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Contents

Data and Knowledge for Medical Decision Support

Jana Zvárová[1]

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The EFMI Special Topic Conference Data and Knowledge for Medical Decision Support held in Prague, The Czech Republic, April 17-19, 2013 (www.stc2013.org) reflected opportunities, challenges and priorities of data and knowledge for medical decision support. The conference was organized by the European Federation for Medical Informatics (EFMI) in cooperation with the Society of Biomedical Engineering and Medical Informatics of the Czech Medical Society J. E. Purkyne. Nearly thirty years after the conference Computer-aided medical decision making held in Prague 1985 [1] this conference showed many new developments of methods and systems focused on medical decision support. Medical decision support is increasingly important. It has spawned research in the areas of standardization, semantic interoperability, formalization of knowledge, knowledge discovery and guidelines. It also led to the development of decision support systems that can be interfaced with clinical information systems. It is very important that the quality of these systems is carefully evaluated. Apart from being used by decision support systems the current medical knowledge also has to be managed so that it is easily accessible by physicians and nurses. Medical decision support is an important constituent in different eHealth applications. Most of the developed decision support systems can be more or less easily integrated into clinical information systems both as part of those systems connected through standardized interfaces or as services to be remotely accessed.

As an outcome of the conference selected full papers in limited number of pages were published by IOS Press [2] and short abstracts of all submissions were published in the International Journal for Biomedicine and Healthcare (www.ijbh.org). In the year 2013 (Volume 9) European Journal for Biomedical Informatics is publishing selected reviewed papers of the conference without restriction on the number of pages. Authors are not paying an article processing fee for the immediate release of peer-reviewed articles, but a small financial support is required in case that the support of projects or sponsors is acknowledged (see Instruction to authors).

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We invite you to propose special topics that would help to accelerate needed changes in health care by easy transfer of a new information and knowledge for health care delivery.

References

[1] Jan H. van Bemmel, Francois Grémy, Jana Zvárová (eds.): Diagnostic Strategies and Expert Systems. Elsevier, North Holland, Amsterdam 1985.

[2] Arie Hasman, Bernd Blobel, Jana Zvárová (eds): Data and Knowledge for Medical Decision Support. IOS Press, Amsterdam 2013.

Selecting Relevant Information for Medical Decision Support with Application in Cardiology

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Abstract

Objectives: The aim of our work was to implement a prototype of a decision support system which has the form of a web-based classification service. Because the data analysis component of decision support systems often happens to be unsuitable for high-dimensional data, special attention must be paid to the sophisticated selection of the most relevant variables before learning the classification rule.
Methods: We implemented a prototype of a diagnostic decision support system called SIR. The system has the ability to select the most relevant variables based on a set of high-dimensional measurements by means of a forward procedure optimizing a decision-making criterion. This allows to learn a reliable classification rule.
Results: The implemented prototype was tested on a sample of patients involved in a cardiology study. We used SIR to perform an information extraction from a cardiological clinical study containing both clinical and gene expression data. The classification performance was evaluated by means of a cross validation study.
Conclusions: The proposed classification system can be useful for clinicians in primary care to support their decision-making tasks with relevant information extracted from any available clinical study. It is especially suitable for analyzing high-dimensional data, e.g. gene expression measurements.

Keywords

Decision support system, web-service, information extraction, high dimension, gene expressions

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1 Introduction

Decision support systems (DSS) offer assistance with the decision-making processes in many areas. Their aim is to solve a variety of tasks and to analyze different information components. In medicine, a decision support system represents an inherent e-health technology tool for diagnostic and prognostic purposes capable to help during the therapy [1]. Recently proposed systems in some areas of medicine are required to extract information also from high-dimensional measurements in order to deduce conclusions for the diagnosis, therapy, or prognosis by comparing the risk corresponding to different alternatives. Some systems have been implemented in a web-based form [2, 3].

Decision support systems have established their place in current healthcare. Their potential for improving the quality of provided care and for generating economic benefits by reducing financial costs and saving human resources have been described in literature [4]. They are known to bring the physician more comfort, a reduction of stress, a higher effectivity, and more time for the patient. The contribution of decision support systems to the patient safety has been summarized in [5]. Another aspect is a benefit for a less experienced physician in a complicated medical case. Also, the systems allow to exploit the level of knowledge reflecting the latest research developments in medicine.

The analytical component within a decision support often happens to be unsuitable for the analysis of high-dimensional data. Decision-making within a clinical decision support system is mostly based only on one of the standard classification procedures of multivariate statistics or machine learning that enables to construct objective classification rules for assigning individual observations to groups. Available classification methods include:

- Linear/quadratic discriminant analysis.
- Neural networks.
- Support vector machines.
- Classification trees.
- K-nearest neighbor.
- Cluster analysis.
- Knowledge-based rules (e.g. [6]).

However, these methods commonly suffer from a so-called curse of dimensionality if the number of variables (e.g. symptoms and signs) exceeds the number of patients [7].

In this work, we have proposed and implemented a prototype of a decision support system in the form of a web-based classification service for diagnostic decision support, which is particularly designed to address the needs for a reliable high-dimensional information extraction. Its organic part is a dimension reduction technique performed in the form of a variable selection. The statistical component of the system uses a variety of sophisticated classification rules, which are reliable also for the analysis of high-dimensional data sets.

We tested the prototype of the system on clinical data in a cardiology study, which includes a whole-genomic study of gene expression measurements. This paper presents the principles and advantages of the proposed system and summarizes results of the testing service on a cardiology study.

2 Methods

We propose a system called SIR (System for selecting relevant Information for decision suppoRt), which is an easy-to-use web-based generic service devoted to data collection and decision support with a sophisticated information extraction component. It is proposed for being used mainly for general practitioners in the primary care, but it is able to handle data from any area of medicine. The decision making of the SIR requires data from a (sufficiently large) clinical study in order to construct the optimal classification rule for the decision making problem.

Data collected within a clinical study represent the training database of the SIR. The SIR can import the whole data set from the clinical study automatically together with a data model. The system cleans the data e.g. by checking if the values of the imported quantitative variables do not exceed given bounds required by the data model.

The next step in the analysis of the data from the clinical study is dimension reduction. Statistics distinguishes between variable selection and feature extraction [8], where the latter searches for a smaller set of linear combinations of all variables. Here, we perform the variable selection, which reduces the set of all measured symptoms or laboratory measurements to a smaller set of relevant symptoms. This step, which is necessary especially for high-dimensional data obtained in genetic studies [7], is performed by a forward procedure optimizing a decision-making criterion.

Categorized data are considered and the contribution of a given variable (say X) to explaining the uncertainty in the response Y (i.e. in the separation among the groups) is quantified by means of the conditional Shannon information, which is denoted as $d(Y|X)$. The first variable (say X_1) fulfils

$$d(Y|X_1) = max\, d(Y|X) \tag{1}$$

over all variables X. Thus, X_1 is the most relevant variable for explaining the classification. Further on, the method successively selects the most relevant variables with the maximal value of the statistical dependence. In other words, other variables are iteratively added to the set with the best improvement of the conditional relevance. If variables $X_1, \ldots, X_s$ have been selected as the most relevant, the next variable (say X_{s+1}) is selected as the variable fulfilling the requirement

$$d(Y|X_1, \ldots, X_s, X_{s+1}) = max\, d(Y|X_1, \ldots, X_s, X), \tag{2}$$

where all variables X not present in the set $\{X_1, \ldots, X_s\}$ are considered. Finally, we consider only such variables for the consequent analysis which contribute to explaining more than 90 % of the inter-class variability. The system allows quantifying the influence of an additional examination (variable) on the diagnostic decision. Additionally, the dimension reduction procedure may take into account the cost of obtaining each clinical or laboratory measurement by using the information theoretical approach of [9].

The process of learning of the classification rule within the SIR has the ability to decide automatically for one of several different methods. A criterion of optimality is adaptively chosen to minimize the risk of a wrong classification result due to special properties of the data and the sample sizes. The implemented methods include the linear discriminant analysis (LDA), which is a multivariate statistical method for separating groups by means of a linear function [10]. The same covariance structure is assumed in each group. Another approach implemented in the SIR is the empirical Bayes inference mechanism, which minimizes the aposterior Bayes risk across all groups of samples. Let us say that the task is the classification to K groups. It uses a discretization of data and we denote the levels of a discrete variable X by $X_1, \ldots, X_r$. The method assumes a conditional independence of the levels of X for each group $k = 1, \ldots, K$.

The construction of the classification rule in the system SIR may additionally allow a combination of data with medical knowledge. To be specific, a clinician may interfere manually the system in order to incorporate ad-

