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A Specialized Shell for Intelligent Systems of Prescribing Medication

V. V. Gribova[a], *, R. I. Kovalev[a], and D. B. Okun[a]

[a] *Institute of Automation and Control Processes, Far Eastern Branch, Russian Academy of Sciences, Vladivostok, Russia*

**e-mail: gribova@iacp.dvo.ru*

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Abstract—This paper analyzes the existing decision support systems for prescription of drug therapy. The main principles of development and architecture of an intelligent clinical decision support system that is implemented as a specialized shell are described. The unique features of the system, as well as information and software components that are part of it, are shown. The presented examples demonstrate all the proposed solutions.

Keywords: ontology, knowledge base, decision support system, cloud technologies

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INTRODUCTION

Computer support for the practitioner in choosing the optimal drug therapy in accordance with the individual characteristics of the user is a very important task. The main reason is the large number of medical errors (ranked third in mortality) [1] caused by both subjective and objective factors. This is due to the huge amount of active substances, their trade names, indications, and contraindications, which must be taken into account when prescribing therapy. In addition, the choice of therapy, dosage, and duration of intake must be taken not only on the basis of the patient's diagnosis, but also considering his complaints, the results of objective, laboratory, and instrumental studies, and life history. This amount of information goes beyond the cognitive capabilities of a person, which leads to an excessive complication of the process of making the right decisions. The aggressive policy of pharmaceutical companies should also be noted, as a result of which more doctors use an irrationally large number of drugs on one patient [2]. The only effective solution that can significantly improve this situation is the introduction of systems that use artificial intelligence technologies in their work into the healthcare system and clinical medicine [3]. These systems combine all available data, clinical, biological, and genetic, and create optimal patient-oriented solutions [4].

The development of such systems is a knowledge-intensive process that requires large expenditures of time, intellectual, as well as financial resources. A huge number of nosologies make it impossible to create and maintain a separate system for each disease (or group of diseases). It is also obvious that a doctor will not be able to use many disparate implementations of this class of system in his daily practice. One of the possible approaches to solving these problems is the creation of specialized software shells, systems focused on solving a certain class of problems and containing both a set of ready-made solutions and tools for automating the creation of information and software components for their solution.

The goal of this study was to describe the principles of creating a specialized shell for building intelligent medical systems for prescribing drug treatment, the requirements for it, and the algorithm for its operation.

1. ANALYSIS AND CLASSIFICATION OF EXISTING SYSTEMS FOR SUPPORT OF A DOCTOR IN THE PRESCRIPTION OF DRUG THERAPY

The systems that assist doctors in prescribing treatment can be divided into three main classes: knowledge-based systems, machine learning-based systems, and medical information systems (MISs).

The most famous solutions, which are considered the prototype of subsequent intelligent systems in medicine, are MYCIN and ONCOCIN. The MYCIN system is designed to assist specialists in diagnosing certain infectious diseases and recommending the required amount of an antibiotic depending on the patient's body weight; ONCOCIN solves the problem of decision support in the treatment of patients receiving chemotherapy. Also, known solution is the AAPHelp expert system, which is designed to find the cause of severe pain and make a decision about the need for surgical intervention and the CASNET system for diagnosing and choosing a strategy for treating glaucoma.

Since the emergence of the first expert system, a huge number of different treatment prescribing systems have been developed. Thus, among the modern developments, we can note the following: the SPELTA system [5] for the treatment of speech and language disorders; RTP-DSS [6] for selection of a radiation therapy regimen; IndiGO (Archimedes) for the formation of individualized protocols for the diagnosis and treatment of diseases in cardiology, endocrinology, as well as a number of other systems [7–13].

The well-known advantages of such systems are assistance to doctors in the selection of therapy and the ability to generate explanations; the disadvantages are orientation to a certain group of diseases, which limits their use, especially in case of combined pathology [14]. Moreover, in real conditions, it becomes necessary to use a variety of heterogeneous systems (for various nosologies), which are usually incompatible and not interrelated. Another disadvantage of such systems is the implementation of their knowledge and data bases, which does not allow domain specialists in medicine field to carry out maintenance without an IT specialist [15].

A typical representative of the second class of systems (based on machine learning methods) is the IBM Watson system [16]. Its implementation required the use of a huge training sample, which made it possible to prescribe treatment for oncological diseases. Currently, this area of research is actively developing and models, methods, and systems that help doctors prescribe treatment for various classes of diseases have been proposed [17–21].

The main disadvantages of systems of this type are that their successful training requires a large number of well-formalized case records, which is almost impossible to provide in real conditions (the process of searching for a training sample, formalizing case records and preparing data is very long, expensive, and laborious), the lack of opportunity for generation of explanations: on the basis of what criteria a particular treatment was prescribed, as well as a focus on one or several nosologies.

The third category includes all kinds of information and reference systems; they are often also called computer-interpreted clinical guidelines. Representatives of this class include Aarogya, Caresoft Hospital Information System, Medstar HIS, MMI Mediface, Clinical Rules, Droice Labs, ISABEL, and Litmusdx [22, 23]. Such systems are based on various databases and medical reference books and use various formalisms for presentation (XML, frame-based models, task-network models, OWL-based, etc.) [24–28]. They have limited functionality and, in fact, are a reference system that helps to check the compatibility of drugs, possible dosages, nosologies for which the drug is used, tell the doctor the treatment protocol according to the reference book, without considering the patient's personal data reflecting the real clinical picture.

Analysis of existing systems in the field of treatment prescription support has shown that there are no software solutions focused on a wide range of diseases that help a doctor to prescribe treatment considering the patient's personal characteristics, which makes it important and relevant to create a software shell for creating decision support systems focused on a wide range of diseases.

2. BASIC REQUIREMENTS AND PRINCIPLES OF CREATION

Let us highlight the following basic requirements for the formation of a specialized software shell (hereinafter referred to as the system) for the prescription of drug treatment:

(1) The system must be expandable, not dependent on a specific disease (or a group of them) or an area of medicine.

This requirement is key, because it is clear that it is impossible to develop and maintain many disparate systems. Moreover, a doctor whose decision-making must be assisted by such systems cannot and must not use many different systems.

