Zbornik 20. mednarodne multikonference

INFORMACIJSKA DRUŽBA – IS 2017

Zvezek A

Proceedings of the 20th International Multiconference

INFORMATION SOCIETY – IS 2017

Volume A

Slovenska konferenca o umetni inteligenci
Slovenian Conference on Artificial Intelligence

Uredili / Edited by

Mitja Luštrek, Rok Piltaver, Matjaž Gams

http://is.ijs.si

9. - 13. oktober 2017 / 9th – 13th October 2017
Ljubljana, Slovenia

A State-Transition Decision Support Model for Medication Change of Parkinson's Disease Patients

Biljana Mileva Boshkoska[1,2]
biljana.mileva@ijs.si

Dragana Miljković[1]
dragana.miljkovic@ijs.si

Anita Valmarska[1,4]
anita.valmarska@ijs.si

Dimitris Gatsios[3]
dgatsios@cc.uoi.gr

George Rigas[3]
george.a.rigas@gmail.com

Spiros Konitsiotis[3,5]
skonitso@gmail.com

Kostas M. Tsiouris[3]
tsiourisk@biomed.ntua.gr

Dimitrios Fotiadis[3]
fotiadis@cc.uoi.gr

Marko Bohanec[1]
marko.bohanec@ijs.si

ABSTRACT
In this paper, we present a state-transition decision support model for medication change of patients with Parkinson's disease (PD), implemented with method DEX. Today, PD patients can be treated with three basic medications: levodopa, dopamine agonist, MAO-B inhibitors, and their combinations. We propose a model which, based on the current patient's symptoms (motor symptoms, mental problems, epidemiologic data and comorbidities), suggests how to change the medication treatment given the patient's current state. The model is based on expert's knowledge of neurologists and is composed of (1) a state-transition model that presents all possible medication changes, and (2) decision rules for triggering the changes, represented in terms of a qualitative rule-based multi-criteria model. The model assesses all states described by the state-transition model and proposes multiple different yet still correct possibilities for medication change.

Categories and Subject Descriptors
H.4.2 [Types of Systems]: Decision support.
J.3 [Life and Medical Sciences]: Medical information systems.

General Terms
Algorithms, Management, Measurement, Design, Human Factors

Keywords
Parkinson's disease, medication change, decision model

1. INTRODUCTION
Parkinson's disease (PD) is a complicated, individual degenerative disorder of the central nervous system for which there is no cure. Hence it requires a long-term, interdisciplinary disease management including typical medicament treatment with levodopa (LD), dopamine agonist (DA), and enzymes (E), such as MAO-B inhibitor. Due to the different combinations of motor and mental symptoms from which PD patients suffer, in addition to existing comorbidities, the interchange of medications and their combinations is patient-specific [1]. In the framework of the EU Horizon 2020 project PD_manager (http://www.parkinson-manager.eu/) [2] we developed a decision support model, called the "How" model, for PD management which suggests how to change the medication treatment given patients' current state. The assessment is based on data that include patients' motor symptoms (dyskinesia intensity, dyskinesia duration, offs duration), mental problems (impulsivity, cognition, hallucinations and paranoia), epidemiologic data (patient's age) and comorbidities (cardiovascular problems, hypertension and low blood pressure). The model is composed of (1) a state-transition model that presents the medication change among levodopa, dopamine agonist, MAO-B inhibitors and their combinations, and (2) decision rules for triggering the changes, represented in terms of a qualitative multi-criteria model. The latter has been developed using the DEX method [4], which integrates the qualitative multi-criteria decision modeling with rule-based expert systems.

2. MODEL DESIGN
The model development was performed with neurologists who work with PD patients. The process of decision analysis led to a design of a model composed of two key elements: (1) A state-transition model that represents all possible combinations of used medicaments and transitions between them, and (2) a multi-criteria DEX model that provides decision rules for each transition.

2.1 A state-transition model
In the state-transition model the medication treatments (states) and transitions among them are represented in a form of a cube as presented in Figure 1. In Figure 1, each medication-treatment state is as a circle and each change of medication treatment is represented with a directed arc. Each state corresponds to the set of medications that constitute the current treatment. The set can be empty (the symbol O indicates no medication therapy), or can consist of any combination of DA, LD and E (Enzymes, such as MAO-B inhibitor). For example, the state DA+E means that the current medication treatment of the patient consists of dopamine agonist (DA) and MAO-B inhibitor. From this state there are three possible state changes depending on the combinations of patient's symptoms: add LD to the treatment (state denoted as LD+DA+E), remove DA from the current treatment (state E) or remove E and use only DA (state DA).