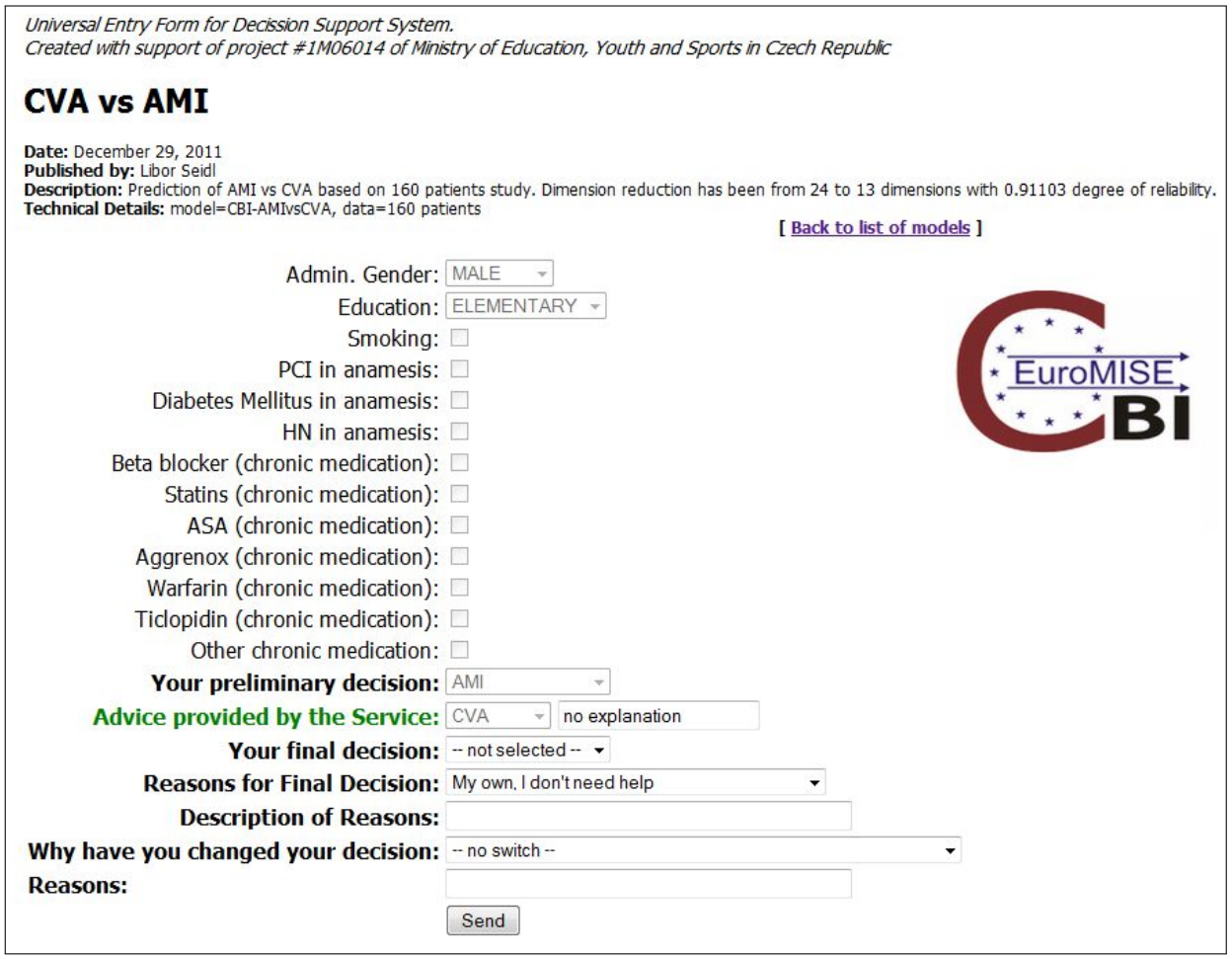

Figure 1: Illustration of the prototype of the system SIR.

ditional expert knowledge based on education, experience, or intuition and can e.g. eliminate a certain diagnosis for a specific combination of symptoms and signs, if their joint occurrence is known to have a zero probability.

From the implementation point of view, the prototype can be understood as four subsystems: an Administration System, a DSS SOAP Frontend, a DSS Web Frontend, and a DSS Backend. The Administration System is devoted to a model creation, data gathering and manipulation, dimension reduction, and DSS publication. The SOAP Frontend provides the classification of a patient on a request by an end-user system (including on-fly generation of WSDL) by working with an internal XML description of the decision support system, which is generated during the process of publication in the Administration System. The DSS Web Frontend provides a HTML Form based user-friendly interface to the SOAP Frontend. All these three subsystems are programmed using PHP5. The main two tasks of the DSS Backend are to learn a new dataset during the process of DSS publication and to classify a new patient during a SOAP Frontend request. The computation in the DSS Backend consists of several R scripts, which are called on demand from PHP5.

A clinician as the user of the decision support service is not required to understand the background of the methods. His/her aim is to determine the diagnosis of a new patient (not included in the clinical study), who can be examined on a distant place. All variables selected by the variable selection procedure are required to enter the decision support system, which can be performed through the automatically generated interface from an electronic health record (EHR) or health information system (HIS), although a manual input of data is also possible, as illustrated in Figure 1. The clinician must specify the prior diagnosis before entering the data to the SIR, because he/she is the only one to carry the legal responsibility for the clinical decision. Now the SIR can be used through the web service to obtain a diagnosis support. Then, the clinician is asked to manually select his/her final decision and only if it is not in accordance with the SIR, the clinician writes a short text justifying the decision.

3 Results

We implemented the prototype of the system SIR and evaluated its performance on a real clinical study of cardiovascular diseases, which incorporated the measurement

Table 1: Sets of personal and clinical variables in the cardiological clinical study.

Set A	Sex, height, weight, education, smoking, diabetes, systolic blood pressure, cholesterol.
Set B	Height, weight, education, systolic blood pressure, cholesterol.

of gene expressions across the whole genome. The study was performed in the years 2006-2011. The aim of the study was to identify a small set of genes and clinical variables associated with excess genetic risk for the incidence of a cardiovascular disease. Clinical and gene expression measurements are measured on a set of 59 patients having an acute myocardial infarction (AMI), 45 patients having a cerebrovascular stroke (CVS), and 77 control persons (CP) chosen as individuals without a manifested cardiovascular disease with the same risk factors as the patients. These 181 individuals serve as a training database for constructing an efficient classification rule for assigning a new individual to one of the groups (AMI, CVS, CP).

A set of 4 personal and 4 clinical variables recorded for each patient is shown in Table 1. The gene expressions of all genes (>39 000 gene transcripts) are measured for each patient using Illumina BeadChip microarrays. We will describe the training of the SIR to classify the samples to one of three groups (AMI, CVS, CP). A routine statistical analysis of a subset of these data was performed in [11]. There, gene expressions AMI patients are compared to those of CPs and values of sensitivity and specificity are presented.

We used the dimension reduction method to select a set of 10 most relevant genes from the high-dimensional set of measurements. We categorized each continuous variable into 4 categories (if possible) and assume an equal importance of each of the variable. The set A was reduced to 5 most relevant variables (set B) shown in Table 1. Set B contains significant instruments of the life style of a particular patient and explains 97.9 % of the intra-class variability of the set A.

Further, the SIR used the linear discriminant analysis on the original data (without categorization) to learn a classification rule into one of three groups (AMI, CVS, CP). Table 2 presents results of an independent validation study performed by leave-one-out cross-validation using various sets of measurements. Thus, the set of all genes has the ability to determine the diagnosis correctly for 85 % of patients.

A reduced set of variables can retain a relatively high classification performance, which is a consequence of redundancy of the remaining variables or their multicollinearity (cf. [12]). Moreover, we have verified the results also with other statistical validation criteria, e.g. leave-10-out cross-validation or bootstrap.

4 Discussion

We implemented an easy-to-use system called SIR (System for selecting relevant Information for decision suppoRt), which has the ability to select the variables relevant for a reliable information extraction from high-dimensional measurements. The system allows a diagnostic decision support by means of a web technology and can be characterized as a practical tool for evidence-based medicine [13]. We believe that a reliable decision support system should be always equipped with a statistical component allowing to extract information from very complex measurements. Without the help of such specialized tool, a clinician would never be able to extract the information from such high-dimensional measurements e.g. in the molecular genetic context.

The SIR simulates a decision making process as performed by a clinician. The system can be used as a purely assistive technology to the clinician, who carries the responsibility for the diagnosis decision making in combina-

Table 2: Evaluation of the system SIR in the task of a diagnostic decision support based on the data from the cardiology clinical study. Percentage of correctly classified samples to one of three groups (AMI, CVS, controls) in the leave-one-out cross-validation procedure using the linear discriminant analysis.

Variables used in the classification rule	**Classification performance**
Set A (8 personal and clinical variables)	0.56
Set B (5 personal and clinical variables)	0.56
All genes	0.85
All genes + set A	0.85
All genes + set B	0.85
10 genes	0.65
10 genes + set A	0.72
10 genes + set B	0.72

tion of a scientific and empirical knowledge to infer the interpretation in all steps of healthcare provision. The clinician determines a prior diagnosis and has the possibility to decide for a different aposterior diagnosis based on the recommendation of the system. In such case, however, the SIR collects a feedback from the clinician.

The prototype version of our system has not been released for a public usage on the internet yet. We plan an intensive validation stage allowing exposing the system repeatedly to real situations starting with formulating requirements, implementation of modifications, multi-level testing under artificial conditions, and testing. Only this will allow tuning all parameters of the system, which must be maintained, supervised and monitored for a long-term period in cooperation with clinicians before introducing a fully public version to real applications following necessary rules of data safety. This will also require a secure access in concordance to current legislation (public-key infra-structure, service versioning, etc.).

In general, the system can be used to analyze different data sets in various areas of medicine. The knowledge from recent medical research can reach clinicians quickly by means of the system, which can assist them as a supporting tool within the decision making process. At the same time, the system SIR is designed to be convenient for a data collection e.g. within a hospital, while the classification rule can be learned continuously during its operation.

So far, we have applied the system SIR to real cardiology data. The system determined a set of 10 crucial genes among more than 39 000 gene transcripts. The selected genes are believed to be associated with the risk of a manifestation of AMI or CVS for a particular patient in the population in the Czech Republic. The paired design of the study allowed eliminating the influence of known risk factors (e.g. systolic blood pressure) on the discrimination. Thus, we revealed the added value of including the gene expression data to the study. A clinician with access to the web classification service may obtain a prediction of the risk of a more severe prognosis or a relapse for new patients. The clinician has the information about the classification reliability of the system. We are preparing other studies for validating the ability of the SIR to select the relevant information from high-dimensional measurements for a reliable decision support.

Acknwoledgements

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References

[1] D.J. Power, Decision support systems: Concepts and resources for managers, Quorum Books, Westport, 2002.

[2] M.J. Romano, R.S. Stafford, Electronic health records and clinical decision support systems: Impact on national ambulatory care quality, Archives of Internal Medicine 171 (2011), 897-903.

[3] F. Sicurello, M. Gündel, A. Donzelli, Data analysis web service using statistical packages. International Journal of Advanced Statistics and ITC for Economics and Life Sciences 1 (2009), 3-7.

[4] K. Kawamoto, C.A. Houlihan, E.A. Balas, D.F. Lobach, Improving clinical practice using clinical decision support systems: A systematic review of trials to identify features critical to success, BMJ 330 (2005), 330:765.

[5] J. Kalina, J. Zvárová, Decision support systems in the process of improving patient safety. In A. Moumtzoglou, A. Kastania (Eds.): E-Health Technologies and Improving Patient Safety: Exploring Organizational Factors. IGI Global, Hershey, Pennsylvania, 2013, 71-83.

[6] P. Berka, J. Rauch, M. Tomečková, Data mining in the atherosclerosis risk factor data. In Berka P., Rauch J., Zighed D.A. (Eds.): Data Mining and Medical Knowledge Management: Cases and Applications, IGI Global, Hershey, 2009.

[7] J. Kalina, Classification analysis methods for high-dimensional genetic data. Biocybernetics and Biomedical Engineering (2013). Accepted.

[8] W.L. Martinez, A.R. Martinez, J.L. Solka, Exploratory data analysis with MATLAB. 2nd edn. Chapman Hall/CRC, London, 2011.

[9] J. Zvárová, M. Studený, Information theoretical approach to constitution and reduction of medical data, International Journal of Medical Informatics 45 (1997), 65-74.

[10] A.C. Rencher, Multivariate statistical inference and applications, Wiley, New York, 1998.

[11] Z. Valenta, I. Mazura, M. Kolář, H. Grünfeldová, P. Feglarová, J. Peleška, M. Tomečková, J. Kalina, D. Slovák, J. Zvárová, Determinants of excess genetic risk of acute myocardial infarction-a matched case-control study, European Journal for Biomedical Informatics 8 (2012), 34-43.

