markov processes and cost-effectiveness analysis are available through the TreeAge Pro Healthcare module.

In addition to being able to display models graphically as both influence diagrams and decision trees, TreeAge Pro offers a wealth of supporting text and graphical reports.

#### **4.2. TreeAge Pro Interactive**

TreeAge Pro Interactive is an ActiveX/COM component (DLL) for use with Windows tools. It allows creating and distributing powerful decision analysis applications. With TreeAge Pro Interactive, TreeAge Pro's powerful decision analysis features can be used to create an automated application to put sophisticated analytical tools into the hands of health care professionals and researchers.

In more detail, TreeAge Pro Interactive allows:

- embedding any decision tree initially created in TreeAge Pro into an application, in order to integrate the model with websites, databases and custom applications and creating interactive applications around models;
- customizing the interface to target a specific audience;
- distributing the application through a web site or an organization's intranet;
- enabling remote users to access the model, make changes to selected values (such as probabilities and costs) and perform analyses, regardless of decision analytic expertise or familiarity with TreeAge Pro.

## 5. Implementation

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### 5.1. The decision tree for managing antithrombotic risk

A decision tree combined with Markov Models (MM) has been implemented to compare the clinical pathways of an AF patient who may undergo to two different treatment strategies for stroke prevention, namely warfarin (oral anticoagulant therapy) and acetyl salicylic acid (ASA), or who takes no therapy at all.

During the Markov process, individuals move among health states according to transition probabilities that are defined for each state. Since each state is characterised by one or more attributes, according to the number of outcomes (i.e. a quality of life coefficient, resource consumption, etc.), by running the model over a number of cycles, the expected values of outcomes (i.e. QALYs, costs, etc) of the process associated with the different strategies can be estimated.

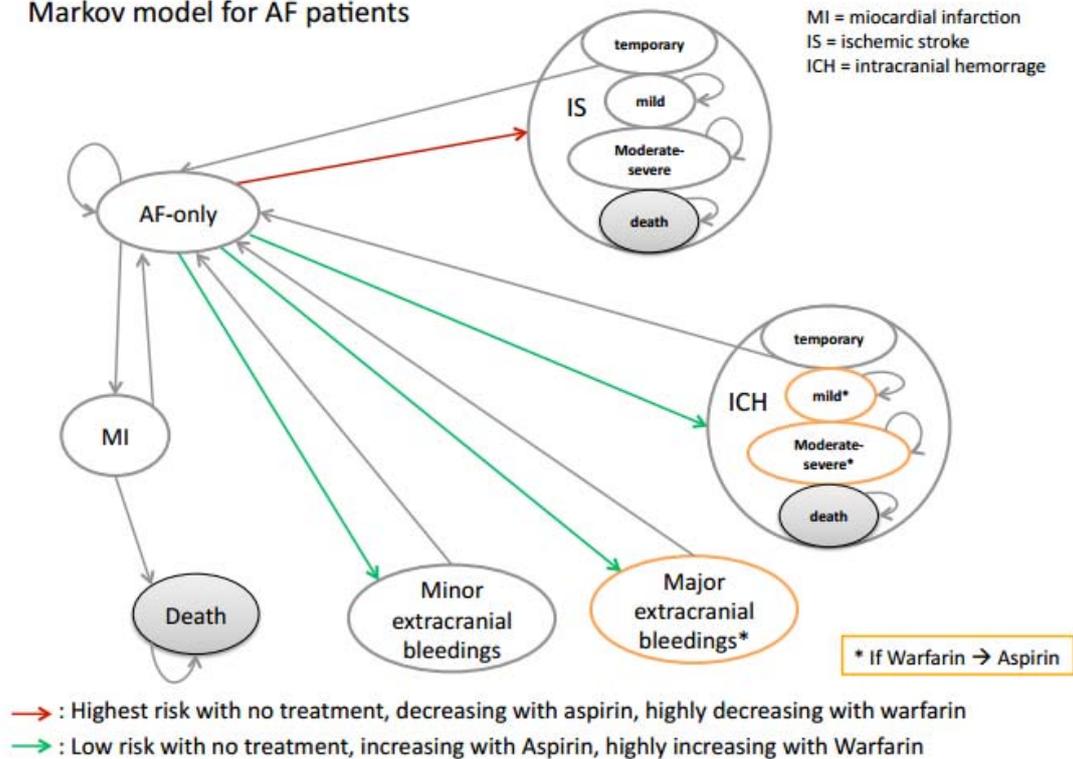
The health states in the implemented model are:

- AF only (i.e. relatively healthy apart from AF)
- ischemic stroke (IS), that can be temporary, mild, moderate-severe, fatal
- intracranial hemorrhage (ICH), that also can be temporary, mild, moderate-severe, fatal)
- myocardial infarction
- extracranial bleedings (minor and major)
- combined events and
- death.

In the model, a 3-months Markov cycle length and a lifetime horizon were chosen. Quality-adjusted life years (QALYs), that are one of the considered outcomes, can be discounted (e.g. at 3.5% annually) or not.

The tree has been developed and analysed by using the TreeAge Software. A simplified representation of the Markov process is reported in Figure 1.

Markov model for AF patients



**Figure 1- Simplified representation of the model. Different arrow colors indicate that there is a trade-off between decreasing the risk of stroke (risk with warfarin < risk with ASA < risk with no-therapy) and decreasing the risk of bleeding (risks going in the opposite way).**

The patient, whose age is read from the PHR, or entered manually by the doctor, enters the Markov process in the AF-only state. Then he can experience events such as MI, IS, ICH, etc., according to the different transition probabilities that depend both on treatment and on patient's risk for stroke, calculated on the basis of CHADS<sub>2</sub> score and stratified into 3 levels: CHADS<sub>2</sub>=0-1, CHADS<sub>2</sub>=2 and CHADS<sub>2</sub>=3-6.

Warfarin and ASA therapies decrease the probability of IS occurrence but increase the probability of ICH and extracranial bleedings; on the other hand, no therapy increases the probability of experiencing an IS but decreases the occurrence of ICH and extracranial bleedings.

Temporary IS or ICH are events that cause only a temporary disability and let the patient recover and go back to the AF-only state. A patient experiencing a more severe event, as mild/moderate-severe IS or mild/moderate-severe ICH, acquires a certain level of permanent impairment that results in quality of life worsening.

