

PROVIDING FLEXIBLE SOLUTIONS FOR CONTINOUS SERVICES (SEAMLESS) IN HEALTHCARE

Doctoral Thesis – Summary

for obtaining the scientific title of Doctor at the Politehnica University of Timisoara in the field of doctoral studies Computer Science and Information Technology

author inf. Oana Sorina LUPȘE

Scientific Superviser Prof.univ.dr.eng. Lăcrămioara Stoicu-Tivadar

October 2018

The PhD thesis with the title "Providing flexible solutions for continuous services (seamless) in healthcare" aims improving the medical act using new technologies, proposing techniques and new algorithms to support the work of doctors in treating patients. The research of the thesis reflects the use of information technology both in the field of general medicine and customized on certain specializations.

Chapter 1 presents the motivation for the proposed theme, the objectives and structure of the PhD thesis. The areas where the author made contributions during the thesis are the following:

- IT is supporting pediatrics, the branch dealing with monitoring children from birth until the age of 18 years. The field of pediatrics is very important in medicine because it is one of the most complex and sensitive specialties. Small children need special care as well as medication based on age and weight. Information technology support for this important area ensures high precision and quality of the medical act through ubiquitous access to data, reducing the number of errors occurring through repeated data entry, ensuring the continuity of medical services by using standards and increasing the quality of treatments identifying incompatibilities.
- Improving electronic prescribing and processing e-prescription systems. In order to get the most effective treatment (improving the health condition as soon as possible), the doctor prescribes a medication as accurate as possible. Each drug can have some side effects, interact with certain allergies, treatments, illnesses (comorbidity), or other concomitant medications. The author proposed solutions that improved the structure and access to drug prospectuses. In the digital age there is information about almost all existing medicines. Each medicine has a leaflet with all the necessary information about it: therapeutic indications, administration mode, contraindications, etc. This information is found under different section names and under different formatting.
- Using ontologies in the development of medical applications, the structuring of different information and the creation of relationships between the elements necessary for the medical act. In support of this research, the author proposed a cloud computing solution to store information for better access to medical information at national level.

The flexibility of solutions is ensured by their generality, their simplicity of adaptation to any medical application, using technologies that ensure interoperability of applications, and

using methods and data files independent of the operating systems used (.xml, .csv files).

Chapter 2 presents the domain of the thesis, generalities about medical informatics and interoperability.

In the first part of this chapter I presented the Romanian medical system extensively, from the point of view of the organization, after this I made a diagram of the flow of information in the medical system in Romania. From this area, it has been taken as a field of research the pediatrics to study and improve the workflow for doctors and patients. Pediatrics takes care of the health of infants, children and adolescents, pursuing their growth and development in order to reach the maximum potential as adults. I extensively presented the pediatric field in which I approached the digital support associated with the child's health status, we identified the requirements of the pediatricians' activity, presented the basic pediatric data, presented the necessary data from the neonatal care, which the electronic dossier should contain and how interoperability can be achieved in pediatric systems. The chapter contains the basics of medical evidence in pediatrics, and consequently the author created a flow chart with pediatric data and analyzed and compared studies in the field of pediatric computer applications such as Artemis, Pediatrics Specific EMR / EHR Software, PCC Complete, etc. because of which we have established the basic pediatric functions and the gaps in this field.

Another area dealt in this chapter is e-prescribing. The thesis analyses the stage of electronic prescribing at European level in different countries, by present each country how was implemented this module by comparing the implementations and times of adopting electronic prescriptions. The chapter contains a presentation of the data that must be found in an electronic prescription followed by identification of the problems that may arise during an electronic prescription in order to support high quality in the field through the research presented in the thesis.

For the correct implementation of the applications, I also studied the most important standards in the field of medical applications for sharing information between them. We tracked their course and how they were applied by medical application developers. We have looked at current interoperability research focusing on the need for standards in medical applications and on how to use them to be integrated by developers in new developed applications. The most widely used standard in the interoperability of medical applications is HL7, the standard used in my application development within this thesis.

Chapter 3 presents an analysis of the structure of medical data and information representation as well as the state of the art in this field. Medical units of any type (cabinets, hospitals, laboratories) collect, store, process and disseminate many data. Data can be numeric (heart rate, pulse, blood pressure) or text (diagnoses, symptoms, recommendations). Thus, medical data refers to this health care information. In Romania, most medical data is on medical handwritten records of patients in the family doctor's office. In some cabinets and hospitals lately, digitization of these data has been done by creating the electronic health records. These (handwritten or digital) handouts contain personal data about the patient and the patient's medical history.