[12] C. Ding, H. Peng, Minimum redundancy feature selection from microarray gene expression data. Journal of Bioinformatics and Computational Biology 3 (2005), 523-528.

[13] H. Chen, S.S. Fuller, C. Friedman, W. Hersh, Medical informatics, Knowledge management and data mining in biomedicine, Springer, New York, 2005.

[14] J. Kalina, L. Seidl, K. Zvára, H. Grünfeldová, D. Slovák, J. Zvárová: System for selecting relevant information for decision suppport. In: B. Blobel, A. Hasman, J. Zvárová (Eds.): Data and Knowledge for Medical Decision Support, Studies in Health Technology and Informatics 186, IOS Press, Amsterdam, 2013, 83-87.

The Medicolegal Certification of Medical Fitness for Work: Necessity of Standardization of the Certificate

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Abstract

Background: One of the crucial medicolegal activity of occupational medical service (OMS) providers is the certification of medical fitness for work issued by examining physician and based on knowledge of working conditions/health risks at work and on results of occupational medical examinations.
Objective: Recommended standards for the content and scope of preventive medical examinations in the listed exposures and loads are available. The employers need clear and standardized final decision about the medical fitness for work without sensitive medical data (diagnosis) issued by examining physician.
Material and Methods: The author analyzed the content of 18 125 certificates of medical fitness for work in the period 1982 – 2012 and compared different written forms of certification based on actual legislation.
Results: In the 30 years period there were used different written forms of certification of medical fitness for work. From this long experience resulted necessary content of certificate of medical fitness assessment for work which was standardized in the new law (Czech Republic Act No 373/2011 Dig., on specific health services and Decree of The Ministry of Health No.79/2013 Dig., on occupational medical services).
Conclusion: Although the content of certificate of medical fitness assessment for work was standardized, different written or electronic forms of certification of medical fitness for work should be unified and standardized for practical needs of OMS providers and employers.

Keywords

occupational health/medical services - medical fitness – certification - standardization of the certificate

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1 Introduction

The Czech Republic Act No 373/2011 Dig., on specific health services (valid since April 1, 2012) [2] defines in paragraphs 53 - 60 Occupational Medical Services (OMSs) as preventive services, which include the impact assessment of work, working environment and working conditions on health, workplace inspections and preventive medical fitness assessment for work aimed at protecting the health and protection against occupational accidents, occupational diseases and work-related diseases, training in first aid and regular surveillance in the workplace.

Providers of occupational medical services are general practitioners (GP´s) or occupational health specialists (certified/recognized occupational physicians)[6]. The employee is obliged to undergo all preventive medical occupational examinations indicated by OMS provider for the evaluation of health status. The employer is obliged to assign of employees to work in compliance with the conclusions of the medical report/certificate about their medical fitness.

2 Methods and Materials

2.1 Competence of OMS Providers

The provider of occupational medical services is required [1, 3, 8]:

- to inform employee about the possible influence of factors of working conditions on his/her health, and with knowledge of the development of his/her state of health,

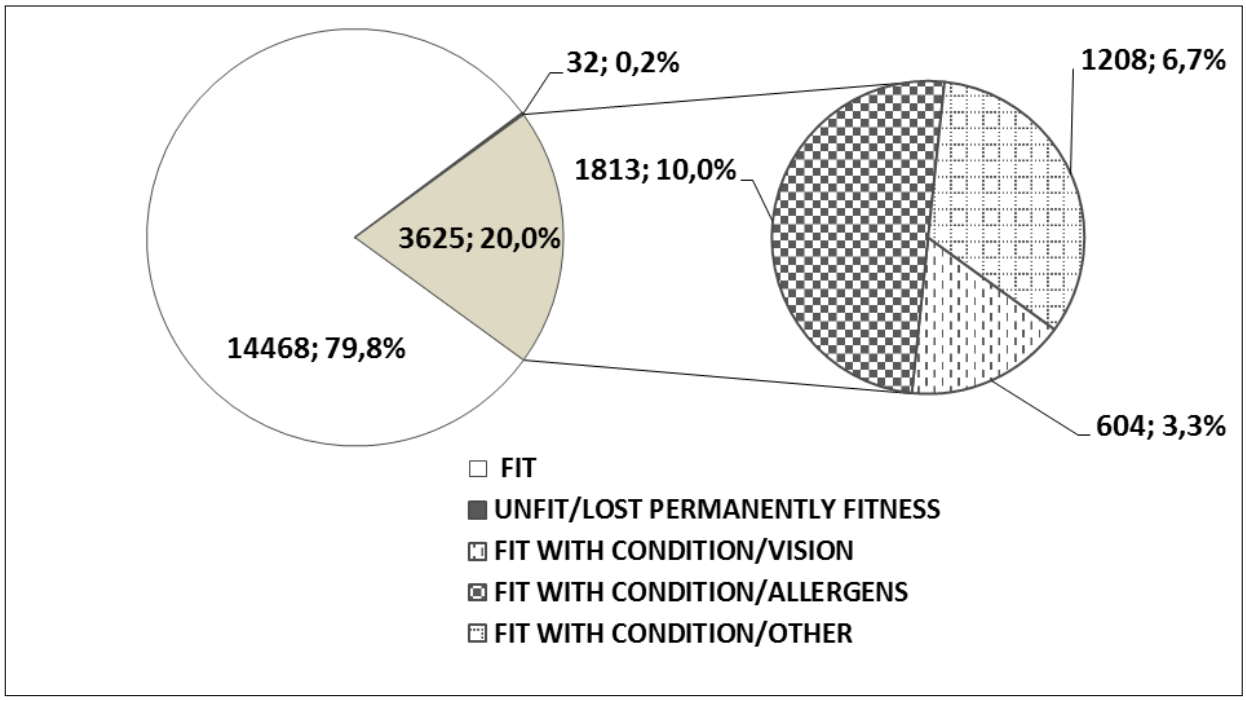

Figure 1: Medical fitness assessment 1982 – 2012 (18 125 certificates).

- to inform employers about the possible influence of factors of working conditions on the health of employees,
- to perform periodic monitoring of the workplace conditions,
- to cooperate with the employer, employee, safety and health at work specialist, governmental inspection authorities and trade unions,
- to notify promptly the employer of serious or repeated facts adversely affecting health and safety at work
- through employer to ensure the measurement/expertise and analysis of the working conditions, working environment including the results of categorization of health risks

Standardized certificate of medical fitness assessment for work must include

- identification of the employer's,
- identification of medical provider and physician/signature, Nr. of certificate,
- identification of the persons employed or seeking employment: the name or names and surname, date of birth, address of permanent residence in the Czech Republic or the address of the registered place of temporary residence,
- details of the job position or employee data of the expected job title of person applying for employment, further information on the nature of work,
- mode of operation, the risk factors in relation to specific work, the degree of working risk factors, job categories expressed by the key risk factors of working conditions,
- the term an extraordinary examination, if such a procedure is justified,
- date of issue of certificate,
- information about the possibility of appeal procedure,
- **final assessment** (4 possibilities):
  - is medically fit,
  - is medically fit with the certain condition/medical restriction,
  - is medically unfit,
  - lost permanently medical fitness.

2.2 Principles of Medical Fitness Assessment for Work and Analyzed Data

One of the crucial medicolegal activity of OMS providers is the certification of medical fitness for work issued by examining physician and based on knowledge of working conditions, knowledge of health risks of work and on results of occupational medical examinations [4].

A keystone of quality performance by an occupational physician is the familiarity with specific working conditions and demands of the respective job and the knowledge of the state of health of individual workers. Occupational

medical examinations of individuals (workers and employees) are initial/entry, periodic, extraordinary, output and consequential [5].

System of categorization of work operations established in the Czech Republic is based on monitoring 13 harmful factors in the workplace (dust, chemical substances, noise, vibrations, electromagnetic fields, physical load, working position, thermal exposure, cold exposure, psychical burden, visual burden, biological agents, high air pressure). Special guidelines for assessment of various types of risks are available.

The category of the work operation and the most important risk factor determine the frequency and range of periodic medical examination of workers and frequency of periodic measurements of different harmful factors at workplaces.

Some occupations (drivers, railway workers, firemen etc.) have besides the examinations above special content of preventive medical examinations [7].

Working population in the Czech Republic currently totals about 4.5 million people working in 74 731 subjects/enterprises (in 2011). Because there is not central register of certificates of medical fitness for work, author based this analysis on his own data (18 125 certificates) since 1982 till 2012 (at about 600 certificates per year). The whole database was not in the electronic form so it was necessary to compare forms and final assessment data from paper health records (Fig. 1).

3 Results and Discussion

Problem of medical fitness assessment for work is not only in the content and scope of preventive medical examination (their effectiveness), but in the amount and form of the legal aspects of certificate of medical fitness assessment for work too, what is utterly incomparable with the simplified situation decades ago (the latest legislation originated in 2013 after 46 years). The list of obligatory requirements of the employer's request and certificate of medical fitness for work is unnecessarily large and ambiguous in details (see part 2.1).

The terms used in law are often very far from an expert terminology (e.g. hazard versus risk). There is only exceptionally available standard form in law (standardized certificate form for medical fitness assessment for road drivers), so the practice is diverse, confusing and legally problematic. The result is a series of cancellations of medical fitness certificates for work in appeal procedures for formal defects. There is another problem: the combination of two approaches to the medical fitness assessment for work – evaluation of working risk factors on one side (e.g. noise, dust) and claims of the job on the other side (eg firemen, vehicle drivers).

There exists an integrated approach called "occupational health characteristics" - maybe less precise, but perhaps more useful for practice. Indeed, many aspects of the medical fitness assessment for work undergo certain rationalization in medical practice.

The content of preventive medical examinations depended on grade of risk of different occupations of examined persons and was not the aim of analysis. The data analysis was focused on the form of the certificate (the form was influenced by unpredictable current requirements and changes in legislation during the analyzed period for different occupations, f.i. drivers) and its conclusions (medically fit, medically fit with the certain condition/medical restriction, medically unfit/lost permanently medical fitness). The main limitation of medical fitness to work was represented by allergic diseases in history and impaired vision. Other limitations (for shift work, work at heights etc.) occurred less frequently (Fig. 1).

4 Conclusions

The certificate of medical fitness for work does not contain sensitive medical data (diagnosis). On the other side there must be clearly expressed that the assessed person is medically fit for the job or medically fit for the job with the certain condition/medical restriction or medically unfit (sometimes permanently) for the job [6]. There are different written or electronic forms for certification of medical fitness for work that should be unified and standardized for practical needs of OMS providers and employers. The introduction of the standard of employer´s request and certificate of medical fitness for work would be useful for the current practice, the correct use of this standard would largely eliminate risk of the annulment of certificate from formal mistakes in appeal procedure. Conceptual unification and cohesion of existing legislation is an obvious prerequisite for the success of standardization [9].