(2) Knowledge in the system must be formed and modified in the process of operation by a domain expert (or by groups of experts) based on her own experience in treating diseases (copyrighted techniques, if it is permissible in a medical institution), or in accordance with clinical guidelines (protocols) adopted in the country.

This requirement imposes, first, a condition on the form of representation of knowledge about treatment (it must be understandable by experts), and secondly, on the tools (editors) for its creation and maintenance (they must shield the user from the peculiarities of the languages of knowledge representation and have an intuitive interface).

(3) Tools for creating knowledge bases, as well as ready-made decision support systems must be available to the wide professional community without the need for additional installation on user computers.

(4) The system must prescribe treatment considering the personal characteristics of a patient, generating detailed justifications for decisions.

One of the solutions to meet these requirements is to use the ontological approach, which, as noted in

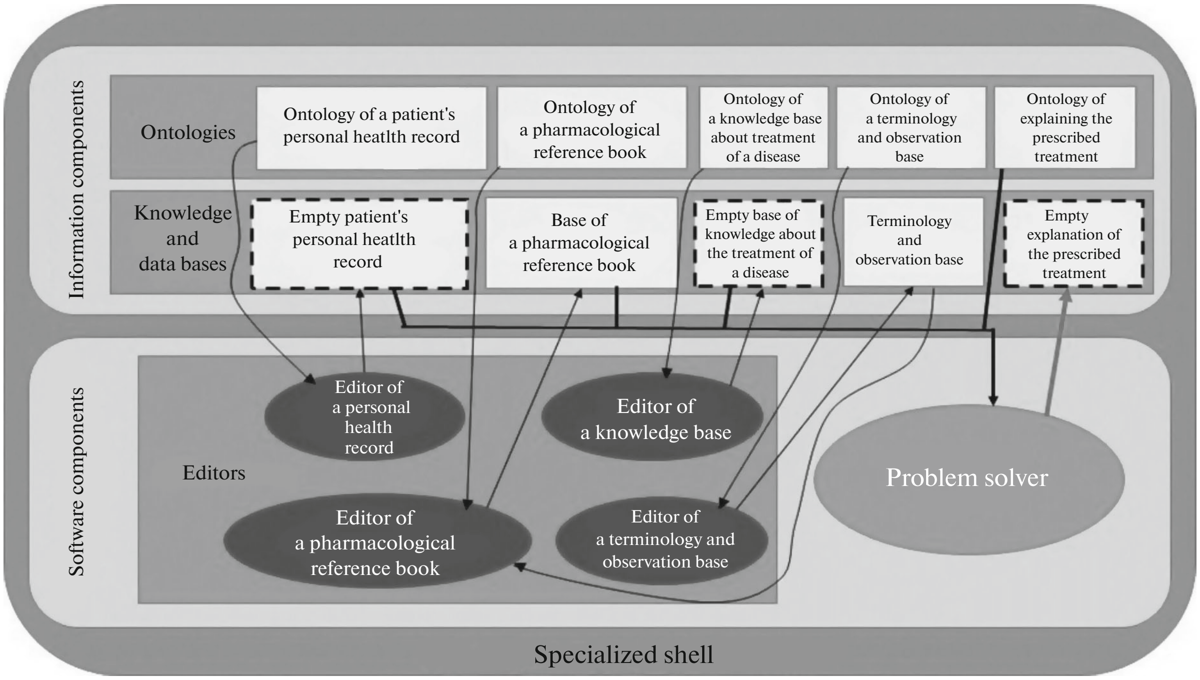

Fig. 1. The conceptual architecture of the custom shell.

[29], has become the de facto standard in the development of systems based on knowledge bases. In the presence of appropriate editors (driven by ontology), it will ensure the comprehensibility of the formation of knowledge, the possibility of implementing a single (unified) ontology-oriented solver, as well as the formation of a detailed explanation. To meet requirement 3, the system must be implemented as a cloud service.

3. THE ARCHITECTURE OF A SPECIALIZED INTELLIGENT SHELL FOR PRESCRIPTION OF DRUG THERAPY

The intelligent shell for prescription of drug therapy includes information and software components (Fig. 1). Information components include ontologies, as well as databases and knowledge bases generated on their basis, and software includes knowledge and data editors, as well as a problem solver.

The shell implementation tool is the IACPaaS platform (https://iacpaas.dvo.ru) [30]. It supports the creation of knowledge base systems based on a two-tier ontological approach. Its fundamental features and differences from other approaches to the formation of ontological knowledge bases are as follows:

– Explicit separation of the ontology from the knowledge base formed on its basis, i.e., the ontology does not contain domain knowledge. In this case, the knowledge base formed as a separate information resource is formed in terms of ontology. This is an extremely important property for the creation of shells, since one ontology can be used as a basis to form many different knowledge bases separated from each other and a single solver, which is independent of a specific content (knowledge base). In fact, the knowledge ontology acts as a formal parameter of the solver, while the knowledge base acts as its actual parameter. Undoubtedly, the creation of the ontology is a separate, complex creative process; the success of the product as a whole depends on the quality of its creation.

– Ontologies, knowledge/data bases are represented by semantic networks, which, according to [31], provides an effective display of the conceptual system of a person.

– The developed language for describing ontologies [32] allows one not only to specify the structure and terminology of the domain, but also, using language specifiers and delimiters, to determine the rules for generating target knowledge bases and ontological agreements that must be met during their construction.

4. THE INFORMATION COMPONENTS OF THE DEVELOPED SHELL

To achieve this goal, the following information components were developed [33, 34]: an ontology of knowledge about the treatment of diseases, which allows describing various models and schemes of drug

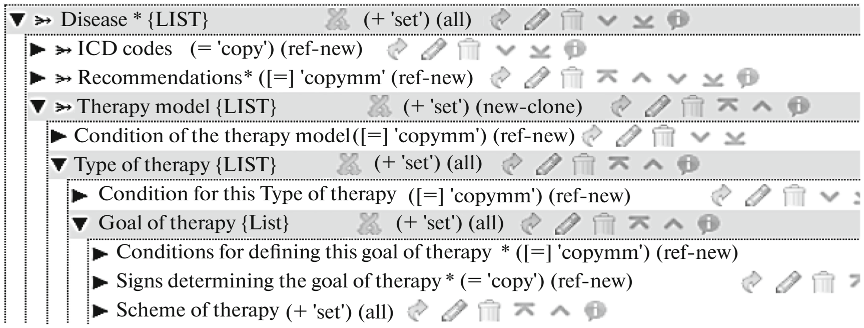

Fig. 2. A fragment of the ontology of the knowledge base on the treatment of diseases hosted on the IACPaaS cloud platform.

therapy considering the patient's personal data, features of the clinical picture of a disease, drug compatibility; ontology of a pharmacological reference book; an ontology of a base of medical terminology and observations; and an ontology of the patient's personal medical electronic record. Based on these ontologies, information resources have been created that make it possible to form modern knowledge about the treatment of a disease regardless of the clinical section of medicine and open the possibility of implementing treatment programs considering the patient's personal data.