Information and medical data are both structured and unstructured. Most structured information is available in English. Various databases with structured information have been created and can be more easily included in medical applications or used by physicians to provide effective treatment for patients. Many researchers have begun to create algorithms or to use new technologies to create the largest possible structured information. Structured information is easier to read and requires less time to be found. It also attempts to retrieve relevant information from various documents in order to use convincing information for certain areas, or to build structured databases with information for doctors.

The field of medical information is an evolving field and has a great need for structured

data. The variety of illnesses and medications met daily by physicians cannot reach each one and improvement of information communication support is a must. Over the last few years, as the chapter present, were developed a lot of applications to help structuring and embedding information in medical applications, databases have been created with a wealth of drug-related information, but most research has been made for English-speaking countries, mainly in the United States. It is still necessary to standardize the data in all countries.

The author examines the structure of medical data and medical databases, especially for medicines, and describing the elements contained in each database.

Chapter 4 presents technologies supporting medical informatics and shows the current state of their use in literature. The chapter presents the technologies (ontologies, cloud computing and neural networks) and their potential to improve medical services. Firstly, there are briefly presented the technologies followed by an analysis of various researches done in medical informatics using the described technologies.

The semantic web is a network of linked information to make it easier to process in computers on a large scale, being an effective way to represent data in the Internet. Ontologies are used to gather information and knowledge in certain areas. Ontology describes concepts and the relationships between them in a specific field. An ontology defines a common vocabulary for sharing information between people in a specific field. It contains definitions of basic concepts in a given field and the relationships between these concepts.

Cloud computing is a relatively new paradigm in which resources are dynamically scalable and virtualized and are provided as Internet services. With this technology, users have available a variety of devices, including PCs, laptops, smartphones, etc., to access cloud computing services, development platforms and data over the Internet. There is a great interest in adopting cloud computing technology in the medical field. Low costs, scalability of resources, or better data protection make this technology an important candidate for medical applications. Since the launch of the technology, architectures have been proposed for the passage of medical databases into the cloud. Using cloud computing technology, the medical act can be greatly improved by accessing as much information as possible and in a very short time on any internet-connected device. Scalability, which is the cloud computing key, can provide more resources for certain operations at any time. Collaboration between medical units is an opportunity provided by cloud computing for healthcare professionals. With this technology, you can check the availability of a doctor, medical specialist, product or service at different times and in different cases, anywhere in the world. Patients can be directed to the right people or units, where they can find what they need. IT infrastructure costs will be cheaper because medical facilities will rent the infrastructure for storing medical data they need and will no longer need the latest equipment to use, manage or maintain applications. They only need computers or devices with Internet access.

Deep learning methods or neural networks have recently influenced many areas, including the processing of natural language. These methods are constantly improved with algorithms and increased performance compared to what exists in each field. Several tools have been developed to enable the implementation of deep learning such as: Caffe, DeepLeaning4J, Eblearn, Keras, Neon, Scikit-learn, TensorFlow, Theano, etc. These tools support optimization in different aspects in learning or developing deep learning algorithms. These deep learning software tools have begun to receive a great deal of attention from the research community being increasingly developed to allow the formation of deep networks with thousands of parameters.

The medical world deals with a great amount of unstructured information. Following the above, results that neural networks can help in dealing with this issue. A lot of free libraries have been created to process the natural medical language from all storage media in order to structure them and make it easier to access relevant information from medical records or medical texts. Recent studies have shown interest in this field as well as in medical research. From the articles presented in the thesis, the reader may see the broad range of areas in the medical field that neural networks cover. With these algorithms, new hypotheses can be created or new treatments can be discovered.

Chapter 5 presents contributions to pediatric medical applications. The systems modelled, developed and presented by the author in articles of the specialized conferences were **cited in more than 70 papers**. The proposed systems have been developed together with specialists in the field of obstetrics at the Bega Hospital in Timişoara and pediatrics at the municipal hospital in Brad. Informatics systems can solve communication problems between the two departments of hospitals and can provide information for building a longitudinal health card. Applications use interoperability solutions for medical systems, making them usable with any other software that supports interoperability. Functions have been created to generate certain automated childhood consultation sheets according to age and all the functions that a pediatrician needs have been added. Implementation of interoperability has been achieved through the HL7 standard, the most commonly standard used in medical applications around the world. Also, cloud computing models have been developed to store hospital data for better financial management and better data accessibility.

