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ESTIMATION OF ACCURACY OF RECOMMENDED DIAGNOSTIC AND TREATMENT ACTIONS BASED ON PRECEDENT APPROACH

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ABSTRACT

The paper is devoted to estimation of accuracy of recommended diagnostic and treatment actions based on precedent approach. For a given clinical case, nearest case search is performed in a database of clinical cases according to defined metrics. The case found is used as a diagnostic and treatment recommendation. Based on representative samples, the accuracy of such recommendations was statistically evaluated for seven mostly widespread nosologies.

KEYWORDS

Medical Informatics; Clinical Decision Support; Precedent Approach

1. INTRODUCTION

The review of Butko (1990) gives an overview of materials of the 5th International Congress for Medical Informatics and discusses the problem of medical knowledge formalization. Medical knowledge was supposed to be scientific or empirical. It was stated that models based on scientific medical knowledge have both generalized and limited character, but empirical knowledge cannot be representative and adequate for population as a whole. Thus, formalized medical knowledge consists of scientific theories and medical practice fixed in databases (DB) and knowledge bases (KB). Over the last few years, both components of medical knowledge continue developing. Due to widespread automation of diagnostic and treatment process (DTP), a new class of systems has risen – Medical Information Systems (MISs). Implementation of MISs has allowed enhancing the value of the empirical component of medical knowledge. There is a considerable body of empirical knowledge in databases of MISs that describes and formalizes millions clinical cases in the form of electronic medical records (EMRs). Recently, there is a growing trend towards the creation of national clinical data banks (Herrett 2015). Scientific components of medical knowledge continue evolving rapidly. New diagnostic approaches as well as new methods of treatment and new drugs are emerging. Recently, personalized medicine is rising that uses the patient's genetic composition to tailor strategies for patient-specific disease detection, treatment, or prevention. According to the paper of (Kohane 2009), personalized medicine is the best practice of clinical decision-making such that the decisions made maximize the outcomes that the patient most cares about and minimize the expenses that the patient fears the most, on the basis of as much knowledge about the individual's state as is available. Such points of view upon personalized medicine focus on clinical decision making and reemphasize the urgency and importance of research and development in this field. Clinical practice is, on the one hand, conservative and traditional, it is based on accumulated and verified experience (evidence-based medicine) and, on the other, there is a clear need to continuously harness new medical knowledge. Decision support systems intended to help physicians are threatened by obsolescence and the knowledge they contain is at risk of being outdated, and it is therefore essential to ensure continued formalization of knowledge and its constant updating. According to (Butko 1990), this is one of the reasons for extremely narrow dissemination and few practical implementations of such systems.

Attempts to overcome critical difficulties in creating clinical decision support systems have led to an expansion of alternative approaches.

The first of them is to supply healthcare professionals with relevant sources of information that could help them to independently take decisions. Frankly speaking, a decision support system of such a kind generates no ready solutions but instead recommends that physicians study the information and get their many questions answered. One example of this approach is the UpToDate system [Evidence-Based Clinical Decision Support at the Point of Care, http://www.uptodate.com/home].

The second approach is based on developing highly specialized decision support systems. Examples are Decision Support Systems of (Nazarenko 2015, Palchunov 2015).

The third approach pretends to being global and aims at developing a cognitive system that is able to self-learning and accumulating knowledge from unformalized text sources. One example is the IBM Watson system [IBM Watson, http://www.ibm.com/smarterplanet/us/en/ibmwatson/]. At the XVII Data Analytics and Management in Data Intensive Domains International Conference, DAMDID/RCDL'2015, the presentation (Arutyunyan 2015, Gavrilov 2015) devoted to the Watson system showed that the results of cognitive approach to creating a clinical decision support system appear to be very poor. Designing a highly specialized decision support system (oncology) led to a long-term training of the system by a team of experts. The hope that a Decision Support System (DSS) could be able to adopt medical knowledge and effectively use it is not materializing.

All of the above-mentioned approaches have shortcomings as well, such as the need of involving experts, regular updating of knowledge bases, and they are highly specialized.

In this paper, we consider a universal precedent-based approach to designing DSS. It is based on a large volume of formalized and verified clinical data (Big Databases). The main idea of precedent-based approach is quite simple – to find a most similar case in a database and use it to support clinical decision making. Precedents of clinical cases could be filtered taking into account the credibility of medical organizations in which precedents were created, the credibility of general practitioners who authored those precedents, and the relevance of precedents to the modern medical technologies.

