УДК 004.89

DEVELOPMENT OF AUTOMATED METHODS FOR REDUCING THE RISK OF CRITICAL CONDITIONS, BASED ON THE ANALYSIS OF MEDICAL RECORDS

Chimit Antonovich NAYDANOV[1], Dmitriy Evgenyevich PALCHUNOV[1,2], Polina Andreyevna SAZONOVA[1]

[1] *Novosibirsk National Research State University*
630090, Novosibirsk, Pirogov str., 2

[2] *Sobolev Institute of Mathematics of SB RAS*
630090, Novosibirsk, Koptyug av., 4

This paper describes the methods of development of ontologies and ontological modes in medicine. We present four-level structure of knowledge representation. Using the basics of ontological methods of presenting knowledge, we developed algorithms to prevent risks of critical conditions and complications. The work is based on the model-theoretic approach to represent medical knowledge, which is shown through partial atomic diagrams of algebraic systems and of a patients' cases data via Boolean-valued models. This data helped to develop ontology and ontological models of the «spinal deformity and spinal degenerative disease». The ontology model contains: a) general knowledge that is applicable for all patients, b) data on specific patients, and c) estimated knowledge that help doctors make recommendations. Estimated knowledge is a set of hypothetical possibilities that could lead to a patient's critical condition or complications. We also developed an algorithm generating the estimated (fuzzy) knowledge based on the analysis of medical records. A software system generating recommendations to help prevent and reduce the risk of a patient's critical condition (life threatening) was implemented. The results used in the study are from data of patients with spinal deformity or spinal degenerative diseases.

Keywords: risk management, critical conditions, ontology model, precedent model, Boolean-valued model, knowledge representation, spinal deformity, degenerative diseases of the spine.

This paper describes methods of ontology and ontological model development for the medical subject area. The ontology development was carried out for the subject domain of «Spinal deformity and degenerative diseases of the spine».

The given approach is based on the four-level knowledge representation: the ontological knowledge level in the subject domain ontology and three levels of knowledge representation contained in the ontological model. In particular, this knowledge representation is the basis for development of methods and algorithms of critical condition and complication risk prevention.

The developed methods are implemented in the software system MedOntoModel. In particular, this software helps predict the probability of occurrence of patient's critical condition and gives appropriate recommendations to doctors. The software system is designed for the subject domain of «Spinal deformity and degenerative diseases of the spine.»

A new approach to the development of the ontological model structure is presented. It is viewed as a four-level one with strict division of knowledge into ontology, general knowledge, specific knowledge and probabilistic knowledge.

Model theoretical approach is used for formal representation of knowledge. This approach allows describing knowledge with different degree of reliability and generality. General knowledge is represented in the model by $\forall$-sentences of the first order predicate language. Specific knowledge about the patients is presented in the form of fragments of atomic diagrams of algebraic systems. Probabilistic knowledge is represented by fuzzy models.

On the basis of ontological model we have developed critical condition risk prevention algorithms

. – *postgraduate student, e-mail: naydanov.fit@yandex.ru*
– *doctor of physical mathematical sciences, leading researcher, e-mail: palch@math.nsc.ru*
– *master student, e-mail: psazonova@gmail.com*

for finding drug contraindications and negative interactions, generation of estimated knowledge. These algorithms have been implemented in the software system MedOntoModel and tested on medical data obtained from patient medical records.

CLINICAL DECISION SUPPORT SYSTEM

This part provides a brief overview of Clinical Decision Support System (CDSS). The most interesting examples of Russian and foreign CDSS's have been considered.

A CDSS is an information technology system that helps doctors to estimate patient's condition, diagnose, choose a course of treatment or prescribe drugs [4]. The system works with patient's characteristics compared with information from a knowledge base. A CDSS outputs recommendations for patients or evaluation of a patient's condition using special algorithms contained in it.

Modern CDSS should automatically warn of critical condition onset, be able to present data in an easy-to-understand form, automate doctor's interaction with other computer systems, be able to verify the medical diagnostic solutions and build assumptions about patient's condition [4].

According to [10], the use of CDSS can reduce the number of medical errors, and improve the treatment process and its outcome. In particular, the work [17] shows a twofold reduction of negative drug interactions leading to serious consequences, due to CDSS.

