2009 Ninth International Conference on Intelligent Systems Design and Applications

On Intelligent Procedures in Medication for Patient Safety: The PSIP Approach

Vassilis Koutkias[a], Katerina Lazou[a], Vassilis Kilintzis[a], Régis Beuscart[b], and Nicos Maglaveras[a]
[a] Lab of Medical Informatics, Medical School, Aristotle University, Thessaloniki, GREECE
[b] Lille University Hospital, EA2694, FRANCE
{bikout, klazou, billyk}@med.auth.gr, regis.beuscart@univ-lille2.fr, nicmag@med.auth.gr

***Abstract*—Adverse Drug Events (ADEs) are currently considered as a major public health issue, resulting in endangering patients' safety and significant healthcare costs. The EU-funded project PSIP (Patient Safety through Intelligent Procedures in Medication) aims to develop intelligent mechanisms towards preventing ADEs, aiming to improve the entire Prescription – Dispensation – Administration – Compliance (PDAC) medication chain. In this regard, PSIP employs data mining and human factor analysis techniques applied on unified patient records and diverse clinical settings respectively, so as to identify the origin of preventable ADEs. This new knowledge combined with existing evidence, in terms of drug interactions and already identified ADE signals reported in the literature, will constitute the basis for constructing contextualized CDSS (Clinical Decision Support System) modules for ADE prevention. In this paper, we briefly present the overall rationale of PSIP and focus on the knowledge engineering approach employed towards the construction of a Knowledge-based System (KBS) regarded as the core part of the PSIP CDSS modules.**

Keywords: Adverse Drug Events; clinical decision support systems; knowledge engineering; patient safety.

I. INTRODUCTION

Nowadays, Adverse Drug Events (ADEs) due to medication errors and human factors constitute a major public health issue, endangering patients' safety and causing significant healthcare costs [1]. Information Technology (IT) is envisioned to play an important role towards the reduction of preventable ADEs by offering relevant knowledge and decision support tools to healthcare professionals [2]. Although there are several efforts towards this direction, their efficiency is impeded by the lack of reliable knowledge about ADEs, and the poor ability of such solutions to deliver contextualized knowledge focused on the problem.

The European project PSIP (Patient Safety through Intelligent Procedures in Medication) aims at preventing medication errors by: (1) facilitating the systematic production of epidemiological knowledge on ADEs, and (2) improving the entire Prescription - Dispensation - Administration - Compliance (PDAC) medication cycle in hospitals via human factor analysis.

More specifically, the first sub-objective involves generating new knowledge on ADEs, i.e., to know as exactly as possible, per hospital, their number, type, consequences and causes, including human factors. Data and semantic mining techniques applied on structured hospital databases and data collections of free-texts (letters, reports, etc.) respectively, are currently employed to identify observed ADEs along with their frequencies and probabilities, thus giving a better understanding of potential risks.

The second sub-objective involves the development of a knowledge-based framework integrating the knowledge discovered in the project with existing evidence in terms of drug interactions and already identified ADE signals reported in the literature, in order to deliver contextualized knowledge fitting the local risk parameters in the form of alerts and decision support functions to healthcare professionals. This knowledge constitutes the backbone of the PSIP platform that is independent of existing Clinical Information Systems, such as CPOE (Computerized Physician Order Entry) and EHR (Electronic Health Record) systems. The PSIP platform will provide the appropriate connectivity mechanisms enabling such systems to access and integrate this knowledge in their local context.

In this paper, we briefly present the overall rationale of PSIP and focus on the knowledge engineering approach employed towards the construction of a Knowledge-based System (KBS) constituting the core part of the CDSS modules for ADE prevention.

II. THE PSIP APPROACH FOR ADE PREVENTION

In order to achieve its objectives, PSIP is organized in the following three stages: (1) Improvement of knowledge on ADEs, (2) development of CDSS modules, and (3) contextualization of CDSS modules and integration in existing IT solutions and usage. Currently, the project is at the middle of the second stage. During the first stage, the available patient databases have been identified residing at the Hospital Information Systems (HIS) of the participating healthcare organizations. In this context, a common data model has been developed to exhaustively define the nature, type, and possible values of parameters that are potentially relevant to ADEs, including drug-related information, diagnostic information, lab results, description of procedures, demographic data, etc [3]. This data model has been used to extract anonymized data from the hospital databases, organize them under the same structure, and prepare them for applying knowledge discovery techniques. It has to be noted that the data model has been designed as generic as possible, enabling this way its reusability for similar research purposes.