To the success of precedent-based approach, there is a need for representative databases of clinical cases. (Herrett 2015) gives an example of the primary care database of anonymized medical records (EMRs) from general practitioners, with coverage of over 11.3 million patients from 674 practices in the UK.

The authors of this publication were involved in designing the INTERIN PROMIS MIS [http://www.interin.ru/] which is widely used in major healthcare organizations of Moscow, Russian Federation. Our estimates suggest that nowadays there is about 3 million EMRs in INTERIN PROMIS. It means that it is possible to create widespread representative nationwide DBs of clinical cases. Precedent-based approach focuses on practical use of knowledge from such DBs. The Institute for System Programming of the Russian Academy of Sciences (ISP RAS) (Karpov 2010) pioneered the use of precedent-based approach for clinical decision support in Russia. Independently, experts of Ailamazyan Program Systems Institute of the Russian Academy of Sciences (Ailamazyan PSI of RAS) carried out R&D in the field of implementation of precedent-based approach in clinical practice (Malykh 2014, Malykh 2015). The research was supported by the Ministry of Education and Science of the Russian Federation and by the Russian Foundation for Basic Research. As a conception, precedent-based approach was represented at the 15th World Congress on Health and Biomedical Informatics (Malykh 2015). Ailamazyan PSI of RAS had a certain advantage because the specialists of this Institute had an access to representative Big Data Bases of clinical cases of the INTERIN PROMIS MIS. In 2015, investigations on statistical evaluation of accuracy of recommended diagnostic and treatment services generated with precedent-based approach were performed using clinical data of the Clinical hospital of the President Administration of the Russian Federation.

In this paper, the authors present the first results of their research. These results are of critical importance as they allow to evaluate both effectiveness and accuracy of precedent-based approach in decision making systems.

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2. PRECEDENT APPROACH TO DECISION MAKING IN CLINICAL PROCESSES

2.1 Model and Methods

For further and deeper understanding of the target formulation, we need to quote the research conducted by (Malykh 2015). Modern medical information systems keep electronic medical records (EMRs) and contain information on millions of various clinical cases formalized to a certain degree. The degree of formalization of the stored clinical data in various MISs may vary. Up-to-date medical information systems contain models of DTP as a time sequence of management events (which include ordering of diagnostic tests and administering of treatment) as well as monitoring events (which describe the patient's state). Management events are better formalized; hospitals keep statistical and economic records on them which include maintaining registers of services rendered, invoicing, planning and centralized control. Medical data associated with monitoring and diagnostic tests are insufficiently formalized.

One of our previous studies describes the possibility of modeling DTP using controlled stochastic Markov processes (Malykh 2014). This model is based on the assumption that DTP is a controlled process. The model sets forth a management notion, u, and a state notion, x. Management means decisions made by a physician and implemented in the future. Management is limited by prescription of various diagnostic and treatment measures by a physician, including diagnostic testing, drug and treatment administration, surgical treatment as well as manipulation, etc. The physician's choice is based on the accumulated medical knowledge about how a certain disease should be treated and on the physician's individual experience. Rather than taking into account all subsets of DTP elements as management options, the physician considers only those subsets that were previously used in similar situations and proved their clinical effectiveness. Management is explicitly case-based reasoning.

Management in the current situation (x^i, u^i) will be determined not only by the state (x^i) but also by the whole history of the process and management at earlier steps of DTP $\{i, i-1, i-2, ...\}$. This is determined by the specific nature of the treatment process. The physician makes decisions based on the life history, disease history, family history, history of allergies and the entire course of the given clinical case. To take account of the DTP memory effect, it was proposed that the data from the above-mentioned histories are included in discrete states of the process, with management integrated. Each control element of the DTP may be associated with a certain integral characteristic of application of this element in DTP. For example, the total dose consumed by a patient will be considered the integral characteristic for a drug and a total radiation dose will be considered the integral characteristic for radiation therapy. Frequency of application of a certain element can also be considered as an integral characteristic (e.g., the number of electrocardiographic examinations).

Figure 1 represents a controlled discrete process with memory where each state **x** contains information about the integral management characteristics **u**, observed values **v** and history values **A** (anamnesis) relevant to a process.

t	*t + 1*	…	*t + n*
v(t)	*v(t + 1)*	…	*v(t + n)*
Σu(i), i<t	*Σu(i), i<t+1*		*Σu(i), i<t+n*
A	*A*	…	*A*

Figure 1. The DTP model

Modeling the DTP with controlled stochastic Markov processes seems appropriate in such cases (Bennett 2013, Malykh 2014), particularly for hospitalized patients because of the clearly manifested periodic observation as well as physician's decision making.