The review conducted by researchers Jeffery et al. [9] shows that the CDSS use for tracking the status of diabetic patients reduces death rate among them. In another paper [15] the authors argue that CDSS use leads to increased performance of medical staff.

Let us consider the most known CDSS used in Russia and other countries.

System IBM Watson for Oncology

This system helps oncologists determine a diagnosis and select a treatment plan. Watson compares the patient data and the knowledge gained from experts and medical texts. The system offers a suitable means of treatment and provides evidence of their efficiency. IBM Watson can process patient information that is derived both from structured sources (electronic medical records) or unstructured (medical records in simple English).

IBM Watson system is able to automatically extract information from medical texts. Knowledge Base of the system is formed by processing more than 290 medical journals, 200 manuals and 12 million pages of text.

System Dxplain

Dxplain was developed in the Computer Science Laboratory at Massachusetts General Clinical Hospital. This system is one of the first CDSS's. Its development began in 1984, and the first version was released in 1986. The Dxplain knowledge base contains a description of 2400 diseases and 5000 different medical data (symptoms, signs, epidemiology, laboratory researches and other).

Input data for Dxplain are data on patients (signs, symptoms, laboratory tests). Output data of the system is a ranked list of presumptive diagnosis. For each of the suspected diagnoses the system provides its rationale in the form of relevant publications from the PubMed database.

Pharm Expert

One of the most interesting systems developed in Russia is Pharm Expert. The system helps doctors make decisions in the preparation of treatment. The main functions of Pharm Expert are:

- detecting drug interactions and contraindications based on the personal characteristics of patient and drug route;
- warning about exceeding the maximum daily dose of drug;
- recommendations for the replacement of a conflicting drug by an optimum one;
- automatic selection of dosages, dosage forms and ways of drug introduction.

There is the possibility of automatic creation of the prescription, collect statistics about the prescribing and reporting on medical errors. The system can be integrated into existing health information systems. Pharm Expert System can analyze the electronic medical records of all common formats.

The system uses the base of medical knowledge named United Medical Knowledge Base. Content of the database is managed by experts from well-known Russian institutions. The Pharm Expert System has been tested clinically.

APPLICATION OF THE ONTOLOGICAL APPROACH TO MEDICAL DIAGNOSTICS

Most of the existing medical decision support systems are based on formalization and conceptualization of subject area [1, 5, 11, 12, 25, 26]. This approach is called «ontology or ontological model» in scientific literature.

A group of specialists headed by A.S. Kleschev developed a series of approaches to the development of ontologies in medicine [2, 13]. Subsequently, they developed an ontology of medical diagnostics [11, 12], ontology of medication treatment [7], filling the knowledge base approaches [3], formal description of a number of diseases, approach to the development of computer simulators in ophthalmology [8] and others.

A model of subject area, incl. the medicine, shall meet the following requirements:

- the knowledge base terms shall be clear to specialists of the subject area;
- the knowledge shall remain useful during the entire system operation;
- the knowledge base shall be available for enlargement;
- availability of automated result accumulation for the verification of decisions made.

The approach to formalization of medical diagnosis is based on the allocation of tasks in the doctor’s everyday activity; on the control of decisions made; on management of knowledge bases, namely specification, extension and debugging of knowledge bases.

The daily work of doctor consists of task groups, such as diagnosis, treatment planning, forecasting, monitoring and examination. Each of these task groups was assigned its own domain ontology, which consists of a description of examined object (patient) and knowledge necessary to make a decision. The first description is called ontology, the second – the ontology of knowledge. They are linked together with ontological agreements.

Knowledge Bases are based on the tasks of doctor’s everyday activity. These bases are filled up by experts and automatically, and later undergo an automated check. If the system detects a task, for the solution of which the knowledge is scarce, the task gets solved in any other way and added to the knowledge base. The newly added knowledge is checked by an expert in the subject area.

A group of specialists headed by A.S. Kleschev has developed a software system that solves the problem of determining a patient's diagnosis based on described approaches [16]. This system outputs a set of estimated diseases and explains the chosen solution. It based on the observed patient signs and symptoms.

THE STRUCTURE OF THE ONTOLOGICAL MODEL «DEGENERATIVE DISEASES OF THE SPINE AND SPINAL DEFORMITY»

Most of the modern ontological models describe the subject area in two levels. First is a meta-level, which describes the generalized concepts. Second level is a factual level, which describes the specific domain objects.