The ontology of knowledge about the treatment of diseases makes it possible to form knowledge of the treatment of a specific disease or a certain group of diseases that have common pathogenetic principles, an etiological component, or clinically important symptomatic manifestations. To implement this idea, the following nodes are provided in the ontology.

Disease is a section of the ontology that defines the name of the pathological process and combines all the elements of knowledge about its treatment. The structure of the section contains the following vertices: *ICD codes* determine the code according to ICD-10; Recommendations are a generalized list of basic rules for correcting lifestyle during treatment; the *Therapy Model* is a logically complete concept of the principles and scope of therapy for a given pathological process, including the *Type*, *Purpose*, and *Regimen of Therapy*. The key element of the ontology is a complexly structured block of conditions that accompanies each section of the ontology and allows one to describe in a formal representation the necessary clinical criteria that determine the conditions for its application in the treatment of a given disease (Fig. 2).

The type of therapy is a term that unites an entire class of concepts that directly describes the type of therapy itself: etiotropic, pathogenetic, symptomatic, empirical, and other types of therapy.

The purpose of therapy is a class of concepts that characterize the goal of the treatment being carried out: hemostatic therapy, antiemetic therapy, antipruritic, detoxification, or mucolytic therapy. The signs that determine the purpose of therapy are the description of clinical data that allow recognizing the achievement of the purposes of therapy.

The therapy regimen is a term that defines the list of active substances, their combinations, and the mode of administration and dosage of drugs for the optimal treatment of the disease. This section of the ontology is structured as follows: The conditions for the use of a given group of drugs, the group of alternatively used drugs, and drugs used in a complex manner.

The group of alternatively used drugs contains the following vertices: active substance and jointly used drugs. Active substance is a list of drugs, from which one drug with the best characteristics for a specific clinical case is selected. Jointly used drugs are a group of drugs that must be used jointly to achieve a clinical result.

Each drug is described by a group of terms that define its clinical need: *Prescription option*, including the elements: *Dosage*, *Form of production*, *Method of application*, *Frequency of use*, *Duration of use*. In addition, the following information is indicated for each drug: Control points for evaluating the effectiveness of therapy, Control of expected side effects, Condition for the active substance, and Trade names of the active substance. *Control points for evaluating the effectiveness of therapy* is an ontology term that allows monitoring the use of an active substance. It includes descriptions of the symptom(s) for monitoring treatment. *Control of expected side effects* is an ontology term that defines the safety of drug use and includes a feature that describes a variant of a side/undesirable effect and the frequency of its control (Fig. 3a).

Drugs used in a complex manner, this ontology section allows one to describe knowledge about multi-

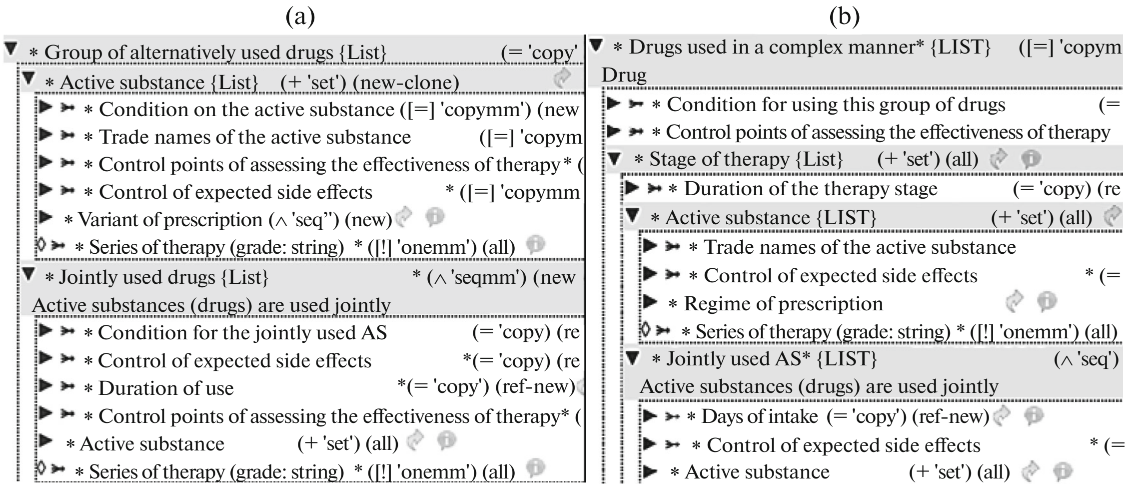

Fig. 3. A fragment of the ontology of the knowledge base on the treatment of diseases: (a) a group of alternatively used drugs; (b) drugs used in a complex manner.