Precedent-based methods of decision making, including physician's decision support, are well known and described in many papers (Zagorujko 1999, Karpov 2010, Varshavsky 2013). The method requires to introduce a metric or a distance into the model to find the nearest neighbour of a given reference case. In the study of (Malykh 2014) an approach to creating a metric for the model was described, including a metric assessment with parameterized measure. In our case, we consider that the most appropriate metric is the weighed sum of rated distances determined for every characteristic of the state. Presence of weights allows to solve the task of training Physician's Decision Support Systems (PDSS) by optimization of metrics. In this study, optimization was not performed, weightages of one point were given, which means an equal informative value of every characteristic of patient's state. Description of a patient's state was not compressed, and the number of characteristics of a patient's state was not reduced.

Metrics could be calculated not only between pairs of states but also between processes. It is also possible to take into account all the process history in metrics defined for a pair of states (Malykh 2015). The Dynamic Time Warping method (DWT) seems promising for building such metrics.

For solving the task of nearest neighbor search, researchers use data structuring on small world graphs (Malkov 2014). By computing experiments, creation of small world graphs with 8 edges for each graph node was chosen. Experiments showed that for properly solving this problem, it was enough to randomly choose only 1% of the total number of graph nodes as a starting point when searching the nearest neighbor, and then, to traverse the graph and find the shortest path between those nodes and the given reference state. Small world graphs were drawn layered, with each layer representing a day of hospitalization (1st day of hospitalization, 2nd day of hospitalization, etc.). The nearest neighbor of a given reference state in the control sample was defined in the layer corresponding to the day of hospitalization from the reference. In average, for a learning sample with a 1000 DTP capacity, it was enough to randomly choose 10 nodes. This approach allows to quickly find the nearest neighbor and generate real-time recommendations about DTP for a physician. Calculating the structure of a small world graph is rather labor-consuming as the volume of calculations needed is proportional to the square root of the number of graph nodes. Adding a new precedent (a new node) into the DB requires the number of metric calculations equal to the number of nodes.

2.2 Results

Based on existing evidence of finished clinical hospitalization cases, models of seven nosologies were calculated (see Table 1). The models contain 8015 clinical cases including 91040 states which represent an average of approximately 11 days of hospitalizations per case. The number of cases for every nosology exceeded 1000, with the exception of J13 nosology which was specially chosen for debugging algorithms and programs because of smaller number of cases. For every nosology, control sample covering 10% of all the cases of a given nosology and spread throughout the period was chosen from all the cases. Every DTP lasted an integer number of days. Patient's state was fixed once per day. Every state was described by a set of characteristics having certain general dimensional values. A dictionary of characteristics describing the states of modeled DTP was created for every nosology. According to the adopted model, management implying diagnostic and treatment actions prescribed by a physician was defined among the set of characteristics. Management values were integrated according to the adopted model. Integral management characteristics are included into the state of the managed object thus reducing memory effect, which allows to get closer to a process where management becomes a function of state. Management capacity was rather high, ranging between 10^2 and 10^3 depending on the nosology.

Within every particular nosology for all states of the control sample which is not terminal (the latest states in DTP implementations), the closest neighbor states were calculated using the defined metric and data from learning sample structured on small world graphs. If closest neighbor states were not terminal in their DTP implementation, integral characteristics of all managed variables for a state following the closest neighbor were accepted as diagnostic and treatment recommendations. Recommended values of integral characteristics of managed variables were compared with actual integral characteristics of corresponding states from control sample. Depending on the resulting comparison, every generated recommendation was allocated into one of two classes: 1) recommended management level for a given characteristic corresponds to the observed control level; 2) recommended management level for a given characteristic does not correspond to the observed control level. These two classes of management are shown in columns 3 and 4 of Table 1. The third class of management corresponds to the cases in which, in control sample, a physician applied management actions (i.e. diagnostic and treatment actions) which were not included into the list of recommendations. This class of management is shown in column 5 of Table 1. For every class, a total number of cases was calculated and a relative number of cases showing the percentage for every class. The results are shown in Table 1.