Our approach to the development of ontologies and ontological model is based on model-theoretic methods of knowledge representation [18–21]. The developed ontology and ontological model primarily intended for the generation of new knowledge and for the integration of knowledge obtained from different sources. In particular, the knowledge is generated by the evaluation of patent’s critical condition probable risk.

The knowledge presented as four levels: the level of ontological knowledge represented in the domain ontology, and three levels of substantial knowledge represented in the ontology model of the subject area.

The first level is the ontology. The ontology presented knowledge about the key (specific) domain concepts. It describes definite specification of the meaning of key concepts. It presents a number of ontological relationships between concepts, such as «is-a», «part-of», different kinds of associative links between concepts and others.

These three levels of knowledge are included in the ontological model:

1. General knowledge that are true in all instances of a given subject area. This knowledge is extracted from regulations (e.g. Ministry of Health and others), monographs on medical topics, articles and other sources. Such knowledge is formally represented in the ontological model by using of universal sentences, i.e., $\forall$-sentences. $\forall$-sentence is a sentence of the first-order predicate logic that starts with universal quantifiers $\forall$. After quantifiers, there is a quantifier-free part of the sentence.

2. Knowledge about individual patient extracted from their medical reports. This knowledge is presented in the form of precedents. Precedent model consist of a set of precedents. This is purely empirical knowledge. It is true for quite specific situations limited in space and time. Formally, such knowledge is represented in the ontological model using quantifier-free sentences. We consider such sentence as fragments of atomic diagram of an algebraic system [14].

We use the previously developed methods at the stage of ontological model filling with the information on specific patients. Besides, we use previously developed software system designed for knowledge extraction from natural language texts and fragments of building atomic diagrams of algebraic systems [14, 24].

3. Probabilistic (estimated) knowledge. This knowledge is used for automated issuance of medical advice. For example, the doctor can get recommendations for the prevention of risks of patient critical conditions. Evaluative knowledge in ontological model replenished by analysis of precedents (patient records) using existing ontological and universal knowledge, as well as general knowledge.

Formally, the probability and evaluative knowledge is represented using fuzzy models [22, 23].

Thus, this paper presents a four-level structure of the ontology and ontological model. This structure allows formalizing the subject area on four levels of knowledge representation. Level of precedents and the level of estimated knowledge have particular importance in the context of this work.

The level of precedents is knowledge of the individual patient. Its level allows describing the subject area in terms of private facts. Each such fact contains only partial information. However, if we bring information from a huge amount of different patient's private data together, we can work out general knowledge. This knowledge is presented in the ontological model on the level of probabilistic (estimated) knowledge.

The level of evaluation knowledge describes the subject area in the terms of «generalized» precedent. The role of this knowledge is the generalization of previously gained experience. Precedents (the patient's medical report) represent this experience. Evaluation knowledge is inexact; any such statement is true only with a certain probability. As a matter of fact, we are dealing with fuzzy truth-values. Therefore, we use fuzzy model for evaluation of knowledge representation [22, 23].