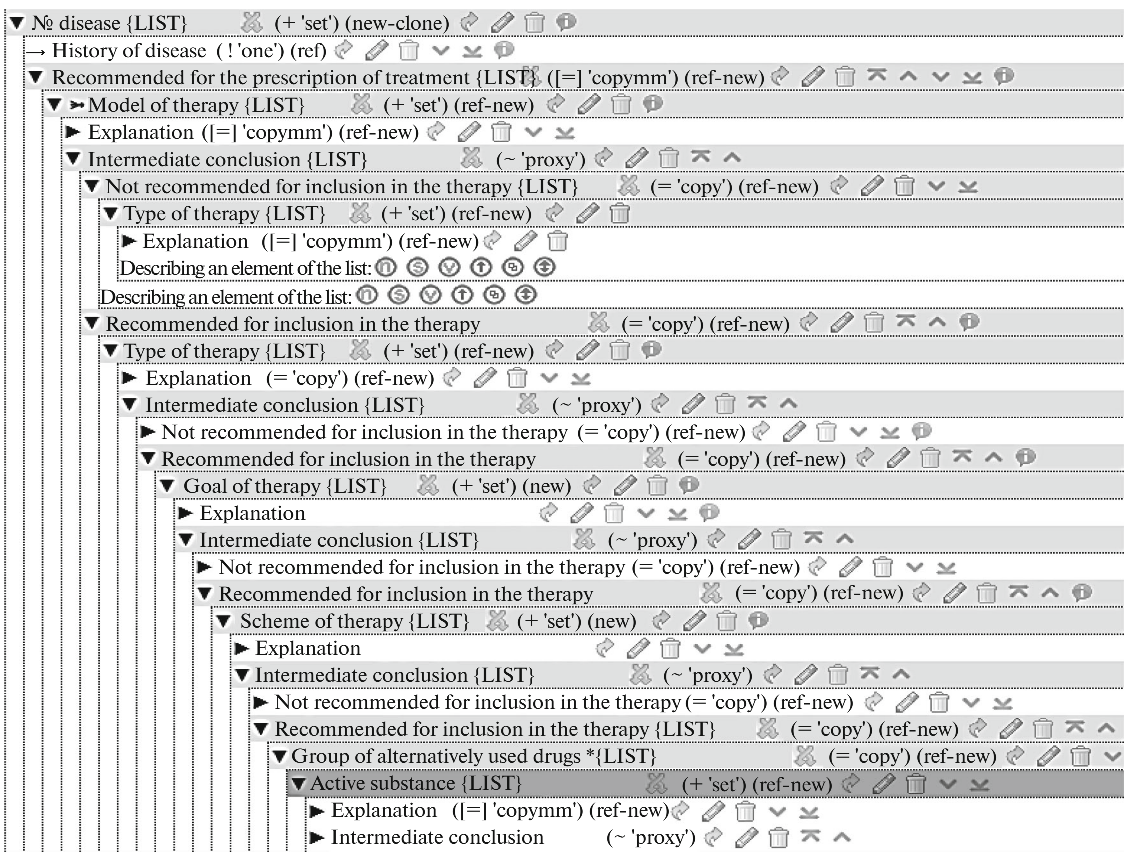

Fig. 4. The structure of the ontology of the explanation of the prescribed treatment.

component and multistage drug therapy, which is based on the structure of drug description (Fig. 3b).

The ontology of an explanation of the prescribed treatment describes the structure of the explanation of the result of the system operation. The structure of the ontology is shown in Fig. 4. An explanation generated from the ontology forms three main blocks:

• the prescribed treatment (a set of active substances with an indication of the form, dosage (daily and course), as well as the explanation of what goals

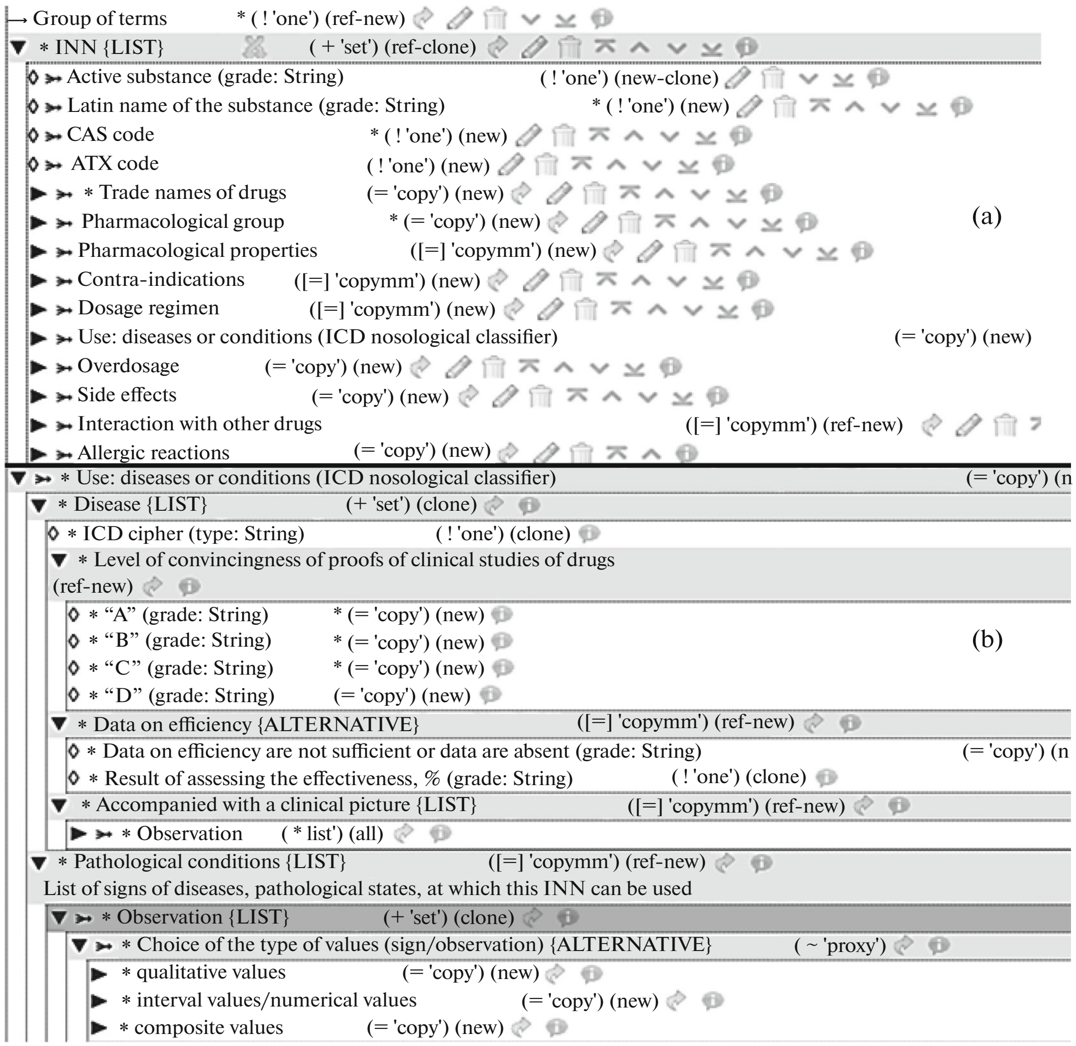

Fig. 5. The ontology of a pharmacological reference book: (a) the main sections of the ontology; (b) the Application block of the ontology.

are achieved by the prescription of each of the active substances).