In this chapter the author presents contributions to IT proved in a pediatric hospital section in order to improve medical services. The author

- developed the pediatric information system according to the real flow of information in the system;
- created the specifications of a complex pediatric application;
- modelled the communication module between the departments of a hospital;
- modelled and implemented the communication between the applications of the pediatric and obstetrics and gynecology departments through the HL7 interoperability standard;
- modelled and implemented the pediatric consultation card, automatically generated according to the situation (preventive or curative or age-based consultation);
- developed and deployed pediatric application with cloud computing using Microsoft Azure Provider;
- modelled the use of cloud computing in a complex medical system in a hospital;
- modelled and implemented cloud communication between two sections of a hospital (pediatrics and obstetrics and gynecology).

Chapter 6 presents the contributions to medical applications for the medical prescription module. A very important module in treating a patient is the one prescribing drugs. To improve this service, the author brings new contributions modeling activities and implementing new modules. The new model uses cloud computing to store treatments for as many physicians as possible. The first contribution is to modeling the e-Prescription module with ontologies, another contribution is to create a module for the collection and suggestion of high-rate treatments for certain illnesses and for patients with the same characteristics, the use of HL7 files for the transmission and acquisition of treatment, the use of cloud for storing information about treatments and a last contribution from this chapter is to create models to use ontologies to create patient profiles to predict certain issues.

I have created a series of application models or modules to be integrated into existing applications. This type of applications may increase physicians' confidence in medical software because all information provided by the system is given by other doctors. Patients will receive better or less untreated treatments for certain diseases. The architecture and tools presented provide a flexible framework for processing large data to achieve better patient outcomes. Physicians have an easy-to-use tool to get personalized treatment information for their patients. The treatment database will improve constantly, in real time, with the results evaluated by

associated physicians.

The author has the following contributions:

- modeling and implementation of an e-Prescription module;
- modeling an ontology-based prescription model;
- modeling a treatment monitoring system;
- modeling and implementing an assisted prescribing system in evidence-based medicine where doctors can propose successful treatments for certain diseases along with all the features of the patient being treated, as well as receive treatment proposals from existing ones for a specific disease and for patients with the same characteristics as those treated;
- modeling and deployment of the assisted prescribing system developed on the Microsoft .Net platform with Microsoft Azure cloud technology;
- shaping the profiles of pregnant women in order to prevent at-risk situations with ontologies;
- modeling a profile-based system in education to select online courses according to learner characteristics;
- modeling and implementing an application to promote physical exercise and dieting;
- presenting related contributions to other research in the field carried out by the team in which they operate.

Chapter 7 presents contributions to extracting and structuring medical information. In some cases, the treatments given by doctors do not take into account certain interactions with other diseases, allergies or concomitant treatments, due to lack of information, resulting in other problems for the patient. To support their activity the author designed and developed a system for structuring data from medical prospectuses that can be used later in medical applications. She developed algorithms for extracting prospectuses from different online sources, made algorithms for browsing and structuring information according to the prospectus sections, and adapted deep learning algorithms to predict section names for new unstructured prospectuses.

Prescribing medicines for certain illnesses in a correct and good healing rate is a challenge for all doctors and healthcare systems worldwide. The number of illnesses and medicines is rising, and new treatments for new diseases requiring new treatments are more and more common. The lack of sufficient information on treatments and the lack of uniformity of existing data on medication, as well as the lack of tools to compare and verify interactions between patient medication, leads to a vulnerable area. Prior to providing a specific treatment, a physician needs data such as: medical history, diagnosis, and complete information about the appropriate medication for the diagnosis.

To structure the medical prospectuses, the author follows the steps:

- extracts the data from 3 medical sources from online sources (CSID.ro, pharmaacistilor.ro and helpnet.ro) the prospectuses have been extracted in HTML and text format;
- structures the HTML format files on sections (indications, contraindications, dosage, composition, etc.);
- proposes a new method for structuring, creating section name files, browsing saved text files and looking for names in each prospect, saving the positions of each section found, refining the results found, and extracting the names and text of each one, followed by saving them in xml files;
- creates a file with the section names from that source in order to make a proper structure for different sources;
- proposes a third method of structuring to eliminate previously mentioned problem; previous structures have been used to train neural networks to produce section names for the supplied files as a result of testing;

- runs three algorithms to extract section names: Scikit-learn library Vector Support Machine Classifier, Scikit-learn library Naïve Bayes Classifier, and 1D Sequencing Model Convolution Network from the Keras library; the three algorithms were run on the data sources and it was obtained an accuracy between 1.99% and 77.47%;
- proposes uniform section names to obtain better precision;
- rs the algorithms on data with uniform sections, obtaining accuracy between 38.26% and 91.78%, confirming the opportunity of the uniformity solution.

After the prospectus were structured, a dictionary of medical terms was created to extract the medical terms from each section to create ontologies for their use in assisted medical applications.