If a patient in the AF-only state is on warfarin therapy, and he experiences a mild/moderate-severe ICH or a major extracranial bleeding, it is supposed that he/she interrupts warfarin therapy that is replaced by ASA, to decrease the probability of bleedings.

An AF patient that has been affected by IS or ICH has 2.6 fold higher risk of experiencing new events in comparison with “healthy” AF patients.

In case of MI, if death occurs, it is supposed happening within 3 months from the event, otherwise the patient recovers back to AF-only state.

Events like temporary IS, temporary ICH and extracranial bleedings (minor and major) lead to temporary decrements in quality of life (disutilities), that have been estimated from the literature, while the utility coefficients of the states related to the permanent disabilities are elicited from the specific patient.

## **5.2. The web interface for the decision tree**

In the first year of the Mobiguide Project, we started implementing a web interface for the decision tree model related to prevention of thromboembolic risk. In the following, we will introduce this interface.

The DT interface can be launched from the caregiver interface when a recommendation suggesting a shared decision is available. In Figure 2, the recommendation detail page is shown.



The screenshot shows the MobiGuide web interface. At the top left is the MobiGuide logo with the tagline "Guiding patients anytime everywhere". To the right, the user is identified as "User: john.smith" with a "logout" link, and the patient as "Patient: Rossi, Mario (AF guideline active)" with a "deselect" link. Below this is a navigation bar with tabs for "Patient Profile", "Clinical History", "AF Diagnoses", "AF Episodes", "AF Symptoms", "Oral Anticoagulant Therapy", and "Other Therapies". The main content area has a breadcrumb trail: "Home > Advice List". The current page title is "R8.1.4-1 Preventing Thromboembolism - Recommendation 1 - Class IIa (A)". A blue information box states: "You selected a recommendation belonging to another patient, so the current patient selected is now Rossi, Mario". The recommendation text is: "For primary prevention of thromboembolism in patients with nonvalvular AF who have just 1 of the following validated risk factors - age greater than or equal to 75 y (especially in female patients), hypertension, HF, impaired LV function, or diabetes mellitus-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. Please consider using Decision Tree "Aspirin vs Anticoagulant"". Patient information includes "Patient: Rossi, Mario", "Advice Date: 2012-02-02 00:00:00", and "Action: Prescribe OAC". There are checkboxes for "Already Read" (checked), "Executed" (checked), "Hide" (unchecked), and "Dt Used" (checked). At the bottom, there is an "Update" button and a set of buttons for decision tree exploitation: "Oral Anticoagulant Therapy", "Aspirin", "Decision Tree Explanation", "Utility Coefficients Elicitation Interface", and "Run Decision Tree".

**Figure 2 - The page of the recommendation for thromboembolism prevention: note in particular the bottom part of the page with links for the decision tree exploitation.**

This page reports the recommendation title, together with the class and the level of evidence of the recommendation, the complete recommendation text and the information related to the patient who has become eligible for the recommendation and the advice date. In addition, where a shared decision is available, a set of buttons is made available at the bottom of the page:



Use comma as decimal separator

Treatment-Specific Variables			
	Warfarin	ASA	No therapy
Proportion of mild ICH	0,088	0,163	0,163
Proportion of moderate/severe ICH	0,318	0,428	0,428
Proportion of temporary ICH	0,078	0,151	0,151
3-months probability of minor bleedings	0,048667	0,018455	0
Proportion of major bleedings that are ICH	0,19	0,219	0,19
Proportion of mild stroke	0,425	0,41	0,41
Proportion of moderate/severe stroke	0,402	0,3	0,3
Proportion of temporary stroke	0,091	0,11	0,11
Tree Defaults			
Patient's age			48
Annual discount rate			0,035
Relative risk for major bleedings on aspirin with respect to warfarin			0,642
Relative risk for stroke on aspirin with respect to warfarin			1,83
Relative risk for major bleedings with respect to warfarin after treatment switch			0,5056
Relative risk for stroke with respect to warfarin after treatment switch			1,83
Need for caregiver visit (0=no 1=yes)			1
3-months cost for domiciliary caregiver			0
Cost for cardiology visit			4,5
Cost for caregiver' time for one visit			0
Cost for ECG visit			3
Cost for INR control visit			7,5
Cost for meals for one visit (one person)			10
Cost for patient' productivity loss for one visit			0
Cost for travel for one visit (one person)			8
Probability of death after MI			0,12
Proportion of mild ICH after treatment switch			0,163
Proportion of moderate/severe ICH after treatment switch			0,428
Proportion of temporary ICH after treatment switch			0,151
Sex (1= male, 0=female)			0
3-months probability of minor bleedings after treatment switch			0,018455
Relative risk for major bleedings on no therapy with respect to warfarin			0,42
Relative risk for stroke on no therapy with respect to warfarin			2,37
N 3-months INR visits			3,475
N 3-months control visit AF			1
Proportion of major bleedings that are ICH after treatment switch			0,179
Relative risk for new events after ICH or IS			2,6
Proportion of mild stroke after treatment switch			0,41
Proportion of moderate/severe stroke after treatment switch			0,3
Proportion of temporary stroke after treatment switch			0,11
Utility coeff. for mild stroke			0,85
Utility coeff. for moderate/severe stroke			0,27

**Figure 4 - The page presenting the values for probabilities and utilities used for the decision tree quantification. These values, in general gathered from the literature, can be changed by the user**

Clicking on the Run Decision Tree button, the page shown in Figure 3 appears. This is the home page of the DT web interface. This page reports a brief introduction to decision analysis and a description of the specific decision tree, which is the one introduced in Section 5.1. From this page it is possible either to return to the model explanation material or to proceed with the running of the decision tree. If this second option is selected, the user is directed to the page shown in Figure 4.

This page lists all the variables specified in the definition of the DT model that the user is allowed to modify if needed.

The DT manages different type of variables:

- Demographic variables (age and sex): the patient-specific values are taken from the PHR
- Probabilities, either specified explicitly (e.g. probability of death after MI) or through variables that can be used for probability computation (e.g. relative risks and proportions)
- Patient's costs related to travel, meals, productivity loss, etc. (see Section 5.4 for details on the cost model).