Acknowledgements

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References

[1] Cikrt M, Pelclová D, Markvart K, Lukáš E, Kříž J. Occupational and environmental medicine in Czech Republic. Int Arch Occup Environ Health 69 (1997), 79-82.

[2] Czech Republic Act No 373/2011 Dig., on specific health services (in Czech)

[3] Leino, T.,Räsänen, K., Kauppinen, T., Liira, j., Jakkola, J., Carnevale,F., Baldasseroni, A., Van Damme, K., Casteleyn, L., Veidebaum,T., Kahn, H., Vilkis, A., Eglite, M., Jekabsone, I., Vanadzins, I., Jankauskas, R., Černá, M., Tuček, M., Málek, B., Cikrt, M., Pelclová, D., Šmerhovský, Z. Comparative analysis of occupational health system and practices as part of preventive health care systems in seven European countries. Part 1 Document based analysis. EU INCO - Copernicus project No. PL 973108, 1999.

[4] Tuček, M., Pelclová, D., Cikrt, M.. Pracovní lékařství pro praxi .(Occupational Medicine for Practice). Příručka s do-

poručenými standardy. (Handbook with Recommended Standards). Grada Publishing, Prague (in Czech), 2005.

[5] Tuček, M. Analýza pracovně lékařské péče v České republice. (Analysis of occupational medical care in the Czech Republic), České pracov. lék. (in Czech, English abstract), 6 (2005), 28-36.

[6] Tuček ,M.: Pracovnělékařské služby jako součást zdravotnické reformy. Zdravotnické fórum (2012), 18-20.

[7] Tuček, M. Transport safety, neurobehavioral disorders and medical fitness standards. Neural Network World, 6 (2010), 723-736.

[8] Westerholm, P., Baranski, B. (eds) . WHO Guidelines on Quality Management in Multidisciplinary Occupational Health Services. WHO European Center for Environment and Health, Bilthoven 1999.

[9] Šubrt, B., Tuček, M: Pracovnělékařské služby (Occupational medical services). ANAG Publishing, Olomouc (in Czech), 2013

In-hospital Death Prediction by Multilevel Logistic Regressin in Patients with Acute Coronary Syndromes

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Abstract

Background: The odds of death of patients with acute coronary syndromes (ACS) in non-PCI (percutaneous coronary intervention) hospitals in the Czech Republic change depending on a number of factors (age, heart rate, systolic blood pressure, creatinine, Killip class, the diagnosis, and the number of recommended medications and treatment of ACE-inhibitor or sartan).
Objectives: We present a detailed description of multilevel logistic regression applied in the derivation of the conclusion described in the Background, namely we compare multilevel logistic regression with logistic regression.
Methods: The above mentioned clinical findings have been derived on the basis of data from the three-year (7/2008-6/2011) registry of acute coronary syndromes ALERT-CZ (Acute coronary syndromes – Longitudinal Evaluation of Real-life Treatment in non-PCI hospitals in the Czech Republic). A total of 32 hospitals contributed into the registry. The number of patients with ACS (n=6013) in the hospitals varied from 15 to 827.
Results: The likelihood ratio test showed that the independence of medical outcomes across hospitals cannot be assumed ($p<0.001$, the variance partition coefficient VPC=8.9%). For this reason, we chose multilevel logistic regression to analyse data, specifically logistic mixed regression (the hospital identity was a random effect). The calibration properties of this model were very good (Hosmer-Lemeshow test, p=0.989). The total discriminant ability of the model was 91.8%.
Conclusions: Considering some differences among hospitals, it was appropriate to take into account patient affiliation to various hospitals and to use multilevel logistic regression instead of logistic regression.

Keywords

Multilevel logistic regression, acute coronary syndromes, risk factors, in-hospital death

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1 Introduction

During the past more than 10 years two important algorithms that estimate the risk scores in patients with acute coronary syndromes (ACS) have been derived [1]. The first is the risk score TIMI (Thrombolysis in Myocardial Infarction), which estimates the risk of death, myocardial infarction, or recurrent ischemia occurred by 14 days after hospitalization [2]. The risk score is available on the Web at http://www.timi.org/. The value of

the risk is estimated based on the following seven risk (binary) variables: at least 65 years of age, at least three risk factors for coronary artery disease (CAD) present (diabetes, cigarette smoking, hypertension, low HDL cholesterol, family history of premature CAD), known CAD, at least two episodes of angina chest pain in the last 24 hours, the use of aspirin in the last seven days, ST-segment deviation of 0.05 mV or more, and elevated serum markers for myocardial necrosis.

The second algorithm is the risk score of GRACE (Global Registry of Acute Coronary Events), which is available on the Web http://www.outcomes-umassmed.org/grace/acs_risk/acs_risk_content.html [3]. To estimate the risk of death or myocardial infarction during hospitalization and in the following six months, eight variables are used: age, Killip class (a classification of seriousness of heart failure), systolic blood pressure, ST-segment deviation, cardiac arrest at admission, serum creatinine, elevated serum markers for myocardial necrosis and heart rate.

Monhart et al. [4] found that the odds of death in non-PCI (percutaneous coronary intervention) hospitals in the Czech Republic in patients with ACS change depending on a number of factors, on which are also based the risk scores TIMI and GRACE. Specifically, the odd of death depends on age, heart rate, systolic blood pressure, creatinine, Killip class, the diagnosis (ST-segment elevation myocardial infarction (STEMI), non-STEMI, unstable angina pectoris (UAP)), the number of the received recommended medications (aspirin, clopidogrel, unfractionated and low molecular weight heparin or fondaparinux, statin, beta-blocker) and treatment of angiotensin-converting-enzyme inhibitor (ACEI) or sartan. In this paper we present a detailed description of statistical analysis by multilevel logistic regression deriving these conclusions.

2 Material

ALERT-CZ (Acute coronary syndromes – Longitudinal Evaluation of Real-life Treatment in non-PCI hospitals in the Czech Republic) is a three-year registry of acute coronary syndromes (1 June 2008 - 30 July 2011), which had been organised by Cardiocentrum of 3rd Faculty of Medicine of Charles University in Prague under the auspices of the Czech society of cardiology. The participation of hospitals in the registry was voluntary. However, none of the hospitals was allowed to have any department of interventional cardiology (non-PCI hospitals). The intervention treatment (if indicated) was provided in any other PCI hospital. A total of 32 non-PCI hospitals from the Czech Republic were involved into the registry for a short time or over a long period.

Data collection was conducted using an electronic form. The application for data collection was created by European Centre for Medical Informatics, Statistics and Epidemiology, which also centrally collected anonymous data. In addition to the basic characteristic of patients (sex, age and cardiovascular risk factors), drug therapy (chronic, acute, at discharge), the severity of the disease, the clinic course of the disease, its complications and the treatment outcomes were recorded in the registry. A total of 7240 disease cases are in the registry. If a person has had more cases of ACS in the reference period, only the data of the first ACS (primarily admitted to non-PCI hospitals) was included in the present analysis (6013 patients).

3 Statistical methods

The influence of potential factors on in-hospital death was analysed using multilevel logistic regression (also called hierarchical logistic regression), and specifically using logistic regression with mixed effects (the identity of the hospital was a random effect), which belongs to generalized linear mixed models (GLMM). When estimating log-likelihood, Laplace and Gauss-Hermite approximations were used. In addition to multilevel logistic regression we also applied traditional logistic regression. To compare the two models we used likelihood ratio test and variance partition coefficient (VPC). Statistical significance of the individual predictors in the model was established using Wald test and likelihood ratio test. The overall fit of the model was assessed on the basis of the values of deviance, Akaike information criterion (AIC), Hosmer-Lemeshow test and ROC (receiver operating characteristic) curve with c-index. We also graphically analysed standardized Pearson residuals and estimated the coefficient of dispersion. In the text the symbol n indicates the number observations. For statistical analysis we used statistical software R version 2.8.0 (libraries lme4, MASS) [5].

4 Results

A total of 32 hospitals contributed into the registry. The number of patients with ACS (n=6013) in hospitals ranged between 15-827 and the time involvement in the registry varied between 0.2-3.0 years (media 2.6 years). The basic characteristics of the patients are shown in Table 1.

Our study was a multicentre study because patients were recruited from the different hospitals (centres). From this reason of hierarchical data organization (hospital-patient) there are possible two kinds of way of the statistical analysis, either to take account of the hierarchical data structure or not to take into account. Table 2 summarizes the results of multilevel logistic regression (taking into account the hierarchical structure of data) and logistic regression (not reflecting the hierarchical structure of data). Laplace approximation was used to estimate the parameters of multilevel logistic regression in Table 2 (the Gauss-Hermite approximation yielded the similar results).

When comparing the 95% confidence intervals in Table 2 it is seen at the first sight that there are not substan-

Table 1: Patients characteristics at admission.

Characteristic	Relative number	n
Age $\leq$ 70 years	53.5%	5987
Heart rate $\leq$ 80 pulses/min.	51.6%	5999
Systolic blood pressure $\leq$ 80 mmHg	58.9%	5985
Creatinine $\leq$ 100 μmol/l	39.3%	5907
Women	41.0%	6013
Diabetes mellitus	36.9%	5996
Hypertension	77.7%	5994
Hyperlipidemia	52.9%	5957
Smokers	28.0%	5925
Recurrence IM	29.5%	5990
Killip class I	74.3%	5996
STEMI	19.0%	5989
Five recommended drugs	41.1%	5922

tial differences between the results of both methods, at least in terms of significance. The intercept represents the odds of death in the "average" hospital, i. e. when the values of the explanatory variables are not taken into account. Specially, the continuous explanatory variables (age, systolic blood pressure) take on the value 0 and the categorical explanatory variables (heart rate, creatinine, Killip class, diagnosis, number of recommended drugs, ACEI/Sartan) are kept at the baseline level (hear rate $\leq$80 pulses/min, creatinine $\leq$100 μmol/l, Killip class = I, diagnosis = STEMI, number of recommended drugs = 5, ACEI/Sartan = Yes). The odds of in-hospital death were increased with increasing age. Patients with heart rate 80-155 pulses/min had the higher odds of death than patients with heart rate $\leq$80 pulses/min. Unlike persons with heart rate 80-155 pulses/min, whose the odds of death was not significantly different from persons with heart rate $\leq$ 80 pulses/min. Higher values of creatinine (over 100 μmol/l) increased the odds of death in comparison with creatinine 100 μmol/l and less. The odds of death were also increased with a higher Killip class, with decreasing number of recommended drugs (aspirin, clopidogrel, unfractionated and low molecular weight heparin or fondaparinux, statin, beta-blocker) received at admission, and if ACE-inhibitor or sartan therapy was not started early. On the other hand, the odds of death were decreased with increasing systolic blood pressure, and the lower odds of death were also observed among persons with final diag-

Table 2: Variables that influence the odds of in-hospital death.