• the nonprescribed treatment, a set of active substances rejected by the system with an indication of why this active substance has not been prescribed for a given patient (based on the analysis of his electronic record).

• a set of active substances, for the prescription of which certain initial data from the electronic record were not enough, for example, information about diseases and the presence of allergies to medicines.

The ontology of a pharmacological reference book includes elements that make it possible to describe the drug directly in the form of an international nonproprietary name (INN) or a fixed combination of INN, as well as a section of specific pharmacological terms. The main sections of the ontology are presented in Fig. 5a.

An important component of this ontology, which distinguishes it from others, is a formal description of the sets of possible signs and their values (ranges of values), which are the patient's complaints, the results of laboratory or instrumental studies, and various factors from the anamnesis of their life. Formally described signs are used to indicate conditions for contraindications, side effects of drugs, and possible allergic reactions.

Another characteristic feature of the ontology of a pharmacological reference book is the block Application: diseases or conditions (ICD nosological classifier) (Fig. 5b). It is necessary to describe the level of effectiveness of using a given drug for a specific disease or pathological condition. This section is important for choosing the most effective drugs from the many possible ones when prescribing treatment.

The ontology of the base of medical terminology and observations describes the structure of medical terms and observations used in practice, as well as the structure of auxiliary terminology that is necessary for the integrity of the description of medical knowledge. The structure of the ontology uses synonymy.

To simplify the search and navigation of terms, they can be composed of term groups, which, in turn, can also contain term groups. Each term is characterized by its own name and many possible synonyms: <(*term name i*, set of *synonyms for term i*)>.

Observations have the following structure: *Observation Group* and *Factor Group*. The observation group contains many grouped signs. Grouping the signs of the observation group will optimize the structure of medical terminology: *Complaints*, *Objective research data*, *Laboratory research data* and *Instrumental research data*. The group of signs has many signs, which can be of the following types: <*Simple sign*, *Composite sing*, *Sign considering the unit of measurement, gender, and age*>.

The factor group allows not only to describe individual elements: *Factor*, *Fact or event*, but also to group them.

A *sign*, *factor,* and *fact or event* can have qualitative, quantitative or composite values. If the value is composite, then it consists of many characteristics. For example, the sign *Headache* in the base of medical terminology and observations is composite and consists of the following characteristics: presence, localization, intensity, severity, frequency, time of occurrence, etc. The base of medical terminology and observations, which is formed according to the corresponding ontology, is a universal resource used for the formation of diagnostic and therapeutic knowledge bases in various fields of medicine. Currently, the base of medical terminology formed by the ontology contains more than 27000 different concepts.

The ontology of a personal health record (PHR) sets the structure for describing a person's health throughout his life. This structure allows one to describe all cases of medical care and preventive measures and promptly provide access to information about studies, cases of outpatient, inpatient and sanatorium-and-spa treatment of the patient, and ambulance calls; it contains a section on contraindications to the use of certain types of treatment for a specific patient and a list of intolerable drugs. The resource created on the basis of this ontology will allow one to quickly find existing information and add new information about all cases of medical care of the patient, as well as generate medical documents in an automated mode. Unlike the existing PHRs, which are part of most medical information systems (MISs), all its structural elements are presented formally (in the MISs, most PHR sections have a text description, for example, complaints, life history, etc.). The names of the terms used (signs, factors, and events), as well as their meanings are selected from the base of medical terminology described above.

Thus, the shell includes a set of ontologies, bases of a pharmacological reference book, ontologies of terminology and observations, in terms of which knowledge bases for the treatment of diseases and an electronic patient record are formed. It is important to note that the use of the ontological approach makes it possible to supplement the indicated bases and knowledge bases without changing the problem solver.

5. THE SOFTWARE COMPONENTS OF THE DEVELOPED SHELL

The software components of the shell are knowledge and data editing tools, as well as the problem solver.

Knowledge and data editing tools are represented by a number of editors (see Fig. 1). The knowledge base editor that is automatically generated according to the ontology (the generator of editors is included in the platform) ensures the generation of target resources (knowledge and data bases) in accordance with the specified rules and controls the implementation of ontological agreements. Moreover, the completeness of the generated knowledge base is automatically checked. Additional means that ensure the quality of knowledge is its formation on the basis of a single terminological base, which provides an unambiguous interpretation of the formed knowledge by the medical community (while the base of terminology and observations allows for synonymy). The platform means also have tools for verifying the knowledge base on the basis of reference examples (in this case, these are PHRs). Thus, the formal completeness of the knowledge base, the syntactic correctness of the formed knowledge base, and, partially, the semantic correctness, are provided by the platform. An additional check of semantic correctness, which cannot be performed automatically, is performed by subject matter experts. First, they can view the knowledge base in a convenient form (there are three ways to visualize the knowledge base), as well as check its correctness using testing on a PHR (Fig. 6). The detailed explanation generated by the system greatly simplifies this process.

The problem solver is an ontological reasoner, which goes through the declarative knowledge base about the treatment of a certain disease in accordance

Fig. 6. The interface of the editor of the knowledge base about the treatment of anemia.

with the ontology in order to prescribe a personalized treatment and compares the information from the knowledge base with the input information, which is the patient's personal medical record (PHR). The task of such a "round" is to search for elements (observations) in the PHR that affect the prescription of treatment and compare their values with the ranges of values of the corresponding observations in the knowledge base with the purpose of building a personalized prescription of drugs with an indication of their one-time, daily, course dosage, compatibility, and features of conducting a course of treatment, as well as constructing a detailed explanation of why this active substance has been prescribed/not prescribed and what additional observations must be carried out in order to prescribe the drugs that are necessary in case of this disease.