Ontology

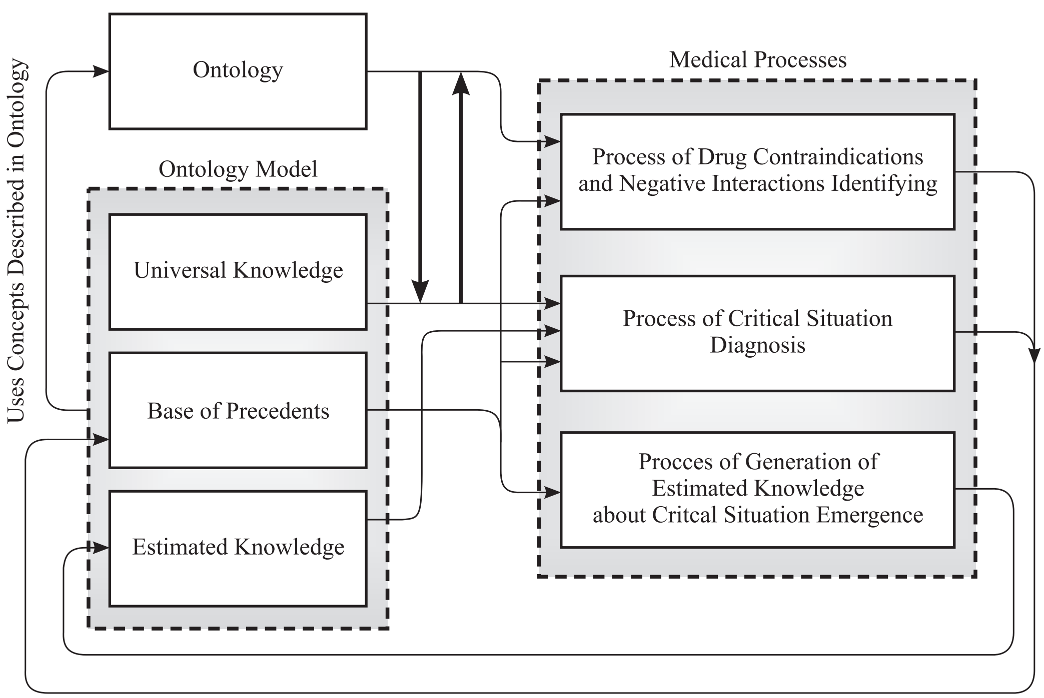
Ontology describes the key concepts of the subject area. It describes the types of objects, types of relationships between objects, object attributes. In developing our ontology, we used Kleschev's, Moskalenko's and Chernyakhovskaya's researches [11, 12].

Condition of patients is presented in the form of medical report in the ontological model (Fig. 1). Information on the results of analysis, surveys, any symptoms, some events, and anatomical and physiological characteristics of the patient are stored as true on this medical report statement. Each medical report has a time scale of non-negative integers representing the number of hours since the start of patient monitoring. All information on the results of analysis, surveys, any symptoms, occurred events is recorded in accordance with this scale.

Base of general knowledge

The database contains information of general knowledge, derived from medical regulatory documents, monographs and articles, as well as by experts of the subject area. In contrast to the ontological knowledge, these statements reflect the properties of the real world. Therefore, some of these statements can become unreliable later.

General knowledge describes the relationship between diseases and complications of critical conditions on the one hand, and the results of analysis and surveys of symptoms on the other hand. If the patient doesn't have a disease, complication or critical condition, the results of analysis and examinations are determined as the relationship between normal reactions and reactions to the impact of events.



The structure of ontology model

All links have several options of manifestation. Which of the options will take place in the situation depends on the anatomical and physiological characteristics of patient and the medical event occurred. Description of the negative drug interactions also refers to the general knowledge base. Negative drug interaction is presented as a cause-effect link where the causes are the use of several different drugs, and the consequence is a negative reaction.

Base of precedents

The base of precedents stores a lot of records of real patients. Each case record is presented as a precedent.

Let us introduce the concept of a formal precedent. Formal precedent is the description of a precedent in some formal language. It is a model containing a set of logical sentences that is true on that model. It describes the patient’s condition during the disease.

The onset of symptoms, diseases or other events is recorded in the form of a logical statement where the predicate is the predicate that indicate an action, such as «Observed». The variables are appropriate terms of symptoms, diseases, and other concepts that reflect with the condition of patient.

The meaning of all symbols that are used as variables and predicates in logical sentences must be defined in ontology. Formally, logically precedent is described in the form of fragments of atomic diagrams of algebraic systems.

Base of probabilistic knowledge

Knowledge stored at the base of probabilistic knowledge generated by the set of precedents (case records of patients). It is generated using algorithms implemented in the functional part of system. In particular, the probabilistic knowledge base contains a set of hypotheses on the probability of patient's critical conditions or complications (Fig. 2).