Variables+)		n	Multilevel logistic regression			Logistic regression		
			Odds ratio	95% CI		Odds ratio	95% CI	
Intercept		5734	0.002	0.002	0.006	0.003	0.001	0.010
Age	[by 10 years]	5734	1.92	1.69	2.19	1.90	1.68	2.16
Heart rate [pulses/min]	$\leq$80	3265	1.00			1.00		
	(80-155]	2408	1.46	1.13	1.89	1.44	1.12	1.84
	>155	61	0.56	0.21	1.49	0.53	0.20	1.39
Systolic blood pressure	[by 10 mmHg]	5734	0.81	0.78	0.85	0.81	0.77	0.84
Creatinine [μmol/l]	$\leq$100	3567	1.00			1.00		
	>100	2167	2.29	1.76	2.97	2.41	1.87	3.11
Killip class	I	4251	1.00			1.00		
	II	1145	2.26	1.72	2.98	2.55	1.96	3.31
	III-IV	338	2.99	2.07	4.31	3.34	2.34	4.77
Diagnosis	STEMI	983	1.00			1.00		
	non-STEMI	3205	0.65	0.48	0.86	0.71	0.54	0.94
	UAP	1546	0.02	0.01	0.05	0.03	0.01	0.09
Number of recommended drugs	5	2362	1.00			1.00		
	4	1560	1.52	1.04	2.23	1.16	0.80	1.66
	3	1039	2.83	1.93	4.14	2.08	1.46	2.96
	2	532	2.91	1.86	4.55	1.77	1.17	2.68
	0-1	241	8.07	4.90	13.30	5.36	3.37	8.52
ACEI/Sartan	Yes	3995	1.00			1.00		
	No	1739	1.82	1.37	2.42	1.78	1.36	2.33

+) If we applied to the ordinal explanatory variables (heart rate, Killip class, diagnosis and number of recommended drugs) the orthogonal polynomial contrasts (under the assumption that the levels are equally spaced), there was also significant polynomial effects of those variables on the odds of death.

Table 3: Akaike information criterion (AIC), deviance and degree of freedom (df).

Model	AIC	Deviance	df	Reduction		p
				Deviance	df	
Multilevel logistic regression						
Intercept	3152.9	3148.9	5732			
Age	2849.1	2843.1	5731	305.8	1	< 0.001
Heart rate	2787.5	2777.5	5729	65.6	2	0.004
Systolic blood pressure	2471.6	2459.6	5728	317.8	1	< 0.001
Creatinine	2325.7	2311.7	5727	147.9	1	< 0.001
Killip class	2211.0	2193.0	5725	118.7	2	< 0.001
Diagnosis	2053.5	2031.5	5723	161.5	2	< 0.001
Number of recommended drugs	1913.3	1883.3	5719	148.1	4	< 0.001
ACEI/Sartan	1898.5	1866.5	5718	16.9	1	< 0.001
Logistic regression						
Intercept	3174.3	2988.9	5733			
Age	2861.0	2699.9	5732	289.0	1	< 0.001
Heart rate	2799.0	2652.4	5730	47.5	2	< 0.001
Systolic blood pressure	2484.6	2371.7	5729	280.7	1	< 0.001
Creatinine	2333.3	2283.8	5728	87.8	1	< 0.001
Killip class	2213.6	2173.8	5726	110.0	2	< 0.001
Diagnosis	2082.9	2039.3	5724	134.5	2	< 0.001
Number of recommended drugs	1968.6	1940.6	5720	98.6	4	< 0.001
ACEI/Sartan	1953.2	1923.2	5719	17.4	1	< 0.001

noses non-STEMI and UAP (compared with the diagnosis STEMI). The only substantial difference between both methods was in the number of the received recommended drugs. Logistic regression did not identify significantly higher odds of death in persons with four received recommended drugs compared with persons with five drugs (OR=1.16; p=0.435). In contrast, multilevel logistic regression showed this difference as a significant (OR=1.52;

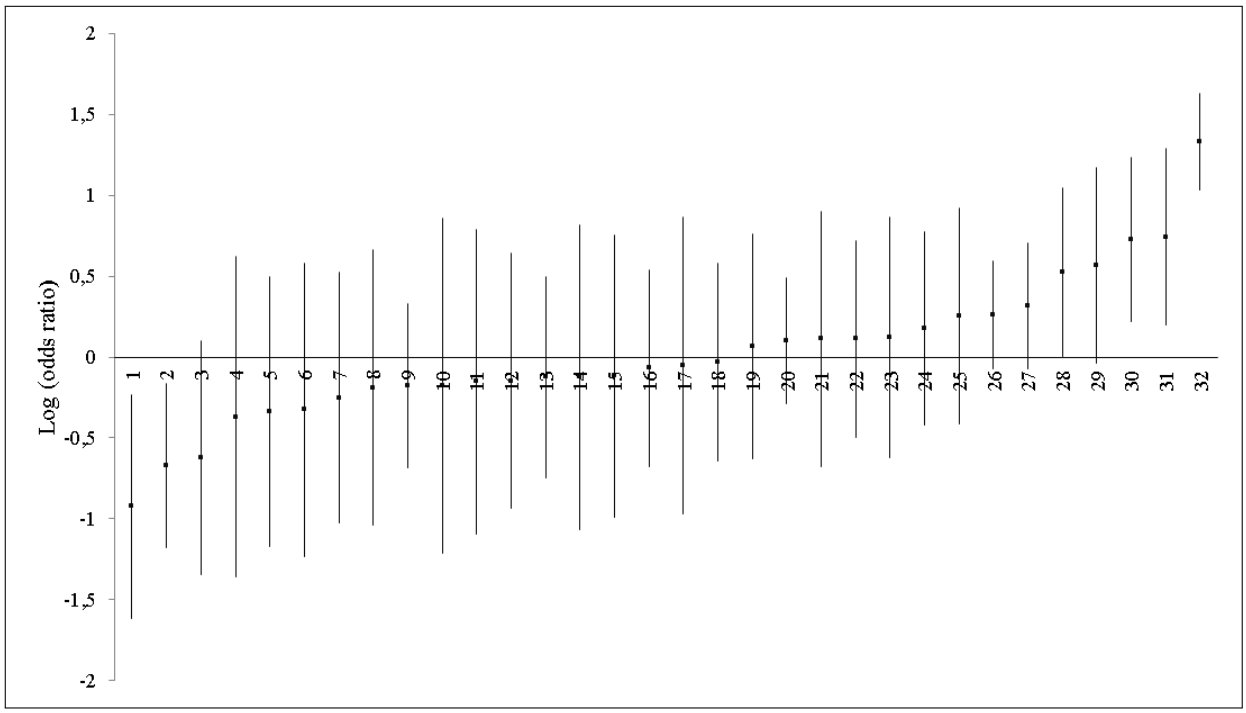

Figure 1: 95% confidence intervals of the natural logarithm of odds ratio of in-hospital death in the 32 hospitals (multilevel logistic regression).

p= 0.031). With the exception of this single difference in significance, let us note that the values of the estimated odds ratio are strongly shifted between both methods in some cases (e.g. in the number of recommended drugs).

The Akaike information criterion in Table 3 is the index that is used for the evaluation of the complexity of the model. Lower values of AIC indicate better model. Deviance measures the appropriateness of the model. The reduction in deviance for each variable, added sequentially first to last, is shown in Table 3. Each variable reduced the deviance significantly. Overall, the significant part of deviance was explained by the final multilevel logistic and logistic regression models (in both cases p<0.001).

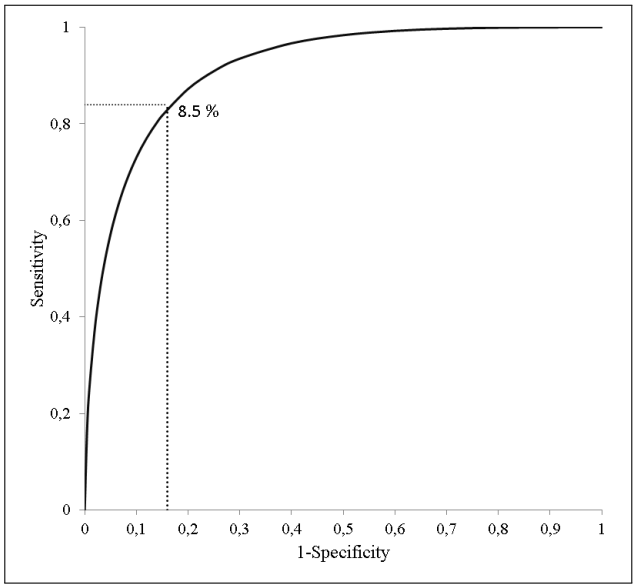

Figure 2: ROC curve - dotted lines mark sensitivity of 83.9% and specificity of 84.0% with threshold risk value of 8.5% (multilevel logistic regression).

When we compare the log-likelihoods of both model, the log-likelihood of multilevel logistic regression (-933.2; df=16) is significantly higher than that of logistic regression (-961.6; df=15), p<0.001. From this reason, we maintain that there is a statistically significant difference in the odds of death among hospitals. Because the VPC is 0.089, we estimate that 8.9% of the total residual variance is due to just hospitals. Although from the statistical point of view, this is a significant difference, from a clinical point of view, the difference may not be significant.

Let us go specify the differences among hospitals. Model of multilevel logistic regression includes, in addition to the intercept of Table 2, which is common for all hospitals, yet another intercepts specific to each hospital (hospital random intercept). Figure 1 illustrates the estimated natural logarithms of odds of in-hospital death in individual hospitals compared to zero value representing the "average" hospital. For a large part of the hospitals, their 95% confidence intervals overlap zero. In fact this means that the odds of in-hospital death in these hospitals did not differ from the average at the 5% significance level. The hospitals, whose 95% confidence intervals do not overlap zero and are above (bellow) the zero line, have the above-average (below-average) odds of in-hospital death. It is, however, necessary to realise that the hospitals with the small sample size have the wide confidence intervals (their estimates values are less accurate) compared with the hospitals with the large sample size. For example, the 95% confidence interval of 10th hospital (n=15) is much wider than 32nd hospital (n=827).

Let us examine in detail the predictive properties of multilevel logistic model. Table 4 shows the observed and expected numbers of in-hospital death across the groups defined on the basis of the percentiles of the estimated risk (probability) of death. There was not any significant difference (Hosmer-Lemeshow test, p=0.989) between the observed and expected numbers of death, and therefore the calibration properties of the model are very good. The highest observed (44.6%) and expected (44.8%) numbers of death were in the group of people with a calculated risk higher than 21.5% (tenth percentile). The discrimination property of multilevel logistic regression model was evaluated by ROC curve, Figure 2. The curve for each value of risk represents the proportion of people with the positive test in the group of the not dead people (1-specificity),

Table 4: Observed and expected relative numbers of in-hospitality deaths (multilevel logistic regression).