Table 2. Evaluation of accuracy of diagnostic and treatment recommendations for seven nosologies

ICD-10 Code / Name	**Power of clinical precedents / Power of control set** Number of States / Number of Controls	The number of accurate recommendations Total / In percent	The number of recommendations not matched by value Total / In percent	Could not recommend Total / In percent
J13 / Pneumonia due to Streptococcus pneumoniae	**166 / 11** 2938 / 118	2865 / 34.4%	3923 / 47.2%	1530 / 18.4%
K80.1 / Calculus of gallbladde with other cholecystitis	**1018 / 128** 12853 / 931	16078 / 35.8%	18390 / 40.9%	10490 / 23.3%
H25.1 / Age-related nuclear cataract	**1205 / 121** 5509 / 293	2983 / 80.4%	539 / 14.5%	189 / 5.1%
H26.2 / Complicated cataract	**1255 / 126** 5778 / 249	2745 / 57.5%	1617 / 33.9%	408 / 8.6%
I67.4 / Hypertensive encephalopathy	**1336 / 134** 23165 / 1431	28115 / 31%	37563 / 41.4%	25060 / 27.6%
I67.9 / Cerebrovascular disease unspecified	**1403 / 141** 24875 / 1518	26202 / 33.7%	32447 / 41.7%	19117 / 24.6%
N20.1 / Calculus of ureter	**1632 / 164** 15922 / 205	7541 / 25.3%	9948 / 33.4%	12291 / 41.3%

3. CONCLUSION

The results given in Table 1 speak for themselves. In average, for all of seven considered nosologies, the results are clear: 1) in 33% of cases, the method permitted to generate absolutely precise diagnostic and treatment recommendations; 2) in 40% of cases, a physician acts according to generated recommendations but changes their integral level (dosage, etc.); 3) in 27% of cases, a physician prescribes diagnostic and treatment actions that are not included in generated recommendations. Account should also be taken of the fact that there were no system training and, thus, the obtained results can potentially be improved. One of the advantages of precedent-based approach is that there is no need to constantly involve and formalize new knowledge. New knowledge (new treatment methods) 'falls' within the precedents as it is inputted into EMRs when databases of MISs are being updated. With this, we could make quite a general conclusion that supporting an empirical component of medical knowledge in MIS requires less effort then formalizing and supporting a scientific one. This offers encouraging prospects for designing and developing decision support systems for physicians based on empirical components of medical knowledge. This approach also corresponds to existing case-based character of management and decision making in medical practice. So far, the results indicate that precedent-based approach has a high effectiveness and could naturally enhance other approaches to supporting physicians decision making, particularly knowledge-based ones.

The constraints of precedent-based approach include the need for a representative database of verified precedents excluding medical errors. From another perspective, precedents with corrected errors are of particular interest to physicians training and further prevention of such errors. The information about the results of these errors and possible ways of correcting them is also valuable. Thus, precedent-based approach could be widely spread as an educational tool. On the other hand, the precedent-based approach does not imply formalization of medical knowledge, which entails poor cognitive justification of generated recommendations. Consequently, justifications only describe how other patients were treated in similar clinical cases. There are also problems with optimization of provided metrics, compression of state descriptions, and construction of training procedures. These problems are connected with high dimensionality of the space of state characteristics and samples of clinical precedents. However, discussion of these issues and possible ways of addressing them has been left outside of this research.

There are two other factors that draw attention to systems based on precedent approach.

First of them is that there are trends in the development of our civilization which include an explosive development of information technologies (among them M2M, Big Data and IoT), their strong need for formalized knowledge and practical absence of qualified experts who could formalize that knowledge. The chief editor of the Rational Enterprise Management (REM) magazine (Russia) holds regular discussions on a wide range of problems including the above mentioned. Results of the discussions are published in the REM editor's column. The guests of a recent discussion (Vasilyeva E. 2015) included Igor Rudym (Intel), Dmitriy Tameev (PTC), Alexander Belotserkovskiy (Microsoft), Igor Girkin (Cisco), Igor Kulinitchev (IBM). All the participants agreed that, nowadays, the key challenge of IT development is not associated with hardware or software, but it needs breakthrough approaches to data analysis.

As for the second factor, it is obvious that nowadays there are no qualified experts in the field of knowledge even in key branches. The actual situation is even more critical as the experts who are able to solve at least a part of these problems are not able to cope with ever increasing information flow. From this point of view, precedent-based DSSs practically need no experts. Experts may be needed for enhancing or optimizing existing DBs and KBs.

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