Chapter 8 evaluates the results obtained in chapters 6 and 7. Usability metrics to demonstrate the effectiveness, efficiency and user satisfaction of using these applications / modules were used. Reviewing the results shows that the implemented applications correspond to usability metrics and satisfy the user's need. For the evaluation of neural network algorithms, charts were created to compare algorithm run results on each database and measurements were made for the precision, recall, and F1-score metrics. The best score for all tested metrics was for convoluted networks on uniformed section sources.

Chapter 9 presents the conclusions of the thesis and describes further developments. This paper addresses the issue of the flexibility of medical services for the continuity of health care services. Flexibility has been ensured using operating system-independent methods, recognized files by any programming environment, and the generic nature of the models used. The models and methods proposed are adapted to the needs of doctors and patients, making it easier for them to work and improving their medical care. The proposed solutions easily adapt to the current healthcare system requirements and bring added performance to the medical field. The main purpose of this paper is to discover new methods and applications in medical informatics to help physicians consult, diagnose and administer treatments for patients. In the paper are proposed methods, algorithms and models for different domains of medical applications on Romanian territory.

The results obtained during the work for the doctoral thesis are supported by **26 published papers**, where the author of the thesis is the first author for **15**. The works published according to the international databases in which they are indexed are the following:

- A paper published in Journal with Impact Factor 0.698 indexed in the Clarivate Analytics Web of Science (ISI Web of Knowledge)
- 8 papers published in the volumes of conferences indexed in the Clarivate Analytics Web of Science (ISI Web of Knowledge)
- 2 papers published in journals indexed in international databases (EBSCO, IndexCopernicus, ProQuest, Google Scholar, PubMed)
- 12 papers published in volumes of conferences indexed in international databases (IEEE Xplore, Scopus, DBLP, PubMed)
- ➤ 3 papers published in volumes of non-indexed specialized conferences.

Published papers received a total of **99 independent citations** (excluding auto citations and co-authors' citations). The citations grouped by the international databases in which they are indexed are as follows:

- 32 citations indexed in the Clarivate Analytics Web of Science (ISI Web of Knowledge)
- ➢ 67 citations indexed in international databases

The PhD thesis includes:

- ➤ 153 pages,
- \triangleright 95 figures,
- \triangleright 22 tables and
- ➤ 156 bibliographic references.

Significant references

- [VID11] M. Vida, O. S. Lupşe, L. Stoicu-Tivadar, V. Stoicu-Tivadar, "ICT Solutions Supporting Continuity of Care in obstetrics-gynecology and pediatrics department", 9-th International Conference on Information Communication Technologies in Health, ICICTH 2011, SAMOS, Grecia, ISBN: 978-960-466-083-4, pp. 108-120, 14-16.07.2011
- [VLS11] Vida, M.; Lupse, O.; Stoicu-Tivadar, L.; Stoicu-Tivadar, V., "ICT solution supporting continuity of care in children healthcare services," Applied Computational Intelligence and Informatics (SACI), 2011 6th IEEE International Symposium on , vol., no., pp.635,639, 19-21 May 2011, doi: 10.1109/SACI.2011.5873081
- [LUP11] Lupse, O.; Vida, M.; Stoicu-Tivadar, L.; Stoicu-Tivadar, V., "Using HL7 CDA and CCD standards to improve communication between healthcare information systems," Intelligent Systems and Informatics (SISY), 2011 IEEE 9th International Symposium on , vol., no., pp.453,457, 8-10 Sept. 2011, doi: 10.1109/SISY.2011.6034371
- [LUP12] Lupşe, OS; Vida, M; Stoicu-Tivadar, L, Cloud Computing Technology Applied in Healthcare for Developing Large Scale Flexible Solutions, LARGE SCALE PROJECTS IN EHEALTH: PARTNERSHIP IN MODERNIZATION, IOS PRESS, Moscow, Romania, ISBN 978-1-61499-052-9, ISSN 0926-9630, APR 18-20, 2012, 6 pag., Special Topic Conference of the European-Federation-for-Medical-Informatics (EFMI), 2012, 10.3233/978-1-61499-052-9-94, WOS:000321182300017
- [LVS12] O.S. Lupşe, M. Vida, L. Stoicu-Tivadar, "Cloud Computing and Interoperability in Healthcare Information Systems", The First International Conference on Intelligent Systems and Applications, INTELLI2012, Chamonix, Franta, Proceedings, ISSN: 2308-4065, ISBN: 978-1-61208-224-0, pp. 81-85, Aprilie 29, 2012 to May 4, 2012
- [VID12] Vida, M.; Lupse, O.; Stoicu-Tivadar, L., "Improving the interoperability of healthcare information systems through HL7 CDA and CCD standards," Applied Computational Intelligence and Informatics (SACI), 2012 7th IEEE International Symposium on , vol., no., pp.157,161, 24-26 May 2012, doi: 10.1109/SACI.2012.6249994
- [VLS12] Vida, MM; Lupse, OS; Stoicu-Tivadar, L; Bernad, E, Flexible Solution for Interoperable Cloud Healthcare Systems, QUALITY OF LIFE THROUGH QUALITY OF INFORMATION, IOS PRESS, Pisa, ISBN 978-1-61499-101-4, ISSN 0926-9630, AUG 26-29, 2012, 5 pag., 24th Medical Informatics in Europe Conference (MIE), 2012, 10.3233/978-1-61499-101-4-280, WOS:000335219500055
- [VID13] M. Crisan-Vida, L. Stoicu-Tivadar, O. Lupse, B. Blobel, E. Bernad, Models Supporting Development of Complex Information Systems in Healthcare. Case study: an Obstetrics-Gynecology Department, EJBI – Volume 9 (2013), Issue 1, ISSN: 1801 – 5603, pp. En18-en23, Decembrie 2013
- [LST12] O.S. Lupse, Stoicu-Tivadar, L., "e-Prescription Ontologies for Cloud Computing Services", Innovation and Cooperation, Proceedings of the 32-nd Conference of the