The absence of a directed arc between two states means that a particular change of medication treatment is not addressed in the model, either because it has been deliberately excluded (transitions from and to state O, which are out of scope of the PD_manager project), or is rarely or not at all used in practice. A

reflexive arc means an increase/decrease of the medication (dosage or intake) [3].

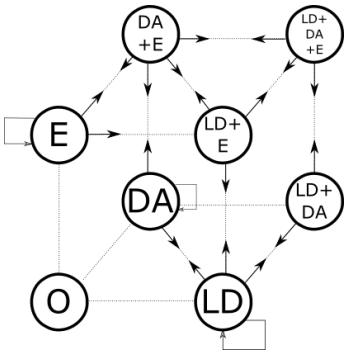

Figure 1: A state-transition model for medication change among levodopa (L), dopamine agonist (DA), MAO-B inhibitors (E) and their combinations. Symbol O represents the state where the patient does not take medications.

2.2 DEX model

The transitions in the state-transition model (**Error! Reference source not found.**) are triggered according to a multi-attribute model, which is responsible for interpreting patients' motor symptoms, mental problems, epidemiologic data and comorbidities, and aggregating them into an overall assessment of the potential medication changes of a given patient. The model is hierarchical and qualitative, developed using a qualitative multi-attribute modelling method DEX [4]. DEX models decompose the decision problem into smaller, less complex sub problems, which are represented by a hierarchy of attributes. Attributes from the decision alternatives are aggregated in order to obtain an overall the evaluation or recommendation. DEX belongs to the class of qualitative multi-criteria decision making methods: it uses qualitative (discrete) variables instead of quantitative (numerical) ones, and employs decision rules rather than numerical aggregation functions for the aggregation of attributes. The method DEX is supported by DEXi [5], freely available software that supports both the development of DEX models and their application for the evaluation and analysis of decision alternatives. DEX was chosen for modelling due to its previous successful usage for implementation of decision support models in health care [6][7].

Using DEX principles of model development, the state-transtion model from Figure 1 is mapped into a qualitative multi-attribute model presented in **Error! Reference source not found.**2. The model consists of basic and aggregated attributes given in a structure that identifies possible transitions in the state-transition diagram for a given patient [8]. The model combines 22 basic attributes including data about motor symptoms (rigidity, tremor, and bradykinesia), mental problems (impulsivity, cognition, hallucinations, paranoia), comorbidities (cardiovascular, low blood pressure, hypertension), and dyskinesia (offs duration, intensity, and duration). In addition, there is data about patient's age and activity, and data about the current therapy (which medications is the patient currently using, and whether or not the maximum dosages of DA and LD have been reached). The values of these attributes constitute model's inputs.

Aggregation of the basic attributes leads to two sets of attributes. The first set is composed of six aggregated attributes: Dyskinesia, MotorSymptoms, CurrentTherapy, PersonalCharacteristics, Comorbidities and MentalProblems. The purpose of this set of attributes is to aggregate several specific symptoms into common indicators, which are used as inputs to the second set of aggregated attributes. For instance, Dyskinesia is a common indicator of patient's involuntary movements caused as a side effect of medications; it is determined by aggregating the basic attributes *offs duration*, d*yskinesia intensity*, and *dyskinesia duration*.

The second group of aggregated attributes forms a set of 15 submodels, which determine the transitions from one medication state to the other one as given in the state-transition diagram (Figure 1). Those submodels are the following:

1. **ChangeDAtoLD:** Change therapy from dopamine agonist to levodopa
2. **ChangeDAtoDA+LD:** Change therapy from dopamine agonist to dopamine agonist and levodopa
3. **ChangeDAtoDA+MAOI:** Change therapy from dopamine agonist to dopamine agonist and MAO-B inhibitors
4. **DecreaseDAdosage:** Decrease the dosage of dopamine agonist
5. **IncreaseDAdosage:** Increase the dosage of dopamine agonist
6. **ChangeLDtoLD+DA:** Change therapy from levodopa to levodopa and dopamine agonist
7. **IncreaseLDdosage:** Increase the dosage of levodopa
8. **IncreaseLDintake:** Increase the intake of levodopa
9. **DecreaseLDintake:** Decrease the intake of levodopa
10. **DecreaseLDdosage:** Decrease the dosage of levodopa
11. **ChangeDA+LDtoLD:** Change therapy from dopamine agonist and levodopa to levodopa
12. **ChangeMAOItoMAOI+DA:** Change therapy from MAO-B inhibitors to MAO-B inhibitors and dopamine agonist
13. **ChangeMAOItoMAOI+LD:** Change therapy from MAO-B inhibitors to MAO-B inhibitors and levodopa
14. **StopMAOI:** Stop using MAO-B inhibitors
15. **AddMAOI:** Add MAO-B inhibitors to the current therapy.