			Relative number	
Risk percentile	**Risk**	**n**	**Observed**	**Expected**
1	<=0.03%	574	0.0%	0.0%
2	(0.03%, 0.13%]	573	0.0%	0.1%
3	(0.13%, 0.37%]	573	0.2%	0.2%
4	(0.37%, 0.75%]	574	0.5%	0.5%
5	(0.75%, 1.38%]	573	0.9%	1.0%
6	(1.38%, 2.53%]	573	1.7%	1.9%
7	(2.53%, 4.66%]	574	3.5%	3.5%
8	(4.66%, 9.07%]	573	6.3%	6.6%
9	(9.07%, 21.50%]	573	15.0%	13.7%
10	>21.50%	574	44.6%	44.8%

and the ratio of people with the positive test in the group of the dead people (sensitivity). The best results were achieved for the threshold risk value of 8.5%, when the values of sensitivity (83.9%) and specificity (84.0%) were high. This means that 83.9% of the dead patients had the risk at least 8.5% (positive test), and 84.0% of the not dead patients had the risk under 8.5% (negative test). The total discriminant ability of the model was 91.8% (size of the area under the curve, c-index=0.918).

5 Discussion

The task of our study was to determine what factors influence whether a patient with ACS dies or does not during his/her stay in non-PCI hospital. Because mortality in some studied subgroups was larger than 10% (e.g. Killip class IV), we preferred (binary) logistic regression to Poisson regression. To be able to apply the traditional logistic regression model, observations within a sample must be independent. In our case, this means that the entries in the registry are not correlated with each other. Our study, however, was a multicenter study (a total of 32 hospitals contributed to the registry). If we did not take into account of hierarchical (hospital-patient) data structure, we would automatically assume that therapeutic results (and hence the medical procedures) are not dependent on which hospital the patient resides. Is it possible to make this assumption? Statistical tests showed that the independence of the outputs cannot be entirely assumed among hospitals. Although the differences between hospitals were not essential from our point of view, it was preferable to apply multilevel logistic regression, namely the logistic mixed regression, which took into account of patient affiliation to various hospitals. Hospital equipment, its accessibility, quality medical personnel and adherence to guidelines can have influence on the medical results.

Principles of multilevel modelling were published e.g. in [8, 9, 10, 11, 12]. Other papers on multilevel modelling can be found at the UCLA website (University of California, Los Angeles, Institute for digital research and education) and at the web sites of the Centre for multilevel modelling in Bristol. Austin et al. compared traditional logistic regression with multilevel logistic regression for patients hospitalized with acute myocardial infarction in Ontario, Canada [13]. The authors emphasize that false inferences can be caused by ignoring data structure. Their logistic regression models increased a level of significance for the effects of variables measured at the hospital-level compared a level of significance indicated by the multilevel model. Multilevel models have been applied for statistical analysis in a number of studies dealing with cardiovascular indicators across hospitals, e.g. [14, 15].

Multilevel models are equivalently called hierarchical models. The term of multilevel models is the term general. It reflects that the model works with some levels of data dependencies, either in the framework of the clusters (in our case they are hospitals), or repeated measurements of individuals. Multilevel model estimates individual-specific effects so called random effects for each level of dependence. If there are both fixed effects, which are the same across all levels of dependencies, and random effects, we are talking about mixed models. Models involving just random effects are called random effect models (variance components model). Models without random effects are called fixed effect models. These are based on the assumption that the observations are independent. Generalized linear models, which are estimated using the maximum likelihood method, belong to fixed effect models. If the assumption of independence of data cannot be made, we can use instead of the maximum likelihood method the generalized estimating equations (GEE) method. GEE is able to take account of data dependence, although in a different way than multilevel models [9]. Unlike them, the dependencies are incorporated into the parameter estimates (fixed effects), which then represent the so-called population-average effects. Population-average model is often referred to as marginal model in contrast to mixed model called individual-specific model. GEE method extends the application of GLM to correlated data. Because our goal was to estimate the effects of predictors on the fate of specific individuals (individual-specific effects) and to quantify the impact of the hospitals, we preferred mixed regression model to GEE.

Let us go back to the conclusions of this model. An adverse effect on our findings may be the fact that many hospitals were not involved in the registry for all-time duration of the registry and in some hospitals there was a small number of patients (for this reason we could not analyse the data in a more complex model, such as with random effect of the trend of the age). The majority of patients (89%) did not have at disposal time from first symptoms of ACS to medical facility contact. The results may be also influenced by the length of stay in hospital (median 5 days, range 0-120 days), which can be dependent not only on the patient's health but also the strategic practices in hospitals. However, when we restrict to the odds of death in first 14 days from hospital admission (87% of deaths were registered in the first 14 days), the results were similar. Despite these shortcomings, our conclusions are more or less in the accordance with the risk scores TIMI and GRACE. Odds of death in patients with ACS in non-PCI hospitals influenced age, heart rate, systolic blood pressure, creatinine, Killip class, diagnosis, the number of the received recommended drugs and ACE-inhibitor or sartan treatment. More detailed clinical description of these conclusions is presented in another publication [4].

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References

[1] Hillis LD, Lange RA. Optimal Management of Acute Coronary Syndromes. From The new England J Med. 2009; 360(21):2237–2240. (translated in Czech: Medicína po promoci 4/2009)

[2] Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, Mautner B, Corbalan R, Radley D, Braunwald E. The TIMI risk score for unstable angina/non ST elevation MI: a method for prognostication and therapeutic decision making. JAMA 2000; 284(7):835–842.

[3] Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger CB, Steg PG, Gore JM, Budaj A, Avezum A, Flather MD, Fox KA; GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6 month post discharge death in an international registry. JAMA. 2004; 291(22):2727–2733.

[4] Monhart Z, Reissigová J, Peleška J, Janský P, Zvárová J, Grünfeldová H, Vojáček J, Widimský P. In-hospital mortality of the acute coronary syndromes patients in non-PCI hospitals. (Submitted)

[5] R Development Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, 2010.

[6] Bencko V, Hrach K, Malý M, Pikhart H, Reissigová J, Svačina S, Tomečková M, Zvárová J. Statistical methods in epidemiology. Zvárová J, Malý M (editors): Biomedical statistics III. Volume 1, 2. Prague: Carolinum; 2003 (in Czech).

[7] Pekár S, Brabec M: Modern analysis of biological data 1, Generalised Linear Models in R, Prague: Scientia; 2009 (in Czech).

[8] Pekár S, Brabec M: Modern analysis of biological data 2, Linear models with correlations in R, Brno: Masaryk University; 2012 (in Czech).

[9] Greenland S. Principles of multilevel modelling. Int J Epidemiol. 2000; 29(1):158-67.

[10] Greenland S. Bayesian perspectives for epidemiological research. II. Regression analysis. Int J Epidemiol. 2007; 36(1):195-202.

[11] Leyland AH, Groenewegen PP. Multilevel modelling and public health policy. Scand J Public Health. 2003;31(4):267-74.

[12] Leylan, A.H., Goldstein, H. Multilevel Modelling of Health Statistics. Wiley; 2001.

[13] Austin PC, Tu JV, Alter DA. Comparing hierarchical modeling with traditional logistic regression analysis among patients hospitalized with acute myocardial infarction: should we be analyzing cardiovascular outcomes data differently? Am Heart J. 2003; 145(1):27-35.

[14] Alter DA, Austin PC, Tu JV; Canadian Cardiovascular Outcomes Research Team. Community factors, hospital characteristics and inter-regional outcome variations following acute myocardial infarction in Canada. Can J Cardiol. 2005; 21(3):247-55.

[15] Park S, Lee J, Ikai H, Otsubo T, Ukawa N, Imanaka Y. Quality of care and in-hospital resource use in acute myocardial infarction: Evidence from Japan. Health Policy. 2013; 111(3):264-72.

Models Supporting Development of Complex Information Systems in Healthcare. Case study: an Obstetrics-Gynecology Department

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Abstract

Objectives: The paper presents a framework and tools for developing models useful for implementing complex Information Systems. It presents a case study for an Obstetrics-Gynecology Department and connected departments. The advantages of using models for creating complex OGD Information Systems together with a standardized communication will lead to an advanced interoperability and also will have benefits in patient care and in time will reduce the medical errors.
Methods: This paper presents the modeling process using the Generic Component Model (GCM) in four steps. The real OGD system is described based on the five RM-ODP (Reference Model of Open Distributed Processing) views. The paper presents the Obstetrics-Gynecology Department model based on the real workflow using Business Process Modeling and Notation and a specialized software - Bizagy. Communication between OGD and other medical units is based on HL7 Clinical Document Architecture CDA. The Obstetrics-Gynecology Department Information System (OGD IS) is developed based on the model, in Visual Studio.NET 2010, using ASP.NET pages and C♯ language, and Microsoft SQL Server 2008.
Results: The paper presents a model represented with Business Process Modeling and Notation and its possibilities to offer support for software developers to create flexible and portable information systems. Based on the workflow in the OGD, including the communication between OGD and other medical units, was developed a model and consequently the OGD IS.
Conclusions: For the future, the OGD IS will be extended with new functionalities: possibilities to introduce medication related to a Database in the cloud to receive suggested treatments. The advantages of using the OGD IS are reflected in a better patient care, and the treatments will be more documented which will determine less medical errors.

Keywords

Model, Obstetrics-Gynecology Department Information System, HL7 CDA, GCM, model, Business Process Modeling and Notation, interoperability

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1 Introduction

Interoperability between different medical information systems facilitates access to information and enhances the safety and quality of patient care despite its location. Information about patients is available much easier electronically and at the same time provides patients and medical professionals with updated and relevant information.

To meet the challenge for efficient, high quality, safe and sustainable care in developing countries, there is a need to extend and improve communication and cooperation between all actors participating in better patients' care by creating interoperable health information systems.

Communication between different systems and their components in a complex and highly dynamic environment must fulfill several requirements [1, 2]: openness,

scalability, flexibility, portability; distribution at Internet level; standard conformance; business process orientation; consideration of timing aspects of data and information exchanged; user acceptance; lawfulness; appropriate security and privacy services.

The paper [3] presents the possibilities offered by Business Process Modeling and Notation in healthcare, based on examples. The paper [4] presents a BPMN model for home peritoneal dialysis. The current paper presents the model and for the model based development process for an Obstetrics-Gynecology Department Information System.

An information system in obstetrics – gynecology department is very helpful in maintaining patient data. It is very helpful for medical staff to have information about the patient in real time. Because its specific characteristics, it can include medical data, ultrasound analysis, monitored information from pregnant's lady home and other relevant information about the patient.