FUNCTION PART OF PROGRAM SYSTEM MEDONTOMODEL

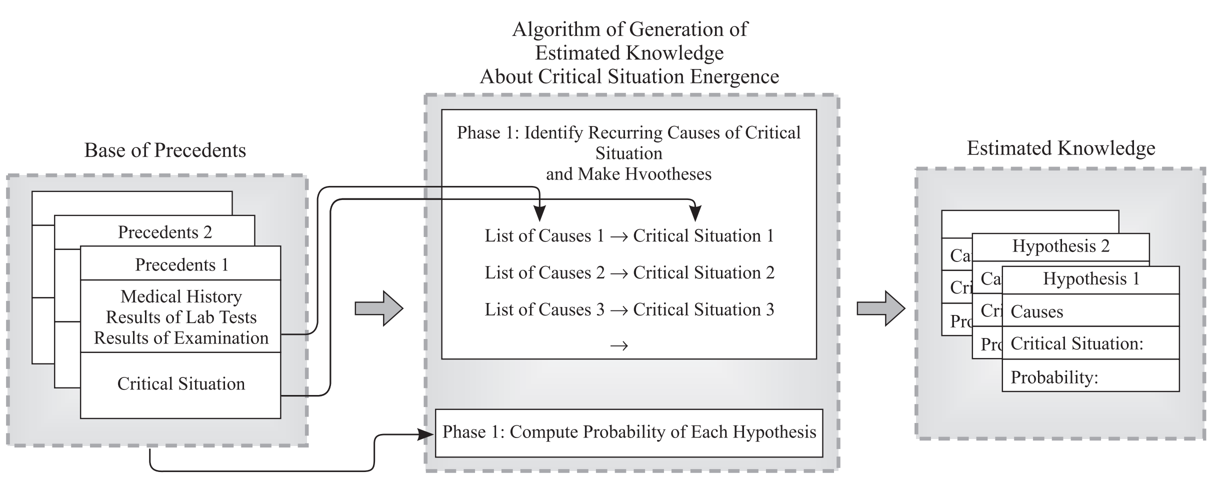
The functional part of the ontological model implements the algorithms of knowledge integration and new knowledge generation. It includes algorithms to detect the risks of critical conditions, finding drug contraindications and negative interactions, algorithms of probabilistic knowledge generation.

In the context of this work, we use the following definition of critical situation, critical states and complications. The critical situation is a situation in which there is a sharp deterioration of patient’s condition or the risk of such deterioration is increased. In particular, it’s an event of critical condition or complication.

Critical condition is an extreme degree of pathology, which requires artificial replacement or support of vital functions.

Complication is a pathological process joined to the main disease. It aggravates the typical course of the disease. This process is not due to the cause of disease, but the additional changes arising in the body in the course of disease.

Developed algorithms are aimed at minimization of the risk of critical situations. They function as follows. First, for all base of precedents (it consist of medical records of patients) an algorithm of generation of evaluating knowledge about the critical condition onset risk is used. The result of the algorithm is a set of hypotheses about the possible critical conditions. Then, for a given individual pa-



Refilling of the base of probabilistic knowledge tient's medical record the algorithm for identifying the risks of critical situations and algorithm for finding drug contraindications and negative interactions are applied. The results of these algorithms is a list of warnings to the doctor about potential negative effects of drug for the individual patient, a list of potential critical situations in this patient and, if necessary, a list of recommended further examination of the patient (Fig. 3).

Let us consider each of these algorithms in detail.

1) Algorithm of generation of evaluating knowledge about the critical condition onset risk.

The algorithm accepts for input a base of precedents, namely the medical records of different patients with critical situations set for them. The algorithm looks for repeated combinations of reasons for each critical situation and thus creates a hypothesis. Hypotheses can be positive (a critical situation occurs) and negative (a critical situation does not occur).

The output of algorithm is a set of hypotheses of cause and effect. For every critical situation, it describes a set of causes. A set of hypotheses forms a base of evaluation knowledge.

2) The algorithm for identifying the risks of critical situations.

This algorithm is based on the algorithm given in [16]. It defines a list of possible critical situations for a particular patient. In addition, algorithm recommends a list of additional surveys to find the risk of critical situations.

The algorithm uses a medical record of individual patient. For each event in the medical record a time of the event is indicated. Also, the algorithm uses ontological model and the base of probabilistic knowledge obtained after application of algorithm of generation of evaluation knowledge about the critical condition onset risks.