The solver is implemented using a multiagent approach and consists of two agents: root and working agents. The root agent is the manager; it initializes (starts) the work of the system through a message to the working agent, passing all input information resources to it and terminates it based on a message from the working agent. The working agent directly implements the main business logic: it receives a personal medical record as input, reads the meaning of the term <Final diagnosis>, and searches for this value in the knowledge base on the treatment of diseases. In accordance with the knowledge base about the disease, it analyzes the models of therapy, their types,

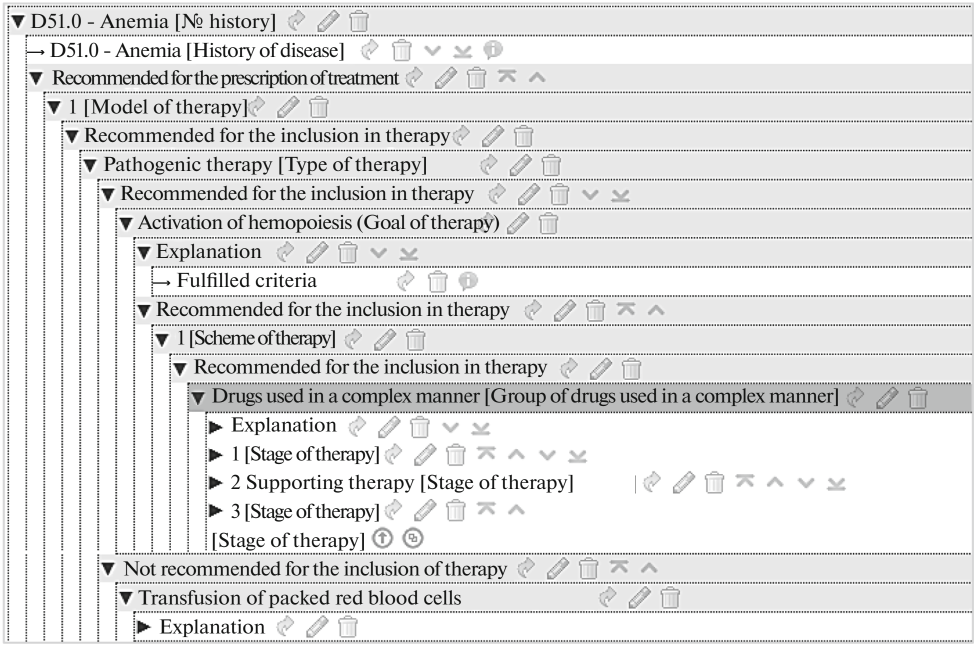

Fig. 7. Explanation of the prescribed treatment.

goals, and intake schemes at each step, checking the appropriate conditions, whose values are analyzed using a medical electronic record. As a result of the work of this agent an information resource with a detailed explanation of the prescribed treatment for a particular patient is formed (Fig. 7), or an explanation is formed why some active substance has not been prescribed: what signs (from the life history, laboratory, instrumental, objective research methods, etc.) are not enough to prescribe treatment.

CONCLUSIONS

This paper provides an overview of the current development of systems that help a doctor to prescribe drug treatment, considering a patient's personal data (life history, concomitant diseases, age, complaints, etc.). The existing systems are divided into three main classes, their characteristics are given, and examples of the systems, their features are presented. The main disadvantages of the proposed systems are their narrow focus on a specific disease or a narrow group of diseases, as well as the impossibility for subject matter experts to independently form and maintain knowledge bases. To eliminate these shortcomings, a new approach and architecture of a specialized shell is proposed for creating decision-support systems in prescribing drug therapy, considering a patient's personal characteristics. The shell is based on the ontological approach and does not depend on a specific nosology.

The features of the developed shell, which fundamentally distinguish it from other medical systems, are as follows:

– Focus on a wide range of diseases; to implement a specific system based on the shell, it must be replenished with relevant knowledge about the treatment of the disease.

– All information resources are formed using knowledge/data editors controlled by appropriate ontologies, which corresponds to the modern approach to the development of intelligent systems; the use of the ontological approach and editor with several versions of the user interface controlled by the ontology makes it possible to include subject matter experts in the development of a medical intelligent system.

– Ontologies, databases, and knowledge bases have a semantic representation (hierarchical semantic networks).

– The presence of the ontology, according to which knowledge bases are formed, controls the integrity of the knowledge base; it is formed considering semantic and syntactic restrictions, which significantly reduce the number of errors in the experts forming the knowledge base and simplify its subsequent debugging.

– The knowledge base is separated from the program code, which allows subject matter experts to ensure its continuous improvement without the participation of programmers (without changing the ontology-oriented solver).

– The result of the operation of the system is not only possible treatment options that correspond to the patient's personal characteristics (at each step of choosing a therapy, the prescription conditions are checked), but also a detailed explanation of why a particular drug has been prescribed/not prescribed, or a hint to the doctor about the need to conduct additional research for the prescription of therapy.

– The presence of the unified ontology for the formation of knowledge bases about treatment planning and the ontological solver allows prescribing treatment for combined pathologies (several diseases at the same time); in addition, possible duplication of prescriptions is monitored.

– The ontology allows description of several models of therapy for the treatment of one disease, which allows one not only to verify the knowledge base with the accumulation of precedents, but also to provide an analysis of the effectiveness of therapy.

– The shell and environment for its management are implemented as cloud services. This allows one to increase the audience of users, as well as develop knowledge bases on treatment for subject matter experts, regardless of their geographic location.

On the basis of the developed shell, applied systems for prescribing drug treatment of gastric ulcer and duodenal ulcer, lambliosis, and symptomatic therapy of cognitive impairments have already been implemented. At the request of the Association of Non-Governmental Medical Institutions of China, this shell was used to implement a system for prescribing the treatment of COVID-19 coronavirus infection by the methods of traditional Chinese therapy. This system was implemented at the height of the coronavirus epidemic (early February 2020) for several days. Information about this system was covered in the Russian and Chinese media [35–37]. The shell made it possible to implement the ready-to-use system in a short time. It should be noted that the system was implemented in Chinese (the IACPaaS platform supports automatic translation into Chinese and English, and experts can manually make changes in case of incorrect automatic translation). The shell also showed its applicability for prescribing treatment by the methods of traditional Chinese therapy. The knowledge base was developed based on the Diagnosis and Treatment Protocols for Patients with Novel Coronavirus Pneumonia prepared by the General Office of National Health Commission of China.