When the page is first accessed, default values are shown. These values are taken from the literature, as detailed in Section 5.1. The caregiver might decide to modify the value for these parameters in different situations:

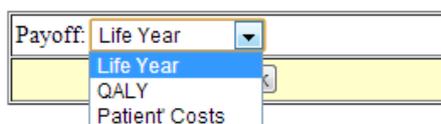
- retrieve the utility coefficients elicited through the specific interface (see section 5.3): this can be done using the Update Values button (bottom right of the page)
- manually editing the textboxes to change costs and/or probability values depending on the specific case.

The page is divided into two sections: in the top part of the form, parameters whose value depends on the specific treatment are listed (in this case we have the three options warfarin, ASA and no therapy). In the bottom part of the form all the other parameters, whose value is independent of the treatment, are shown.

This page allows to proceed with several options (accessible through the buttons at the bottom of the page): to reset to default values, to run the tree (RollBack), to run a Monte Carlo simulation (Simulation), to perform 1-way sensitivity analysis (Sensitivity) and to load elicited utility coefficients.

### Rollback Analysis

Use this form to specify the payoffs.



Payoff:	Life Year	▼
	Life Year	
	QALY	
	Patient Costs	

**Figure 5 - Payoff selection. The graphical results will refer to this choice**

To perform the RollBack analysis, the user has to select the payoff. In the current version of the implementation, this is done in a separate page, as shown in Figure 5. Up to now, the available options are: Life Years, QALYs and Patient's costs. At the moment the analysis is run on all the available payoffs and the payoff selection is used for a graphical representation of the executed tree.

Once the rollback is completed, the results page is displayed. The results are shown both in a synthetic tabular format for all the available payoffs (see Figure 6) and with a graphical representation of the decision tree (Figure 7), but only for the selected payoff.

Tabular Output for the selected payoff

Expected Values			
Payoff	Warfarin	ASA	No therapy
QALYs	15 years 12 months	15 years 10 months	15 years 0 months

Tabular output for all payoffs

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 €
<input type="button" value="Submit"/>			

Tabular Output

Time spent in each Markov state			
Markov states	Warfarin	ASA	No therapy
well	12 years 7 months	13 years 10 months	13 years 5 months
well-therapy switch	5 years 6 months	3 years 3 months	2 years 5 months
well total	18 years 1 months	17 years 1 months	15 years 10 months
stroke temporary	2 months 9 days	4 months 11 days	4 months 18 days
stroke temporary-therapy switch	2 months 6 days	1 months 12 days	1 months 2 days
stroke temporary total	4 months 15 days	5 months 22 days	5 months 20 days
mild ischemic stroke	5 months 25 days	1 years	1 years 2 months
mild ischemic stroke-therapy switch	8 months 1 days	5 months 29 days	5 months 5 days
mild ischemic stroke total	1 years 2 months	1 years 6 months	1 years 8 months
moderate to severe ischemic stroke	7 months 5 days	1 years 3 months	1 years 8 months
moderate to severe ischemic stroke-therapy switch	1 years 1 months	10 months 11 days	10 months 11 days
moderate to severe ischemic stroke total	1 years 8 months	2 years 2 months	2 years 6 months
mild ICH-therapy switch	1 months 18 days	1 months 12 days	0 months 28 days
moderate to severe ICH-therapy switch	9 months 24 days	8 months 3 days	5 months 30 days
stroke & ICH	7 days	7 days	6 days

**Figure 6 - The page showing the results of the decision tree: expected values of the three payoffs (first two tables), and time spent in the different health states according to the strategy (last table)**

The top table in Figure 6 shows the expected values for the payoff selected in the analysis (the one also represented in graphical format), while the second one shows a summary of the expected values for all the available payoffs. Clicking on the Submit button under the second table allows storing the analysis results. Currently, this is done by storing a DT exploitation ID to identify a single run of the model together with the

expected values for each payoff and for each option. In addition, for every exploitation, information about patient, caregiver, exploitation date and decision tree used (in the case many are available) are stored. The third table reports, for each decision option, the time spent in each health state according to the Markov model. This is particularly useful to understand the results obtained when considering Life Years and QALYs as payoff. For example, in Figure 6 the analysis for ASA resulted in a huge difference between the expected life years (22 years and 1 month) and the QALYs (15 years and 10 months). To understand this difference, it is worth considering the information reported in the Markov state table: the expected value for life years is given by the sum of the time spent in each Markov state for ASA, while the QALYs value is given by the sum of the time spent in each state weighted by the corresponding specific utility coefficient. The result obtained for the QALYs payoff reflects the fact that different time intervals are spent in the various health states for the different treatment strategies.

The solution presented by the model represents in any case only just a suggestion for the physician and the patient, who will then take the final decision (that might potentially be different from the suggestion). Such decision will then be recorded in the Mobiguide System via the Caregiver Interface (this component is described in D5.1). For example, Figure 6 shows that the solution optimizing the QALYs is to prescribe Warfarin (QALYs = 16 years). If the caregiver, together with the patient, decides to follow this suggestion, to complete the decision process, he will go to the therapy management page in the Caregiver Interface and prescribe a suitable dosage.

Figure 7a presents a synthetic view of the decision tree, showing the three decision options, all leading to a Markov node implementing the model described in Figure 1. We have expanded the ASA branch to show the starting of the Markov model: after a Markov node, all the possible states must be displayed (here we show only a subset just for simplicity), with their initial probabilities. In our case a patient starts the process in the AF-only state (probability=1). Then, all the transitions from a state to another one must be represented.

Figure 7b shows a snapshot of the decision tree after execution with TreeAgePro. At the decision node the best result in terms of the selected payoff (in this example QALYs) is

shown. The best option (the one leading to the best result) is highlighted by a coloured branch (in our example Warfarin).

Given the high complexity of the model, the graphical representation is not very easy to understand and to navigate. For these reasons, we are considering the possibility of removing it from the results page, leaving only the tabular representation and a link to a downloadable version of the graph.