At the top of each submodel, there is the *root* attribute which represents the overall assessment of medication change under consideration. For example, the submodel **ChangeDA+LDtoDA** estimates the change of medication from dopamine agonist and levodopa to dopamine agonist based on the information whether the patient already takes DA (*usingDA*) and LD (*usingLD*), if the patient has increased mental problems (*MentalProblems*) and/or cardiovascular problems (*cardiovascular*).

All submodels were obtained through expert modelling. In this case, decision-support models were developed in collaboration between the neurologists (experts) from and the decision analyst. The work proceeds in the form of a question-answer dialogue, led by the analyst, aimed at identifying the important indicators and decision rules used, implicitly or explicitly, by the expert when making decisions.

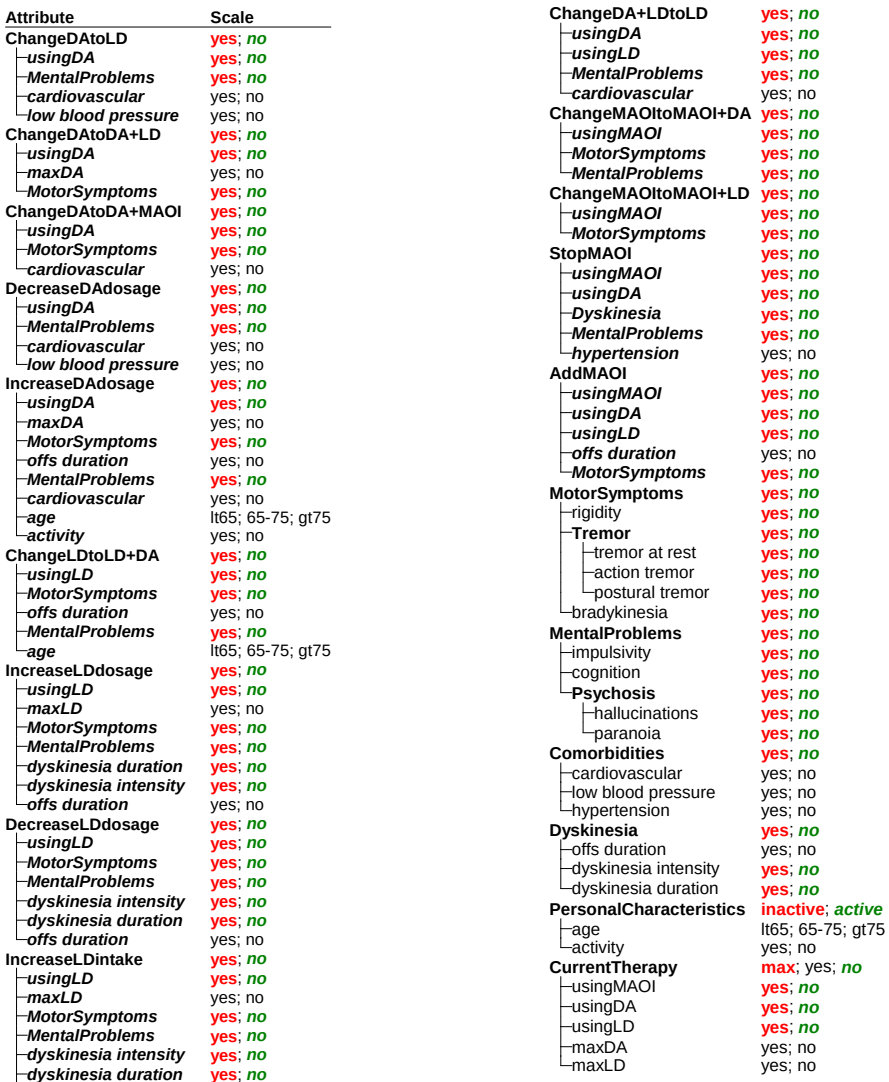

Figure 2: Structure and value scales of the "How" medication change model

Figure 2 shows the value scales and structure of the model. It shows that most attributes in the model are binary, each taking one of the two corresponding values: *yes* or *no*. Coloured values indicate that the corresponding attribute is ordered from left-to-right, so that the leftmost (**red**) value indicates a problematic, and the rightmost (***green***) a non-problematic patient's condition. The red/left values generally indicate a problem that should be addressed by medication change.

2.3 Decision rules

For each aggregate attribute in the DEX model, it is necessary to define the values of that attribute for all possible combinations of lower-level (input) attribute values. For example, the **IncreaseLDdosage** aggregate attribute depends on seven lower level attributes that correspond to current patients' medication treatment and symptoms. These attributes are binary, so there are $2^7 = 128$ possible combinations of their values. The DEXi software was used to represent, manage and define such combinations in the form of decision tables. All decision rules contained in the model are presented in a tabular form together with a verbal interpretation. Table 1 is an example of a decision table that defines the decision rules for the aggregated attribute **ChangeDatoLD**. The symbol '*' used in the decision tables denotes any value that can appear at that position. For instance, in connection with an attribute than can take the values "yes" and "no", the '*' stands for "yes or no".