Currently, systems for the prescription of treatment for a number of nosologies are being implemented on the basis of the shell. The team of authors continues to work on improving the shell. In the future, it is planned to create subsystems for the inductive formation of a knowledge base based on a training sample (PHR), as well as to form a knowledge base from texts of clinical guidelines.

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REFERENCES

1. Makary, M.A. and Daniel, M., Medical error—the third leading cause of death in the US, *BMJ*, 2016, p. 353. https://doi.org/10.1136/bmj.i2139
2. Masnoon, N., Shakib, S., Kalisch-Ellett, L., and Caughey, G.E., What is polypharmacy? A systematic review of definitions, *BMC Geriatr.*, 2017, vol. 17, p. 230. https://doi.org/10.1186/s12877-017-0621-2
3. Lysaght, T., Lim, H. Y., Xafis, V., and Ngiam, K. Y., AI-assisted decision-making in healthcare, *Asian Bioethics Rev.*, 2019, vol. 11, no. 3, pp. 299–314. https://doi.org/10.1007/s41649-019-00096-0
4. Kobrinskij, B.A., Features of medical intelligent systems, *Informatsionno-izmeritel'nye i upravlyayushchie sistemy*, 2013, vol. 11, no. 5, pp. 58–64.
5. Robles-Bykbaev, V.E., López-Nores, M., Pazos-Arias, J.J., and Arévalo-Lucero, D., SPELTA: An expert system to generate therapy plans for speech and language disorders, *Expert Syst. Appl.*, 2015, vol. 42, no. 21, pp. 7641–7651. https://doi.org/10.1016/j.eswa.2015.06.011
6. Watkins, W., Kowalchuk, R.O., Luu, A.N., and Siebers, J.V., A radiation therapy treatment planning decision support system (RTP-DSS) for selecting patient-specific optimal treatment, *Int. J. Radiat. Oncol., Biol., Phys., Suppl.*, 2016, vol. 96, no. 2, p. S82. https://doi.org/10.1016/j.ijrobp.2016.06.207
7. Khozeimeh, F., Alizadehsani, R., Roshanzamir, M., Khosravi, A. Layegh, P., and Nahavandi, S., An expert system for selecting wart treatment method, *Comput. Biol. Med.*, 2017, vol. 81, pp. 167–175. https://doi.org/10.1016/j.compbiomed.2017.01.001
8. Jiang, X., Wells, A., Brufsky, A., and Neapolitan, R., A clinical decision support system learned from data to personalize treatment recommendations towards preventing breast cancer metastasis, *PLoS One*, 2019, vol. 14, no. 3, p. e0213292. https://doi.org/10.1371/journal.pone.0213292
9. Abu-Naser, S. and Al-Dahdooh, R., Lower back pain expert system diagnosis and treatment, *J. Multidiscip. Eng. Sci. Stud.*, 2016, vol. 2, no. 4, pp. 441–446.
10. Zhang, Y.F., Gou, L., Tian, Y., Li, T.-C., Zhang, M., and Li, J.-S., Design and development of a sharable clinical decision support system based on a semantic web service framework, *J. Med. Syst.*, 2016, vol. 40,