When selecting the Sensitivity option, a page to select the variable on which to perform the analysis is displayed. It is possible to select any variable, including utilities and costs. When the variable is selected, the user must edit some analysis settings (Figure 8). The form reported shows: the name of the variable selected for the 1-way sensitivity analysis, the range of variation of the variable (Low and High fields), the number of intervals of discretization of the variable range and the target payoff. The values shown when the page is opened are the default values of the tree and, when the user updates them, a control is present to check the validity of the modified values. Clicking on the button at the bottom of the page the sensitivity analysis is launched, and, when it is completed, the page on Figure 9 is displayed. First, a summary of the most relevant results is provided. In the following of the page, the results are presented both in a graphical and in a tabular way. The graphical representation presents a plot of the behavior of the payoff for the available decision options as a function of the values of the variable chosen for the analysis. Such variable is discretized into the selected number of intervals, that are also visualized on the plot. The tabular output presents the same information synthesized in a table. The sensitivity analysis is useful to determine whether there is a threshold value for the variable that causes the inversion of the result: in Figure 9 we can see that, for values of the *relative risk for major bleedings* less than 0.33, the best option becomes ASA instead of Warfarin. The current version of the implementation includes only univariate sensitivity analysis. In the following releases we will introduce also multivariate analysis.

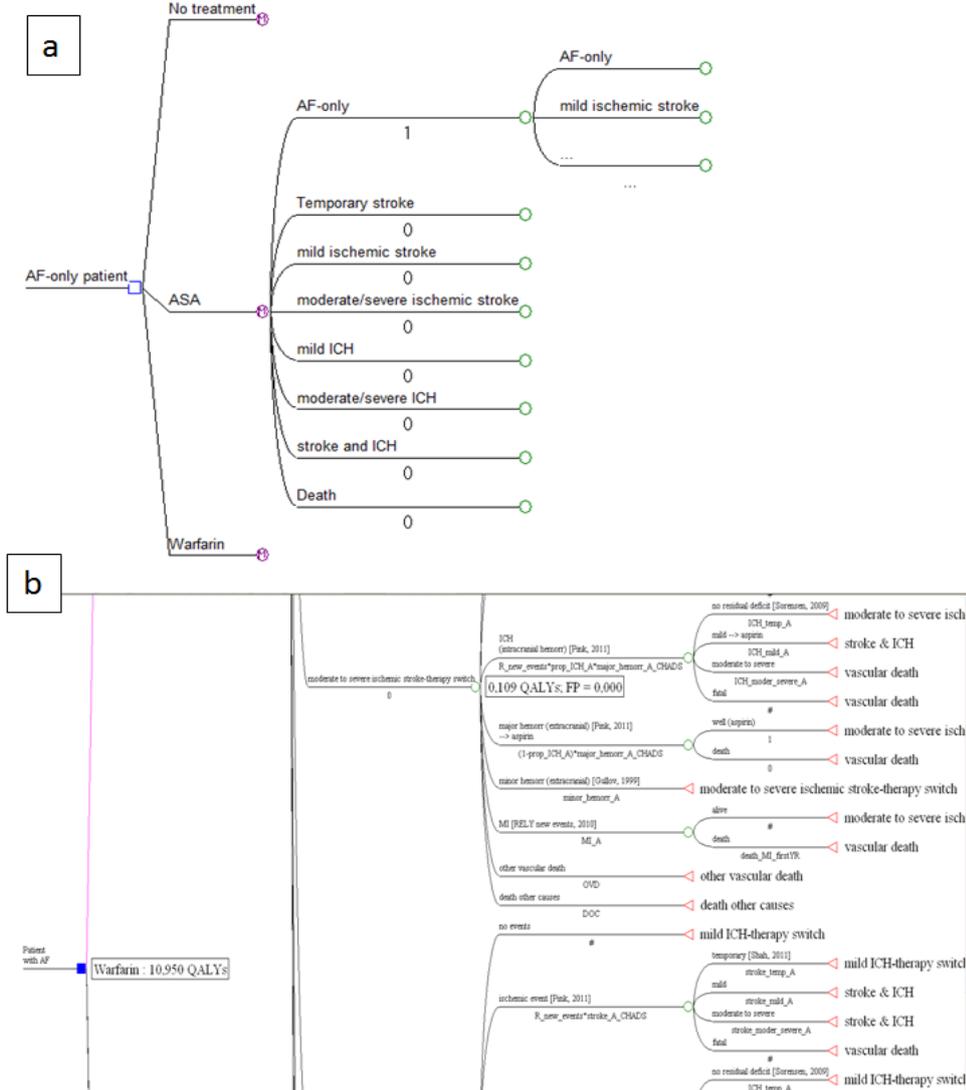


Figure 7 – (a) A simplified view of the decision tree. (b) A portion of the decision tree as represented by the tool TreeAge Pro after execution.

## Sensitivity Analysis

Use this form to specify the sensitivity analysis range and intervals for the selected variable.

<b>Relative risk for major bleedings with respect to warfarin after treatment switch</b>	
Variable:	<b>Treatment</b>
Low:	<input type="text" value="0.1"/>
High:	<input type="text" value="1"/>
Intervals:	<input type="text" value="4"/>
Payoff:	<input type="text" value="Life Year"/> ▼
<input type="button" value="Sensitivity Analysis"/>	