The paper presents the possibility to create complex healthcare information systems using models using as case study the current workflow in OGD modeled using Business Process Modeling and Notation. The communication between OGD and other medical units is ensured using HL7 CDA.

2 The Generic Component Model

The GCM is: "an architecture framework that enables the representation of any real or virtual system; includes the system architecture from its business prospective and the system's development process for ICT solution supporting or enabling that business" [1] which was developed by professor Bernd Blobel from University Hospital Regensburg, Regensburg, Germany. The GCM is presented in Figure 1.

The Generic Component Model (GCM) provided the modeling framework for an obstetrics-gynecology department [5].

The steps reflecting the system development process based on the RM-ODP views are:

- defining the analyzed system, in this particular case the OGD IS,
- separation of the domain of current interest (here the medical one) from other domains which are not relevant for the moment (e.g., financial, administrative, security),
- composition/decomposition of the analyzed system, considering four granularity levels (business concepts, relations network, aggregations and details),

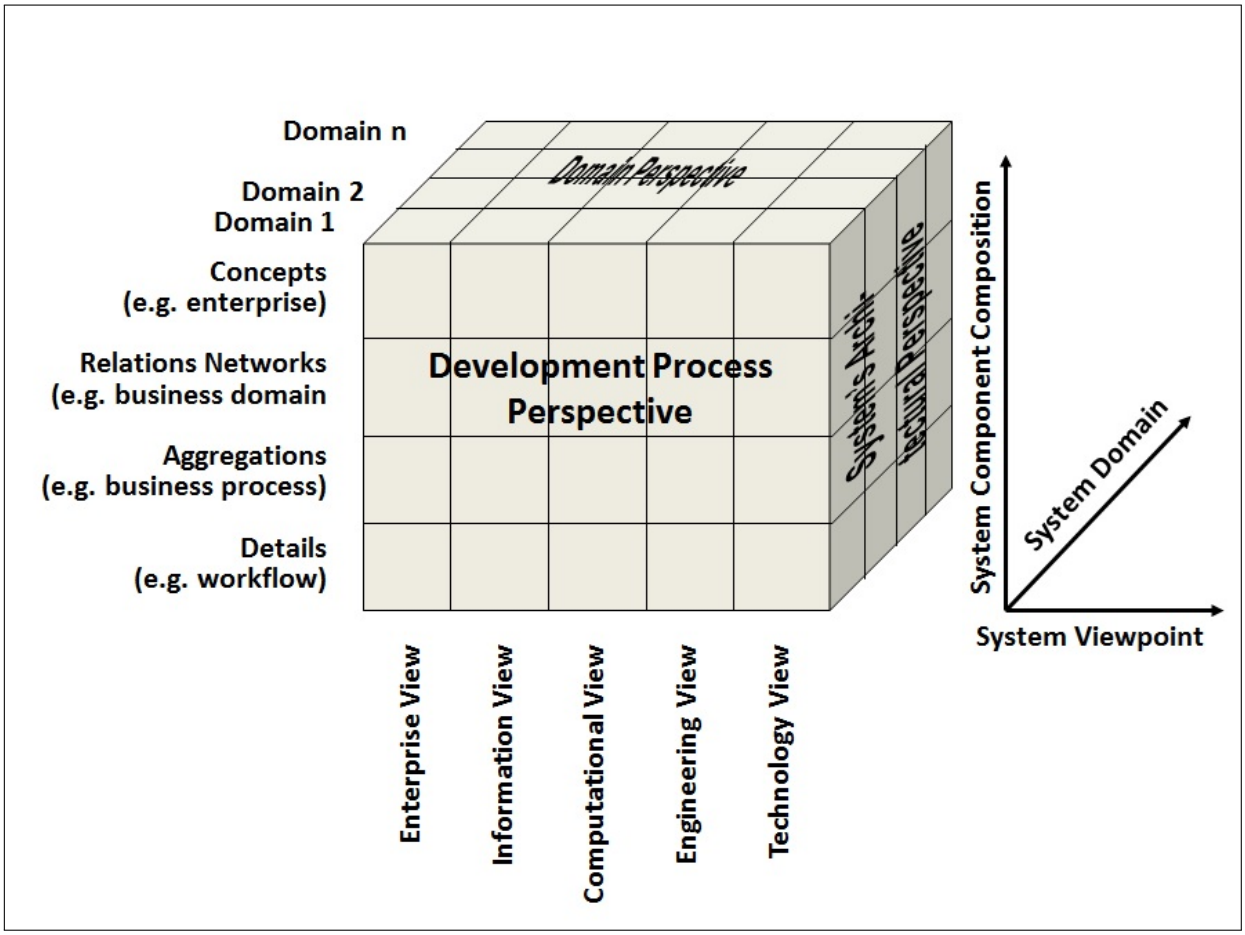

Figure 1: Generic Component Model.

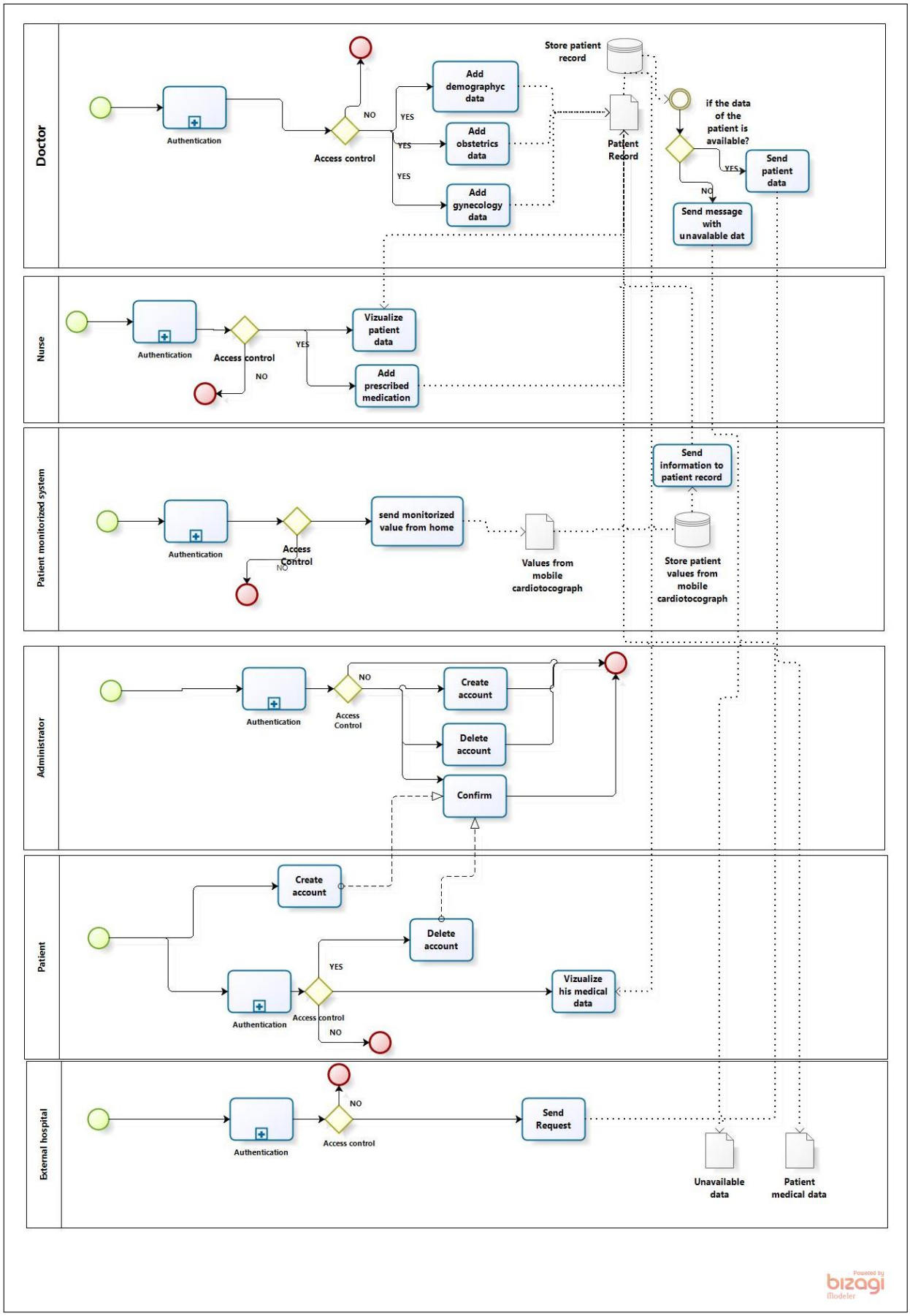

Figure 2: The real workflow in OGD.

- model-driven development of the real OGD system based on the five RM-ODP views previously mentioned.

The OGD system is modeled using Business Process Modeling and Notation, and using Bizagy software. The paper [8] presents a previous version of the model of OGD workflow, and the current paper presents a new model which has more actions, including a monitoring component of the patient status. The OGD IS design and development process was presented in [6, 7]. For the future new functionalities will be available for the system. The model described in the following represents the Enterprise View.

3 Modeling the Obstetrics-Gynecology Department

Figure 2 presents the real workflow in the OGD using Business Process Modeling and Notation language using Bizagy Software [8].

The model connects several actors: Doctor, Nurse, Patient, Administrator, Patient monitoring system and External Hospital.

In Process 1 the main actor is the doctor. If he wants to introduce new data about a patient the first step is to authenticate and after the system verifies if the actor has access to introduce new data about a patient, proceeds. In the correct role he/she can input patient data (demographic, gynecology and obstetrics) into a Patient Record (this record is previously created) which has the data stored on a cloud or a server [8].

In Process 2 the main actor is the nurse that has access to the report for patient data and the monitoring report. She can add information about patient medication administration. Firstly, she has to authenticate herself and after the system checks that she has the appropriate rights, she can visualize the reports or input information about medication [8].

In Process 3 the main actor is the Patient monitoring system. The hospital can receive information about the patient monitored from home. If the patient monitoring system will send monitored information, the first step for the user is to authenticate himself/herself and after the system verifies if the actor has correct access rights, the data will be received and recorded in Patient Record.

In Process 4 the main actor is the administrator. If changes are needed into the system the first step is authentication and after the system verifies if the actor has access, the changes into the system are operated. If the actor has the correct role then he/she has the possibility to create new accounts, delete accounts, to confirm the created or the deleted accounts [8].

In Process 5 the main actor is the patient who can create a new account after the authentication and the system verifies if the actor has access. If the actor has the correct role then he/she can express the will to delete an account or request a report about monitored information about the pregnancy [8].

In Process 6 the main actor is an external hospital which requests data about a patient. Firstly, it has to authenticate and the system checks the rights and if they are correct sends a request to OGD. If he has rights to access the information and if the information is available, the OGD IS will send an XML in HL7 CDA format or in the case if the information are not available than the external hospital will receive a message were will be written that the information about the patient requested are not available [8].