no. 5, p. 118.
https://doi.org/10.1007/s10916-016-0472-y

11. Goldstein, M.K., Hoffman, B.B., Coleman, R.W., Tu., S.W., Shankar, R.D., O'Connor, M., Martins, S., Advani, A., and Musen, M.A., Patient safety in guideline-based decision support for hypertension management: ATHENA DSS, *Proc. AMIA Symp.*, 2001, vol. 2001, pp. 214–218.
12. Peleg, M., Shahar, Y., Quaglini, S., Fux, A., García-Sáez, G., Goldstein, A., Elena Hernando, M., Klimov, D., Martínez-Sarriegui, I., Napolitano, C., Parimbelli, E., Rigla, M., Sacchi, L., Shalom, E., and Soffer, P., MobiGuide: a personalized and patient-centric decision-support system and its evaluation in the atrial fibrillation and gestational diabetes domains, *User Mod. User-Adapted Interact.*, 2017, vol. 27, no. 2, pp. 159–213. https://doi.org/10.1007/s11257-017-9190-5
13. Koutkias, V., Kilintzis, V., Stalidis, G., Lazou, K., Niès, J., Durand-Texte, L., McNair, P., Beuscart, R., and Maglaveras, N., Knowledge engineering for adverse drug event prevention: On the design and development of a uniform, contextualized and sustainable knowledge-based framework, *J. Biomed. Inf.*, 2012, vol. 45, no. 3, pp. 495–506. https://doi.org/10.1016/j.jbi.2012.01.007
14. Bilici, E., Despotou, G., and Arvanitis, T.N., The use of computer-interpretable clinical guidelines to manage care complexities of patients with multimorbid conditions: A review, *Digital Health*, 2018, vol. 4, pp. 1–21. https://doi.org/10.1177/2055207618804927
15. Zacharias, V., *Development and verification of rule based systems—A survey of developers, Rule Representation, Interchange and Reasoning on the Web. RuleML 2008*, Bassiliades, N., Governatori, G., and Paschke, A., Eds., Lect. Notes Comput. Sci., vol. 5321, Berlin: Springer, 2008, pp. 6–16. https://doi.org/10.1007/978-3-540-88808-6_4
16. IBM Watson graduated a medical institute and took up a job. http://habrahabr.ru/company/ibm/blog/169067/. Cited May 25, 2020.
17. Rajkomar, A., Dean, J., and Kohane, I., Machine learning in medicine, *N. Engl. J. Med.*, 2019, vol. 380, no. 14, pp. 1347–1358. https://doi.org/10.1056/NEJMra1814259
18. Yahyaoui, A., Jamil, A., Rasheed, J., and Yesiltepe, M., A decision support system for diabetes prediction using machine learning and deep learning techniques, *2019 1st Int. Informatic and Software Engineering Conf. (UBMYK), Ankara*, 2019. https://doi.org/10.1109/UBMYK48245.2019.8965556
19. Anakal, S. and Sandhya, P., Clinical decision support system for chronic obstructive pulmonary disease using machine learning techniques, *2017 Int. Conf. on Electrical, Electronics, Communication, Computer, and Optimization Techniques (ICEEECCOT), Mysuru, India*, 2018. https://doi.org/10.1109/ICEEECCOT.2017.8284601
20. Ray, M. and Qudwai, U., Machine learning in medicine: calculating the minimum dose of haemodialysis using neural networks, *Ann. Technical Conf. IEEE Region 5, 2003, New Orleans,* 2003, pp. 23–27. https://doi.org/10.1109/REG5.2003.1199705
21. Hwang, Y., Oh, M., Jang, G., Lee, T., Park, C., Ahn, J., and Yoon, Y., Identifying the common genetic networks of ADR (adverse drug reaction) clusters and developing an ADR classification model, *Mol. BioSyst.*, 2017, vol. 13, no. 9, pp. 1788–1796. https://doi.org/10.1039/C7MB00059F
22. Chanchal, S., What is hospital information system & our top 15 picks. www.softwaresuggest.com/blog/top-hospital-information-system/. Cited July 28, 2020.
23. Shahsavarani, A.M., Abadi, E.A.M., Kalkhoran, M.H., Jafari, S., and Qaranli, S., Clinical decision support systems (CDSSs): State of the art review of literature, *Int. J. Med. Rev.*, 2015, vol. 2, no. 4, pp. 299–308.
24. Jenders, R.A., Adlassnig, K.-P., Fehre, K., and Haug, P., Evolution of the Arden Syntax: Key technical issues from the standards development organization perspective, *Artif. Intell. Med.*, 2018, vol. 92, pp. 10–14. https://doi.org/10.1016/j.artmed.2016.08.001
25. Peleg, M., Tu, S., Bury, J., Ciccarese, P., Fox, J., Greenes, R.A., Hall, R., Johnson, P.D., Jones, N., Kumar, A., Miksch, S., Quaglini, S., Seyfang, A., Shortliffe, E.H., and Stefanelli, M., Comparing computer-interpretable guideline models: A case-study approach, *J. Am. Med. Inf. Assoc.*, 2003, vol. 10, no. 1, pp. 52–68. https://doi.org/10.1197/jamia.M1135
26. Shiffman, R.N., Agrawal, A., Deshpande, A.M., and Gershkovich, P., An approach to guideline implementation with gem, MEDINFO 2001, Patel, V., Ed., Studies in Health Technology and Informatics, vol. 84, Amsterdam: IOS Press, 2001, pp. 271–275. https://doi.org/10.3233/978-1-60750-928-8-271
27. Peleg, M., Shahar, Y., Quaglini, S., Broens, T., Budasu, R., Fung, N., Fux, A., García-Sáez, G., Goldstein, A., González-Ferrera, A., Hermens, H., Elena Hernando, M., Jones, V., Klebanov, G., Klimov, D., Knoppel, D., Larburu, N., Marcos, C., Martínez-Sarrieguig, I., Napolitano, C., Pallàsi, À., Palomares, A., Parimbelli, E., Pons, B. Rigla, M. Sacchi, L., Shalom, E., Soffer, P., and van Schooten, B., Assessment of a personalized and distributed patient guidance system, *Int. J. Med. Inf.*, 2017, vol. 101, pp. 108–130. https://doi.org/10.1016/j.ijmedinf.2017.02.010
28. Jafarpour, B., Abidi, S.R., and Abidi, S.S.R., Exploiting semantic web technologies to develop owl-based clinical practice guideline execution engines, *IEEE J. Biomed. Health Inf.*, 2014, vol. 20, no. 1, pp. 388–398. https://doi.org/10.1109/JBHI.2014.2383840
29. Gavrilova, T.A. and Strahovich, J.V., Visual-analytical thinking and intelligence maps in ontology engineering, *Ontol. Proekt.*, 2020, vol. 10, no. 1, pp. 87–99. https://doi.org/10.18287/2223-9537-2020-10-1-87-99
30. Gribova, V.V., Kleschev, A.S., Moskalenko, F.M., Timchenko, V.A., Fedorishchev, L.A., and Shalfeeva, E.A., IACPaaS cloud platform for the development of intelligent service shells: current state and future evo-

lution, *Software Syst.*, 2018, vol. 31, no. 3, pp. 527–536. https://doi.org/10.15827/0236-235X.031.3.527-536

31. Ausubel, D.P., *Educational Psychology: A Cognitive View*, New York: Holt, Rinehart and Winston, 1968.

32. Gribova, V.V., Kleshchev, A.S., Moskalenko, F.M., and Timchenko, V.A., A model for generation of directed graphs of information by the directed graph of metainformation for a two_level model of information units with a complex structure, *Autom. Doc. Math. Linguist.* 2015, vol. 49, no. 6, pp. 221–231. https://doi.org/10.3103/S0005105515060059

33. Gribova, V.V. and Okun, D.B., Ontologies for the formation of knowledge bases about disease treatment in medical intelligent systems, *Inf. Syst. Uprav.*, 2018, no. 3, pp. 71–80. https://doi.org/10.22250/isu.2018.57.71-80

34. Gribova, V.V., Petryaeva, M.V., Okun, D.B., and Tarasov, A.V., Software toolkit for creating intelligent systems in practical and educational medicine, *2018 3rd Russian-Pacific Conf. on Computer Technology and Applications (RPC), Vladivostok, Russia*, 2018. https://doi.org/10.1109/RPC.2018.8482130

35. Bondarenko, A., Artificial intelligence makes a diagnosis, *Ross. Gaz.*, 2020, no. 23. https://rg.ru/2020/02/04/reg-dfo/uchenye-privlekut-iskusstvennyj-intellekt-dlia-diagnostiki-koronavirusa.html. Cited August 30, 2020.

36. Assistant in treating coronavirus with artificial intelligence: Know-how from Primorye, 2020. www.vesti.ru/videos/show/vid/825790. Cited August 23, 2020.

37. Chinese doctors in Wuhan will use coronavirus diagnosis software developed in Primorye, 2020. http://www.interfax-russia.ru/FarEast/news.asp?sec=1671&id=1101675. Cited August 23, 2020.

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