Figure 8 - The interface for performing sensitivity analysis

### Sensitivity Analysis Results

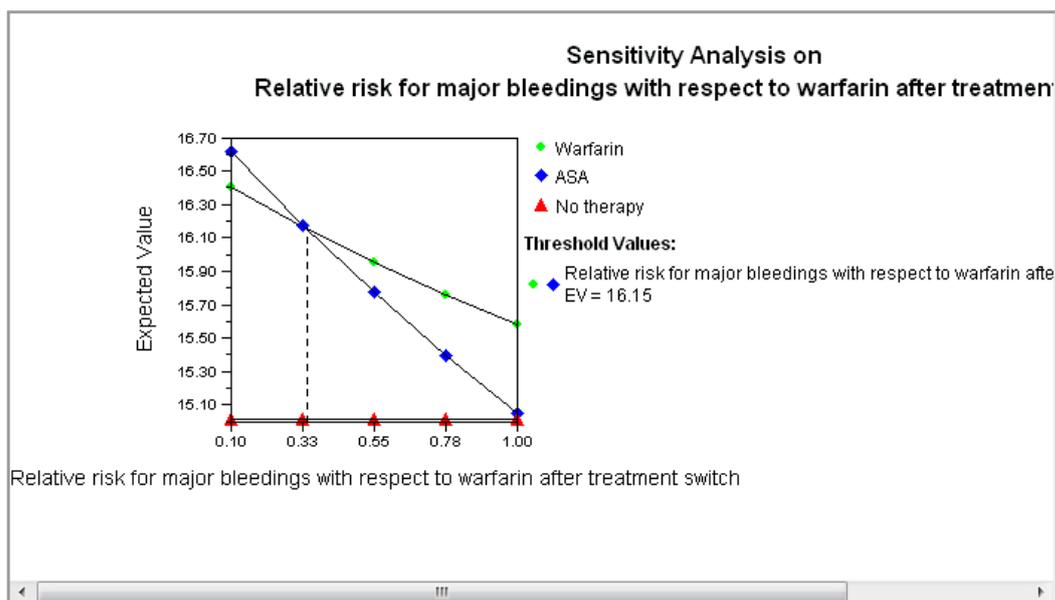
Here is the sensitivity analysis generated using the value range you specified:

**Summary:**

1 effectiveness threshold(s) found:

Between 0.1 and 0.3381, ASA has the highest effectiveness. Between 0.3381 and 1, Warfarin has the highest effectiveness.

**Graphical output:**



**Tabular output:**

Relative risk for major bleedings with respect to warfarin after treatment switch	Warfarin	ASA	No therapy
0.1	16.40520952	16.619990965	15.014838758
0.325	16.166219788	16.177331727	15.014838758
0.55	15.950831886	15.771176734	15.014838758
0.775	15.755553237	15.39655788	15.014838758
1	15.577469193	15.049248878	15.014838758

**Figure 9 - The results of the sensitivity analysis, allowing to test the robustness of the decision tree results.**

Besides sensitivity analysis, the interface gives also the possibility of running a Monte Carlo simulation (Figure 10). With this analysis, it is possible to study the probability distribution of a selected payoff for a specific decision option, derived from a set of

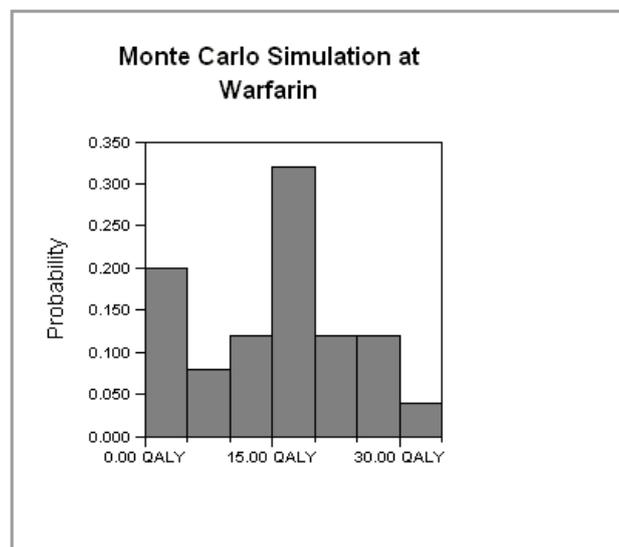
random trials. This is shown by a histogram and a table with the summary statistics for the distribution.

### Monte Carlo Simulation

#### Probability Distribution (simulation)

The results of simulation at the Warfarin node are displayed below. To see the results of different random trials, simply rerun the analysis by choosing the Refresh command in your browser window.

Here is the graphical distribution of outcomes from the last set of simulation trials:



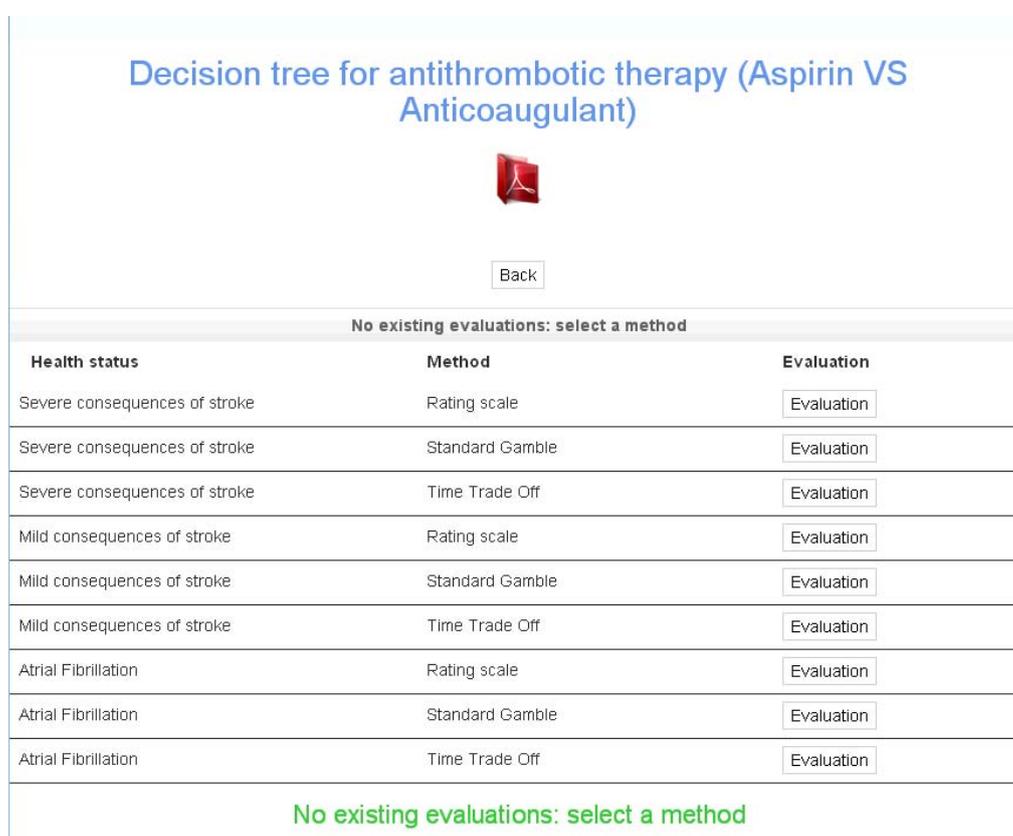
Here are the basic statistics of the simulation:

Mean	15.7996491206704
Median	15.9550092450529
Low Value	0.09575
High Value	36.3793948065114
Std Dev	8.14164948334498
5% percentile	1.04701864472251
10% percentile	4.20178296599887
90% percentile	26.5882976451376
95% percentile	30.0491924939588

**Figure 10 - The results of the Monte Carlo simulation, allowing to check the distribution of the expected payoffs**

### 4.3 The web interface for utility coefficient elicitation.

As stated in Section 5.2, when a recommendation suggesting a shared decision is available, the Utility Coefficients Elicitation Interface button is shown (see Figure 2) that links to the Utility Coefficients Elicitation Interface. The page displayed is the one shown in Figure 11. The page is specific for the selected patient and the decision model involved in the recommendation. When this page is first accessed, no existing evaluation is available, and a table is displayed providing a link to the specific evaluation for each combination of health state and elicitation method.



**Decision tree for antithrombotic therapy (Aspirin VS Anticoagulant)**



**No existing evaluations: select a method**

Health status	Method	Evaluation
Severe consequences of stroke	Rating scale	<input type="button" value="Evaluation"/>
Severe consequences of stroke	Standard Gamble	<input type="button" value="Evaluation"/>
Severe consequences of stroke	Time Trade Off	<input type="button" value="Evaluation"/>
Mild consequences of stroke	Rating scale	<input type="button" value="Evaluation"/>
Mild consequences of stroke	Standard Gamble	<input type="button" value="Evaluation"/>
Mild consequences of stroke	Time Trade Off	<input type="button" value="Evaluation"/>
Atrial Fibrillation	Rating scale	<input type="button" value="Evaluation"/>
Atrial Fibrillation	Standard Gamble	<input type="button" value="Evaluation"/>
Atrial Fibrillation	Time Trade Off	<input type="button" value="Evaluation"/>

**No existing evaluations: select a method**

**Figure 11 - The page for eliciting patient’s values for the health states characterizing the actual decision tree**

In the case some elicitation has already been performed, a page as the one depicted in Figure 12 is displayed. It is divided into three parts:

- Utility coefficients already calculated: this is a table presenting for each health state and method, the value of the calculated utility coefficient and the date

of the evaluation. The date is colored in red if it is antecedent to the actual date. For each row, it is either possible to elicit a new value for the coefficient or keeping the old value as the present evaluation (in this case the evaluation date is updated with the current date and it is colored in green).

- The average list: as different methods for elicitation are available, the interface provides a form for calculating the average of such values (the decision tree allows imputing only one coefficient per health state). In this section we can see the available calculated average, the date when this value was calculated, the manually adjusted value and the motivation for the adjustment and a button linking to the form for a new average calculation.

- Health condition/method pairs still to be evaluated.

Utility coefficients already calculated					
Health status	Last Evaluation	Method	Utility coefficient calculated	New Evaluation	Keep the value as today evaluation
Atrial Fibrillation	2012-09-17	Rating scale	0.78	<input type="button" value="New Eval"/>	<input type="button" value="Keep"/>
Atrial Fibrillation	2012-09-03	Time Trade Off	0.9816	<input type="button" value="New Eval"/>	<input type="button" value="Keep"/>

The average list					
Health status	Date	Calculated average	Manually set up average	Recalculate average	Motivation
Atrial Fibrillation	2012-09-03	0.9816	----	<input type="button" value="Recalculate"/>	----

Health condition/method pairs still to be evaluated:		
Health status	Method	Calculate
Severe consequences of stroke	Rating scale	<input type="button" value="Select"/>
Severe consequences of stroke	Standard Gamble	<input type="button" value="Select"/>
Severe consequences of stroke	Time Trade Off	<input type="button" value="Select"/>
Mild consequences of stroke	Rating scale	<input type="button" value="Select"/>

**Figure 12 - Health states values can be elicited with different methods, and then an average value can be calculated**

### 5.2.1. Rating Scale

In case of rating scale method selection the page shown in Figure 13 is displayed. The top part of the page is the same for each method and it is characterized by a brief description of the selected health state (in this case severe consequences of stroke), a picture, linked to a PDF document containing educational materials, and a link to an explanatory video. All this material is useful for the caregiver to better explain to the patient the different health states.

Once the caregiver has determined that the patient has well understood the selected health state, it is possible to proceed with the proper elicitation.

In the case of the rating scale, both a visual scale with 6 smileys and a scale of numbers (ranging from 0 to 100) are displayed. Initially, the value of the bar is set to 50, indicating a state considered exactly in the middle between the perfect and the worst state (death). The caregiver, after discussion with the patient, will position the bar at the most appropriate value.

We are also evaluating other options to present the rating scale method, based on the fact that If DEATH is 0, then many of the relevant options might be close to each other within the upper interval. That makes it very difficult to assign any meaningful values to them. One example of solution presented in the literature is the one proposed by the PANDEX system [15], which first finds the value of the worst non-death outcome, fixing it to be the 0, and then "stretches" the scale accordingly.

## Rating Scale

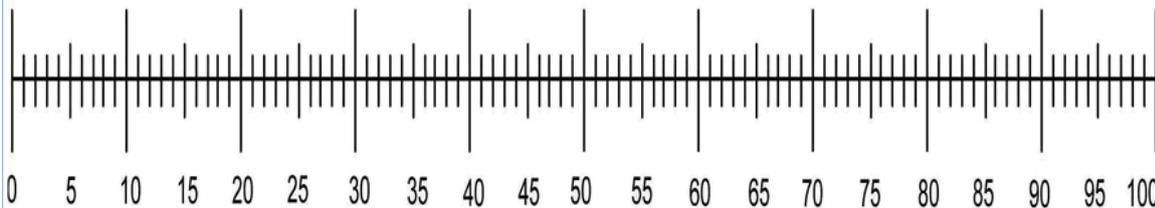
Severe strokes often result in combinations of significant motor, sensory and cognitive deficits. Individuals who have experienced a severe stroke constitute the most disabled group of stroke patients and represent the greatest rehabilitation challenges



Health status:  
Severe  
consequences of  
stroke



Move the cursor to position the health status



You choose the value

**Figure 13 - The interface for the rating scale method**

Once the value (e.g. 80) has been confirmed, it is used for rating the health state with respect to the other states considered in the tree, and the page shown in Figure 14 is displayed.