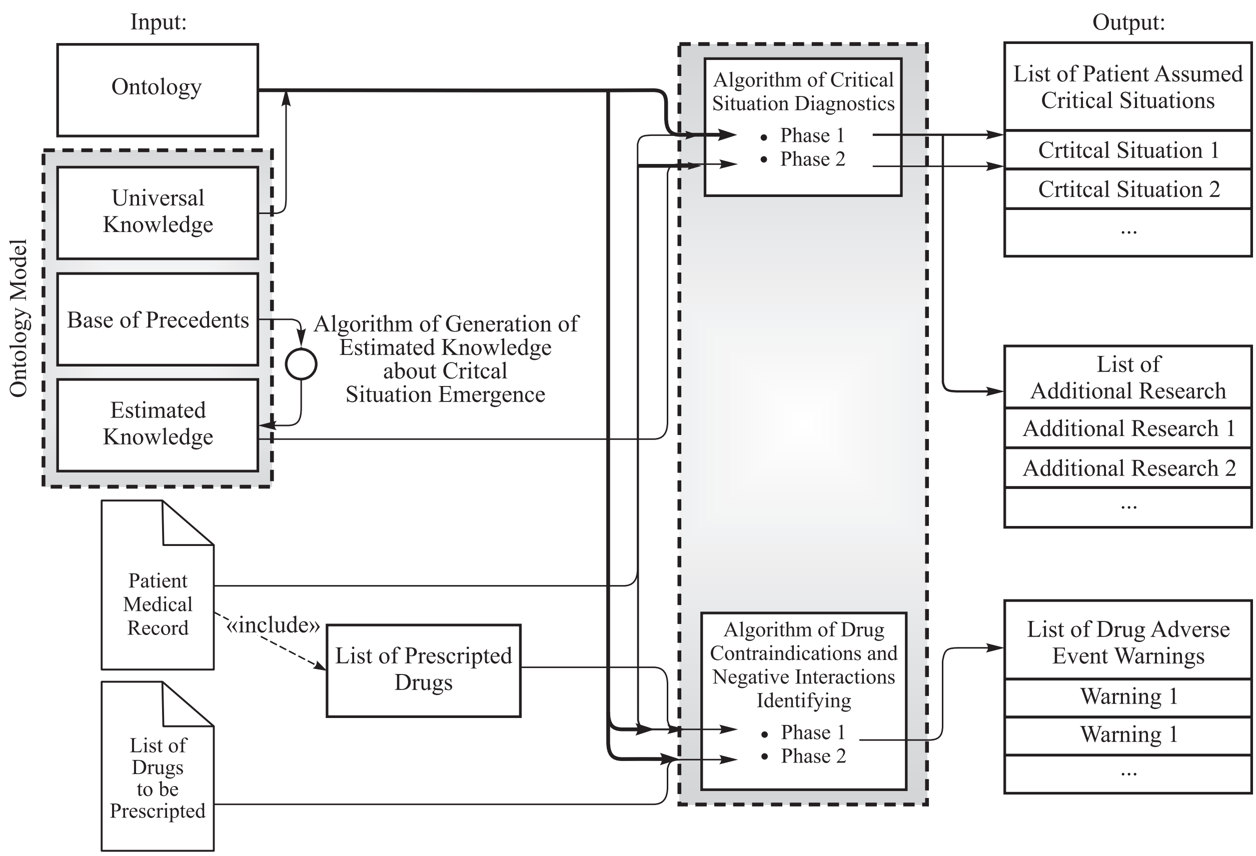
3) The algorithm for finding drug contraindications and negative interactions.

One of the most common causes of critical situations [6] and later mortality is prescribing contraindicative drugs to patient. In particular, the combination of drugs can be dangerous if it includes incompatible substances.

To prevent such cases we have developed an algorithm for finding drug contraindications and negative interactions.

Whenever a doctor prescribes a new medication to a patient, the algorithm checks the correctness of choice using the knowledge from ontology and ontological model.

For example, if contraindications read «liver disorder», the system concludes that the drug is also contraindicated to patients with hepatitis, cirrhosis



Functional part of the system

and other, because hepatitis and cirrhosis are certain cases of liver disorder.

RESULTS

The software system MedOntoModel has been tested on clinical data – medical records of more than 250 patients. As a result, the system has revealed possibility of occurring of neurological and inflammatory complications in about half of the patients. On this basis, appropriate warnings have been issued for doctors.

Approximately in one fourth of medical records system could not accurately determine whether there was a probability of critical situations or not, and requested additional information. With additional information, these patients were identified for the probability of critical situations and appropriate warnings for physicians were given.

In all cases where the possibility of occurrence of critical situations was found, the actual existence of critical situation was confirmed by the information from the patient's medical record.