Romanian Society of Medical Informatics (ROMEDINF 2012), Timisoara, Romania, pp. 38-43, 15-17.11.2012, ISBN: 978-606-8054-95-7

- [LUP13] O.S. Lupşe, L. Stoicu-Tivadar, "Ontologies for e-Prescription Systems in the Cloud", Scientific Bulletin of the Politehnica University Timisoara, Romania, Transactions on Automatic Control and Computer Sience, BS-UPT TACCS Volume 58(72) No. 1 / March 2013, pp. 65-69, ISSN:1224-600x
- [LGS13] Lupse, O.S.; Stoicu-Tivadar, L.; Golie, C., "Assisted prescription based on successful treatments," E-Health and Bioengineering Conference (EHB), 2013, vol., no., pp.1,4, 21-23 Nov. 2013, doi: 10.1109/EHB.2013.6707286
- [VID14] Vida, M; Lupse, O; Gomoi, V; Stoicu-Tivadar, L; Stoicu-Tivadar, V; Bernad, E, Using Web Services to support the interoperability between healthcare information systems and CDS systems, CONTROL ENGINEERING AND APPLIED INFORMATICS, ROMANIAN SOC CONTROL TECH INFORMATICS, ISSN 1454-8658, 113, 8 pag., 2014, WOS:000333724500012
- [VLS14] M. Crişan-Vida, O.S. Lupşe, L. Stoicu-Tivadar, "Assisted prescription for improving treatments in Obstetrics-Gynecology Department", Proceedings IWBBIO 2014 International Work-Conference on Bioinformatics and Biomedical Engineering, I.S.B.N: GR 738/2014,pp. 473-843, 07-09.2014
- [LUP14] Lupşe OS, Crişan-Vida M, Stoicu-Tivadar L, Bernard E, "Supporting diagnosis and treatment in medical care based on Big Data processing", Studies in Health Technology and Informatics, Volume 197, IOS Press, Proceedings of the EFMI Special Topic Conference, STC2014, Budapesta, Ungaria, pp. 65-69,26-29.04.2014
- [LST14] Lupşe OS, Stoicu-Tivadar L., "e-Prescription in pediatrics based on ontologies and treatment suggestion", Studies in Health Technology and Informatics, IOS Press – Proceedings of MIE 2014, Istambul, Turcia, pp. 403-408, 31.08-03.09.2014
- [LUP18] Oana-Sorina LUPȘE and Lăcrămioara STOICU-TIVADAR, Extracting and Structuring Drug Information to Improve e-Prescription and Streamline Medical Treatment, Applied Medical Informatics, Vol. 40, No. 1-2 /2018, pp: 7-14
- [LST18] Oana-Sorina LUPȘE and Lăcrămioara STOICU-TIVADAR, Supporting Prescriptions with Synonym Matching of Section Names in Prospectuses, Stud Health Technol Inform. 2018;251:153-156
- [LCS18] Oana-Sorina LUPȘE, Ciprian-Bogdan CHIRILA and Lăcrămioara STOICU-TIVADAR, Harnessing ontologies to improve prescription in pediatric medicine, Studies in Health Technology and Informatics, Vol. 255, 2018