4 Obstetrics-Gynecology Department Information System

OGD IS is an application developed in Visual Studio.NET 2010, using ASP.NET and C♯ language. The database is using Microsoft SQL Server 2008. In the future the system will provide the possibility to receive data from systems which are for monitoring the patient from home (a mobile cardiotocography will give the possibility to send information about the pregnant woman to the doctor). There will be available a possibility to send patient medication to a database in a cloud connected to an application suggesting treatments based on previous doctors experience. The current doctor will have the possibility to choose that treatment or not.

Figure 4 presents an image from OGD IS where the doctor can add a consultation regarding gynecology data.

Figure 3 presents a screen shot from Obstetrics-Gynecology Department Information System where the doctor can add information about the examination.

Figure 3: Entering system examination.

It is important that the OGD IS has the possibility to communicate with other medical units, based on implemented interoperability between medical information systems. Figure 5 presents the communication framework between the OGD IS with other medical units.

To achieve interoperability we use XML files based on HL7 CDA standard. An example is in the case of OGD IS and Pediatrics Department communication. When the data of a new born child is added in the database of the

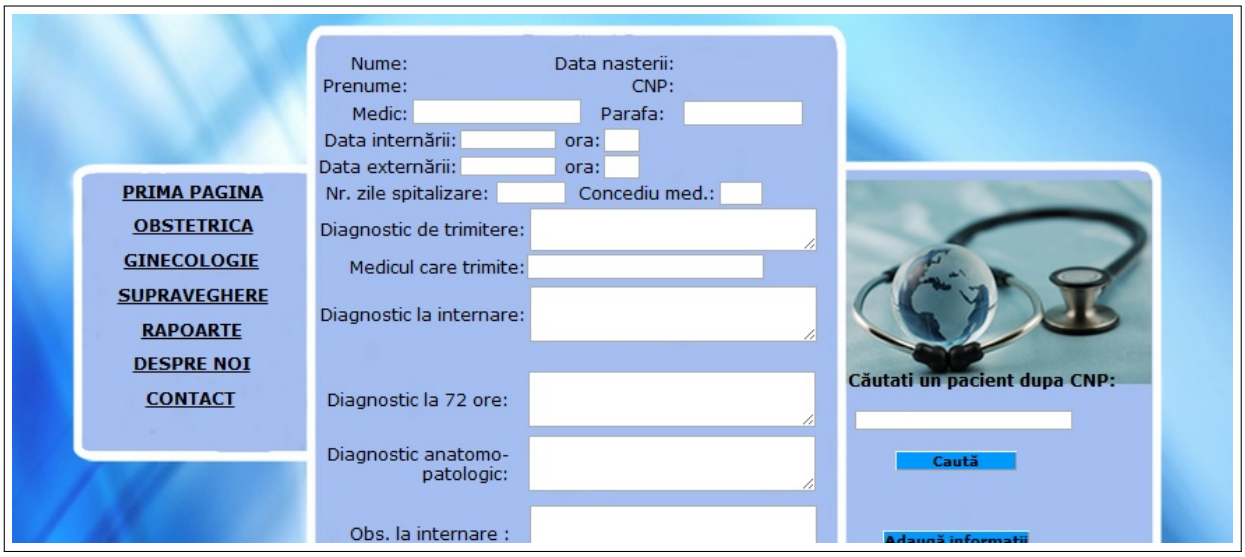

Figure 4: Entering gynecology data.

pediatrician, the physician will be asked if he/she wants to add the data manually or retrieve it from the database of the hospital, which technically is located in the server or private cloud of the Obstetrics and Gynecology unit, where the baby was born. When the data acquisition from the Obstetrics and Gynecology unit option is chosen, the Pediatrics application will create an XML file with the Personal Identification Number of the mother, date of birth of the child. The XML file with these data will be sent to the data server from the private cloud of the unit of Obstetrics and Gynecology. When these dates are available in the server, via a specific application it will check the validity of the received message will analyze the request and if the data exists in the server the application will form another XML file which contains the medical data record of the baby from birth until to the day of discharge. These XML file is created in HL7 CDA standard format, and it will be sent to the unit who requested the data [9].

Once received, the required medical data in XML format, the Pediatrics application will read the XML file and will display the medical records to the location point where the physician adds the patient. The received medical data will be saved in the database server of the private cloud of the Pediatrics unit. The pediatrician will have access to the medical history of the baby from birth and during pregnancy, information important for monitoring and treating the child [9].

In Figure 3 the communication is realized using web server, but in the future will be uploaded in the cloud. The advantage of using the cloud solution is that information is always and anywhere available.

Applications communicate with each other better and more effectively using the HL7 CDA standard, due to its

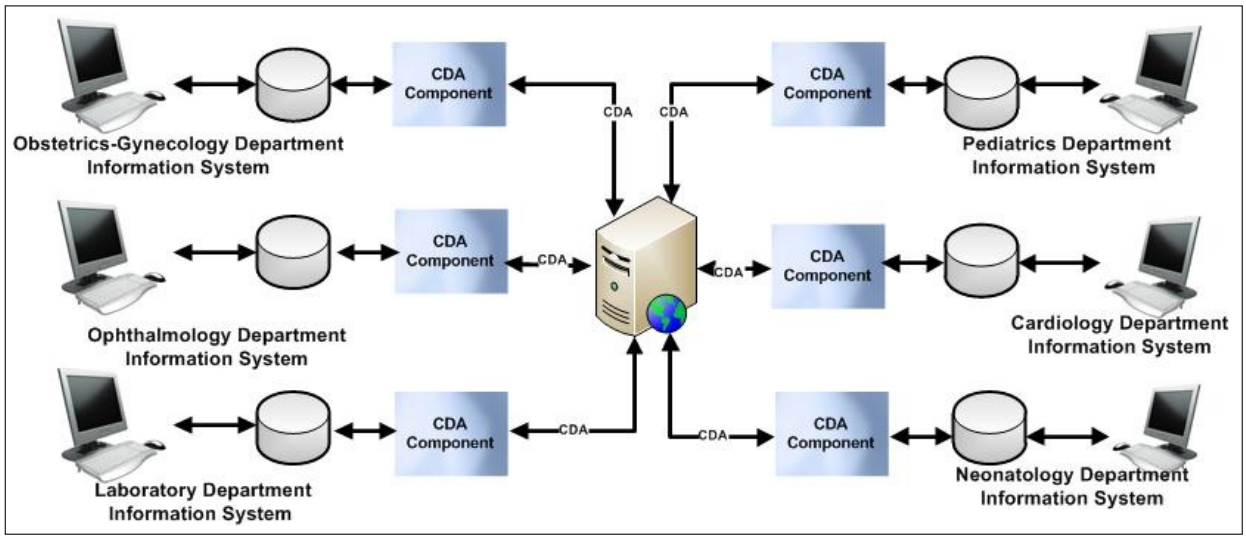

Figure 5: Communication between OGD IS and other medical units.

features structuring the medical data on several levels and with certain codes that can be read by any application that uses these medical standards [9].

5 Conclusions

The paper presents the possibility to create complex healthcare information systems using models. It presents a case study for OGD IS modeled using Business Process Modeling and Notation with its processes. [8] presents a previous version of the model for the OGD workflow, and this paper presents a newer version which brings more actions related to the OGD. Based on the previous model the OGD IS basic system was developed, and in the future the new actions described by this paper model will be implemented. The communication between OGD IS and other medical units is using HL7 CDA with examples presented in the paper. A new component that will be added in the future is the possibility to use a specialized software tool that has as functionalities receiving treatments from different specialist from different locations and checking between given treatments, and suggesting a treatment. The doctor may or may not use the suggestion, having the possibility to approve it or not.

The paper [10] presents the steps and metrics for evaluating the interoperability of an Obstetrics-Gynecology Department Information System used in this paper and applied in Bega Clinic Timisoara regarding its readiness for interoperability in relation with similar systems. [10] presents also the amount of data related to the current system exchanged between the Obstetrics-Gynecology Department and other medical units. The obtained results were relatively good for the investigated data and structure of the system.

The work presented in this paper prepares a framework for flexible and quick development of OGD information systems supported by increased interoperability. Using the OGD IS medical staff will have a support for better patient care, the access to patient information will be in real time in the case of an emergency.

Using models before implementing an application improves the quality of the software, increases development speed, leads to a better maintainability and reusability, and also ensures better portability and interoperability.

References

[1] B. Blobel, Advanced EHR architectures—promises or reality, Methods Inf. Med. 2006; 45 (1): 95–101.

[2] Lopez D., Blobel B. A development framework for semantically interoperable health information systems. International Journal of Medical Informatics 2009; 78:83-103

[3] M. Richard and A. Rogge-Solti, BPMN for Healthcare Processes, CEUR Workshop Proceedings, Vol. 705, 2011

[4] Monteleone, Home Peritoneal Dialysis: a BPMN model and use of 5S principles, Available on: http://www.modernanalyst.com/Resources/Articles/tabid/115/articleType/ArticleView/articleId/2650/Home-Peritoneal-Dialysis-a-BPMN-model-and-use-of-5S-principles.aspx

[5] Lopez D. and Blobel B. Formal Design of Electronic Public Health Records, Medical and Care Compunetics 3, 2006

[6] M. Vida, O. Lupse, L. Stoicu-Tivadar, V. Stoicu-Tivadar, ICT Solution Supporting Continuity of Care in Children Healthcare Services, 6th IEEE International Symposium on Applied Computational Intelligence and Informatics, SACI, 2011, 635-639

[7] O. Lupse, M. Vida, L. Stoicu-Tivadar, V. Stoicu-Tivadar, Using HL7 CDA and CCD standards to improve communication between healthcare information systems, 9th IEEE International Symposium on Intelligent Systems and Informatics, SISY, Serbia, 2011, 435-457

[8] M. Vida, L. Stoicu-Tivadar, B. Blobel, E. Bernad, Modeling the framework for obstetrics-gynecology department information systems, IHIC Conference, 2012, published in European Journal for Biomedical Informatics Vol. 8, Issue 3 "Standard and Solutions for ehealth Interoperability of the European Journal of Biomedical Informatics", 2012

[9] O. Lupse, M. Vida, L. Stoicu-Tivadar, Cloud Computing and Interoperability in Healthcare Information Systems, Proc. The First Internatonal Conference on Intelligent Systems and Applications, INTELLI2012, Chamonix, Franta, pp. 81- 85

[10] M. Vida, L. Stoicu-Tivadar, B. Blobel, E. Bernad, Interoperability Evaluation Case Study: An Obstetrics-Gynecology Department and Related Information Systems, Studies in Health Technology and Informatics, Volume 186: Data and Knowledge for Medical Decision Support, pp. 177 - 181