In particular, clinical data of patient with a preliminary diagnosis of «osteochondrosis of the lumbar spine» were entered into the system. There were patient personal information (date of birth, sex, etc.), characteristics of the patient’s body (intolerance, height, weight, etc.), medical record, results of examination and blood tests among the entry data.

On the basis of knowledge about infectious endotoxicosis the system MedOntoModel has found symptoms of occurrence of post-operative complications in clinical data. This result has been confirmed by the presence of infectious endotoxicosis in the patient’s medical record.

In some patient prescriptions the system found contraindicated drugs and drugs with a negative interaction of active ingredients. The system issued a list of warnings to physicians in form of enumeration of drugs and whether conflicting drug or patient's contraindications to it from the medical record.

With the help of a separate sample of patient medical records the system MedOntoModel generated hypotheses about the causes of neurological complications. Generated hypotheses were added to the estimated knowledge and were used in the following work of the system. In particular, the added knowledge was used to identify the risks of neurological complications that are not described in the general knowledge.

CONCLUSION

We present methods for developing ontologies and ontological models based on the four-level model of knowledge representation. The subject domain knowledge is represented on the following levels: ontology, general knowledge, specific knowledge (precedents) and estimated (probabilistic) knowledge. On the basis of this representation the ontological model of the «Spinal deformity and degenerative diseases of the spine» subject domain has been developed.

We have developed specific algorithms for identifying the risks of critical situations, finding drug contraindications and negative interactions. These algorithms have been implemented in the software system MedOntoModel. This system helps predict critical conditions of patients and provides recommendations for doctors. It has been tested on the data from medical records of patients with spinal deformity and degenerative diseases of the spine.

ACKNOWLEDGMENTS

The reported study was partially supported by RFBR, research project No. 14-07-00903-a.

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РАЗРАБОТКА АВТОМАТИЗИРОВАННЫХ МЕТОДОВ ПРЕДУПРЕЖДЕНИЯ РИСКОВ ВОЗНИКНОВЕНИЯ КРИТИЧЕСКИХ СОСТОЯНИЙ, ОСНОВАННЫХ НА АНАЛИЗЕ ЗНАНИЙ, ИЗВЛЕЧЁННЫХ ИЗ ИСТОРИЙ БОЛЕЗНЕЙ ПАЦИЕНТОВ

Чимит Антонович НАЙДАНОВ[1], Дмитрий Евгеньевич ПАЛЬЧУНОВ[1,2], Полина Андреевна САЗОНОВА[1]

[1] Новосибирский государственный университет
630090, г. Новосибирск, ул. Пирогова, д. 2.

[2] Институт математики им. С. Л. Соболева СО РАН
630090, г. Новосибирск, пр. Академика Коптюга, д. 4.

Статья посвящена методам разработки онтологий и онтологических моделей предметных областей в медицине. Предложена четырёхуровневая модель представления знаний. На основе онтологических методов представления знаний разрабатываются алгоритмы предупреждения рисков возникновения у пациентов критических состояний и осложнений. Работа основана на теоретико-модельном подходе к представлению медицинских знаний. Используется представление знаний при помощи фрагментов атомарных диаграмм алгебраических систем, а также представление знаний о пациентах в виде булевозначной прецедентной модели. Разработаны онтология и онтологическая модель предметной области «Деформации позвоночника и дегенеративные заболевания позвоночника». Онтологическая модель содержит универсальные знания, истинные для всех пациентов, данные о конкретных пациентах и оценочные знания, служащие для выдачи рекомендаций врачу. Оценочные знания являются вероятностными гипотезами о возможности возникновения критического состояния или осложнения у пациента. Разработан алгоритм порождения оценочных знаний на основе анализа историй болезней. Реализована программная система, предназначенная для выдачи рекомендаций по предупреждению и уменьшению риска возникновения критических состояний и осложнений у пациентов. Программная система была протестирована на данных о пациентах, имеющих деформации позвоночника и дегенеративные заболевания позвоночника.

Ключевые слова: управление рисками, критические состояния, осложнения, онтологическая модель, прецедентная модель, булевозначная модель, деформации позвоночника, дегенеративные заболевания позвоночника.

Найданов Ч А *– аспирант, e-mail: naydanov.fit@yandex.ru*
Пальчунов Д Е *– д.ф.-м.н., в.н.с., e-mail: palch@math.nsc.ru*
Сазонова П А *– магистрант, e-mail: psazonova@gmail.com*