This page, which is the same for any of the elicitation methods, shows a table listing both patient information (name, surname, age, sex, etc) and encounter information (selected tree, health state, method and utility coefficient calculated). These information are stored in the PHR in order to be used by the DT web interface for running the tree model (from the specific button in the page in Figure 14).

## Encounter data

12-ott-2012

<b>Encounter Code:</b>	1965
<b>Selected tree:</b>	Decision tree for antithrombotic therapy (Aspirin VS Anticoagulant)
<b>NI Number:</b>	4444444444444444
<b>Name:</b>	Nome 4
<b>Surname:</b>	Cognome 4
<b>Born on:</b>	1988-01-01
<b>District:</b>	Crotone
<b>Sex:</b>	M
<b>Race:</b>	Bianca
<b>Encounter date:</b>	2012-10-12
<b>Age:</b>	24
<b>Health status:</b>	Severe consequences of stroke
<b>Used method:</b>	Rating scale
<b>Utility coefficient calculated:</b>	0.8

Save and back to the health status selection

Don't save and go back

**Figure 14 - Summary page showing the elicited coefficient for the health state “severe consequences of stroke” in the specific patient**

### 5.2.2. Time trade-off

Choosing the time trade-off method the page in Figure 15 is shown. The top of the page is similar to the one described for the rating scale method.

Below the health state description, the patient’s life expectancy in years and months is displayed. Since this interface will be run at FSM Hospital in Italy, this value is calculated according to the Italian population statistic. As well, the Spanish statistics will be used for the application concerning pregnancy complications.

When the page is first displayed, the bar will be colored in green, and its value is set to the expected life. With this method, the patient will indicate how many years he would be willing to give up for living in perfect health. Based on the indicated value, it is

possible to have an index of how much the selected health state is considered severe by the patient.

When the caregiver moves the bar, four textboxes are automatically filled: the first two (in blue) being the years and months to live in perfect health, while the other two (in red) represent the years and months to give up. In the case of Figure 15, the life expectancy is 35 years and 4 months, and the choice of the patient is to give up 4 months.

### Time Trade Off method

Severe strokes often result in combinations of significant motor, sensory and cognitive deficits. Individuals who have experienced a severe stroke constitute the most disabled group of stroke patients and represent the greatest rehabilitation challenges



Health status: **Severe consequences of stroke**



You are 45 years old. Your life expectancy according to the Italian population statistics is 35.0 years 4.0 months

Do you prefer to live all your life with "Severe consequences of stroke"

or to live  years and:  months in perfect health? (That is to give up  years and  months)

**Figure 15 - Interface for the time trade-off method for utility elicitation**

Once the value is confirmed, the utility coefficient is calculated as described in Section 3.1.2.2 and stored for future usage through the page shown in Figure 14.

#### 5.2.3. Standard Gamble

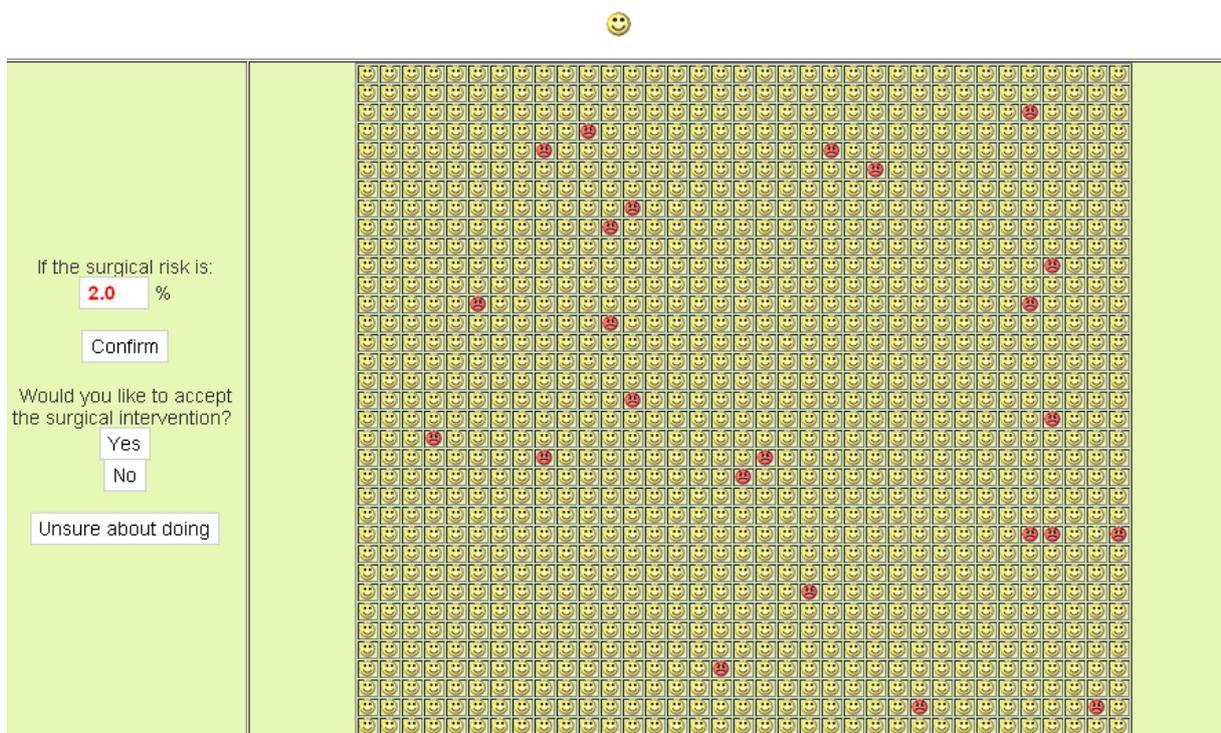
If the caregiver decides to elicit coefficients using the standard gamble strategy, he is directed to a page with the layout shown in Figure 16. This page is divided into two panels:

- on the left hand side there is the question the caregiver asks to the patient. It is related to the risk of death a patient would be available to take in the case there existed a surgical intervention able to make him living in perfect health thereafter;
- the panel on the right hand side provides a table of 35x35 smileys useful to graphically give an idea of such a surgical risk. The choice of using this kind of graphical representation was also motivated by the results reported by [8].