According to the decision rules presented in Table 1, one may read that the change of medication treatment from DA to LD should happen only when the patient already takes DA (*usingDA*). The change may take place in in three different cases: the patient has mental problems, cardiovascular problems, or low blood pressure. Otherwise, the change to LD should not happen.

The whole model contains 21 other decision tables such as Table 1, corresponding to the remaining aggregate attributes in the model.

Table 1: Decision rules for submodel ChangeDatoLD

	usingDA	Mental-Problems	cardio-vascular	low blood pressure	Change-DAtoLD
1	yes	yes	*	*	yes
2	yes	*	yes	*	yes
3	yes	*	*	yes	yes
4	*	*no*	no	no	*no*
5	*no*	*	*	*	*no*

3. CONCLUSIONS AND FUTURE WORK

Using the DEX method, we developed a state-transition model and decision rules for medication change of PD patients. This approach assured that the model fulfils the following important characteristics: completeness (it provides outputs for any possible inputs), robustness (it works even if some input data is missing), consistency (the model is free of logical errors), transparency (the model is fully "open" for the inspection of contained decision rules), comprehensibility (the embedded decision rules are easy to understand and explain). The model assess all combinations of possible medication changes that arise from the state-transition model thus allowing interpretation of several different and yet correct scenarios for medication change for patients that suffer from PD.

The future work in the framework of the PD_manager project will be focused on model evaluation and implementation. We intend to verify and validate the model on (1) real-life examples of medication-change decisions, such as the Parkinson Progression Marker Initiative dataset [9], (2) on real case patient's scenarios, (3) and in comparison with neurologists from different EU countries. The model will be integrated in the PD_manager m-health platform for Parkinson's disease management [2].

4. ACKNOWLEDGMENTS

The work of the authors was supported by the PD_manager project, funded within the EU Framework Programme for Research and Innovation Horizon 2020, under grant number 643706.

5. REFERENCES

[1] Gatsios D, Rigas G, Miljković D, Koroušić-Seljak B, Bohanec M, Arredondo MS, Antonini A, Konitsiotis S, Fotiadis DI. 2016. Mhealth platform for Parkinson's disease management. CBHI, *18th International Conference on Biomedicine and Health Informatics, February 25-26, 2016, Dubai, UAE*.

[2] PD_manager: m-Health platform for Parkinson's disease management. EU Framework Programme for Research and Innovation Horizon 2020, Grant number 643706, 2015–2017, http://www.parkinson-manager.eu/

[3] Bohanec, M, Antonini, A, Banks, A, Fotiadis, D.I, Gasparoli, E, Gatsios, E, Gentile, G, Hovhannisyan, T, Konitsiotis, S, Koutsikos, K, Marcante, A, Mileva Boshkoska, B, Miljković, D, Rigas, G, Tsiouris, K.M, Valmarska, A. Decision support models. PD_manager project, *Deliverable D5.2, 2017*

[4] Bohanec M, Rajkovič V, Bratko I, Zupan B, Žnidaršič M. DEX methodology: Three decades of qualitative multi-attribute modelling. *Informatica* 37, 2013, 49–54.

[5] Bohanec, Marko. *DEXi: Program for multi-attibute decision making user's manual : version 5.00*, (IJS delovno poročilo, 11897). 2015.

[6] Bohanec M, Zupan B, Rajkovič V. 2000. Applications of qualitative multi-attribute decision models in health care, *International Journal of Medical Informatics*; 58- 59:191-205

[7] Šušteršič, O, Rajkovič, U, Dinevski, D, Jereb, E, Rajkovič, V. 2009. Evaluating patients' health using a hierarchical multi- attribute decision model. *Journal of international medical research; 37(5):1646-1654*.

[8] Mileva-Boshkoska, Biljana, Miljković, Dragana, Valmarska, Anita, Gatsios, Dimitros, Rligas, George, Konitsiotis, Spyros, Tsiouris, Kostas M., Fotiadis, Dimitrios I., Bohanec, Marko. 2017. Decision support system for medication change of Parkinson's disease patients : a state-transition model. V: LINDEN, Isabelle (ur.). *Proceedings of the 2017 International Conference on Decision Support System Technology, ICDSST 2017, with a theme on Data, Information and Knowledge Visualisation in Decision Making, 29-31 may 2017, Namur, Belgium*.

[9] Parkinson Progression Marker Initiative: The Parkinson Progression Marker Initiative (PPMI). *Progress in Neurobiology 95(4), 2011, 629–635*.