When the elicitation starts, the textbox containing the risk percentage is set to 0.0% and all the smileys are yellow. The caregiver starts by indicating a percentage of risk to the patient and asking whether he would be willing to accept it (in the case of Figure 16 this value is 2%). To help the patient understanding the meaning of the *risk* he is asked to evaluate, a random set of smileys corresponding to this percentage is turned into red. According to the answer of the patient, the system increases/decreases the proposed risk value until the patient states he is unsure on what he would do in the presence of a certain value of the risk. This specific value is then used to calculate the utility coefficient as described in Section 3.1.2.3 and store it for future usage through the page shown in Figure 14.

In this case we have chosen to increase/decrease the risk percentage starting from a value selected by the caregiver. Another option might be to ask questions to the patients using a "ping-pong" method ("Is the value more than 90? Is it less than 10?").

## Standard Gamble Method



😊

If the surgical risk is:  
**2.0** %

Would you like to accept the surgical intervention?

**Figure 16 - A matrix-like picture to help a patient understanding the risk concept**

### 5.3. The cost model

Among the payoffs, the implemented decision model includes also the costs. These are the so-called out-of-pocket costs related to the patient and to the economic impact a specific decision option has on his activities.

For the current implementation of the model, we have considered three categories of costs:

1. Costs related to the visits the patient has to undergo during his treatment;
2. Costs related to domiciliary care the patient may be in need of;
3. Home adaptation costs.

### 5.3.1. Follow-up Visits Costs

As regards follow-up visits costs, we have considered those visits specifically related to AF, namely visits for INR control, cardiological visits and ECGs. As the currently implemented model will be run at FSM Hospital that is located in Lombardy (Italy), and the Italian national health care service (SSN) is based on a regional management, costs values were taken from the regional price list for Lombardy. In particular, the visit for INR control has a cost calculated as the sum of the cost for the INR test and the cost of the visit for oral anticoagulant therapy assessment that is always performed in conjunction. The value for the costs of the considered visits depends on the position of the patient with respect to the national healthcare service, as some patients can have the visits costs totally covered by SSN. In the case the model will be used outside Italy or other decision models will be implemented, cost values will have to be adapted to the specific cases.

Besides the specific costs of the visits, we also took into account non-healthcare resources that are:

- the cost of the travel to the center where the visit is performed: this is a patient-specific value that depends on the distance the patient has to travel, the transportation, etc.;
- the cost of the meals that the patient might have to pay for during the visit day (for example INR checks last from the morning to the afternoon);
- patient's productivity loss, in case the patient is self-employed;
- 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.

### 5.3.2. Domiciliary Care and Home Adaptation Costs

The inclusion of the category of the costs related to domiciliary care is based on the fact that, after a mild/moderate-severe stroke/ICH, the patient needs 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 mild/moderate-severe stroke/ICH is not only the one provided by a home caregiver, but may also imply some home adaptation to manage the impairments the patients may suffer from after the event. These costs are assessed based on the results presented in [6]. This paper presents an analysis of the overall social costs of stroke in Italy, in terms of direct costs and productivity losses. Particular attention is devoted to the identification of non-healthcare actual resources consumed by the patient, including home adaptation costs.

## 6. Discussion

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In this deliverable we described the tools used for developing the interaction between two types of users (patients and caregivers) and decision models.

We motivated our decision to use a commercial product, namely TreeAge Pro together with TreeAge Pro Interactive, to develop and publish decision trees. In addition to the technical and background-based motivations described in this document, we want to stress out that, avoiding to develop a tool from scratch, allowed us to put more efforts in the tree modeling activity. As a matter of fact, building a decision tree involves acquiring a big amount of knowledge from both the literature and medical experts, which is a very time-consuming, conceptual task.

During this first year, just one tree has been developed, concerning the prevention of thromboembolism in Atrial Fibrillation (AF) patients. As regards the AF domain, in the next years we plan both to build additional trees (one for the ablation treatment choice and one for choosing the treatment after several cardioversion failures) and to update the already developed tree. This last work will be necessary because it is very likely that a new drug (Dabigatran, known as a “NOAC” or NewAnticoagulant) will enter the Italian market. This drug will in some cases replace Warfarin and the main difference is that it does not require the frequent INR measurements that Warfarin does [1,3,12,16]. As a consequence, a new branch in the tree will be introduced. As regards the Gestational Diabetes and Hypertension domain, we will support the CSPT team in investigating the presence of situations where it might be useful to apply the shared decision model framework (e.g. for insulin schedule for type 2 Diabetes). In that case, the specific decision tree model will be implemented.

Another limitation of the work done so far is related to the values elicited through the rating scale method. Since in fact they are not suitable to be used for QALY calculation, but only to obtain from the patients their relative, subjective ranking, the interface will be slightly changed, allowing the patient to put all the tree states in the same visual-analog

scale. The values will then be used to check for coherence of the utility coefficients elicited with the SG and TTO methods.

Eventually, there is an issue related to the validation of the interface. It has been shown to medical partners of MobiGuide in Pavia. They suggested some modifications in the terminology used. Then, the interface underwent a careful, but only internal evaluation, i.e. it has not been tested by users different from the system developers. Therefore, a test phase with physicians and patients is needed in the next year.

Often, the result of the “shared decision” module will be the decision to follow some protocol or ancillary guideline. For example, if the decision is to use warfarin, the patient should be educated to correctly follow the oral anticoagulant therapy. The administration of this therapy is handled by the Mobiguide Guideline Application Engine (part of WP5) through a patient-specific recommendations set. The system will then proceed to provide these recommendations, in a context-sensitive manner, to the patient. This process can be followed recursively whenever, within this administration protocol, there is a decision that involves the patient.

## 7. Conclusion

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The work done within this work package task has been exploited during the “Hello Tallinn” demonstration of the MobiGuide work-in-progress, held on September 4th -9th. In this way, we had the chance to test the connection functionality with the other components of the MobiGuide architecture. The demonstration was satisfactory, and was a source of useful discussion.

## 8. References

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