Knowledge discovery activities in PSIP focus primarily on the identification of clinical cases that are potential ADEs. Thus, initially, an analysis has been performed in 3,000 patient records exported from RegionH hospitals

978-0-7695-3872-3/09 $26.00 © 2009 IEEE
DOI 10.1109/ISDA.2009.207

(Copenhagen, Denmark), and 10,000 records exported from the General Hospital of Denain (Denain, France). Among the techniques employed for knowledge discovery on ADEs are multivariate correspondence analysis, hierarchical classifications, decision trees, and association rules [4]. The outcome of these activities resulted in knowledge in the form of: (1) A set of association "rules" in the form: *(Condition-1 & Condition-2 & ... & Condition-N)* → *Effect-X*, e.g., *Drug(quinolone[antibiotic])=1 & Drug(proton pump inhibitor)=1* → *Appearance of hyponatremia*, and (2) characterization of hospital stays, according to their probability of showing an ADE. Most of such identified "abnormal" cases are attached to a rule.

The outcomes of knowledge discovery are subsequently filtered and validated, in order to eliminate artifacts or clinically irrelevant results [5]. In this context, two validation methods are employed: (1) As the extracted rules associate information on drugs with biochemical information along with some clinical outcomes, these rules are confronted with the existing clinical pharmacological knowledge available in the scientific literature and/or in specialized information repositories, such as the VIDAL® EXPERT (expertise available in the PSIP Consortium). (2) Since the identified abnormal stays are characterized by a large amount of data describing each patient's case (starting with the entry of the patient and the reason for hospitalization, while ending with the patient's discharge or death), human experts, i.e., specialized physicians or clinician pharmacologists, extensively review these data, in order to decide whether the corresponding patient stays present or not potential ADEs. As most of the abnormal stays are also attached to one or several rules, their review by human experts also allows assessing the capacity of the clinicians to understand the (complex) rules obtained, and the contextual clinical relevance of the rule(s) attached to each reviewed stay.

Following the knowledge discovery and validation phase, a knowledge engineering framework has been established to articulate and electronically encode this knowledge, so that it may be efficiently incorporated in CDSS modules. At the current stage of the project, the design and development of such CDSS modules constitute the primary activity, with particular emphasis on knowledge modeling, representation, management, and inference issues. Equally important, connectivity issues are also explored, aiming to effectively support the provision of the CDSS services and functionality to the clinical environment via a highly interoperable and robust connectivity platform. The knowledge engineering part is presented in the following section.

III. KNOWLEDGE ENGINEERING FRAMEWORK

A. Knowledge Sources

The knowledge sources considered for ADE identification in PSIP are: (a) ADE rules originated from data mining techniques, (b) knowledge on drug interactions available in the Consortium, e.g., drug to drug, drug to allergy class, drug to contraindications, and so forth, that is already known and registered in existing databases, (c) tacit knowledge derived from human experts, providing their knowledge and experiences on ADEs, (d) human factors and clinical procedures, constituting complementary knowledge about factors related to ADEs and associated with human errors within the context of PDAC, and (e) knowledge reported in the literature concerning ADEs.

These knowledge sources constitute the basis for constructing the PSIP Knowledge Base (KB); thus, they were analyzed in detail, in order to design a suitable knowledge model, appropriate engineering processes, and an effective overall KBS architecture. Issues considered were the format/syntax and possible formalization of each source, the required terminologies, the expected size and complexity, as well as special requirements in expressiveness and processing. As a result of this analysis, the major knowledge engineering methodologies that were considered particularly favorable in PSIP are ontology engineering [6], rule-based systems (RBSs) [7], and electronic guidelines and protocols modeling [8]. These methodologies are envisioned to be complementarily employed towards the construction of a common knowledge framework for ADE prevention.

In particular, ontology engineering in PSIP is essential towards the construction of the vocabulary/terminology of concepts/variables related to ADEs that take part in the rules originated by the data mining techniques, as well as for the drug interaction rules. Rule modeling is essential as the project elaborates on rule-like patterns, thus, rules have to be effectively represented in the KB and executed by the KBS engine. Finally, guideline/protocol modeling is particularly important as rules elaborated are rather complex, i.e., each rule typically comprises of several intermediate rules; thus, encoding of each rule involves the construction of a conditional workflow that may be effectively encoded as a guideline/protocol. In addition, guideline/protocol modeling is favorable for representing procedures that are relevant to the PDAC chain currently applied per hospital/department. In general, guideline/protocol modeling enables the unification of domain knowledge (via ontologies) and task/procedural knowledge (e.g., rules) into an efficient problem-solving model that is particularly suited to develop a CDSS [9].

B. Knowledge Modeling

Knowledge employed in PSIP can be considered as belonging in three categories: a) *domain knowledge*, in terms of types and facts, which is generally static and structured via concepts (i.e., classes), relations – associations, attributes, and rule types (expressions); b) *task knowledge*, in terms of functional decomposition, and control; in this regard, knowledge is elaborated with respect to combination of tasks to reach a goal/workflow, or oppositely, decomposition of complex tasks into separate processes; c) *inference knowledge*, in terms of basic reasoning steps that can be made in the domain and are applied by tasks.

The proposed PSIP knowledge model architecture is depicted in Fig. 1. Roughly, its components are discriminated into the following categories:

a) *Drugs*: Defines all possible drugs, containing also their categories and subcategories, based on the ATC (Anatomical Therapeutic Chemical) standard classification.

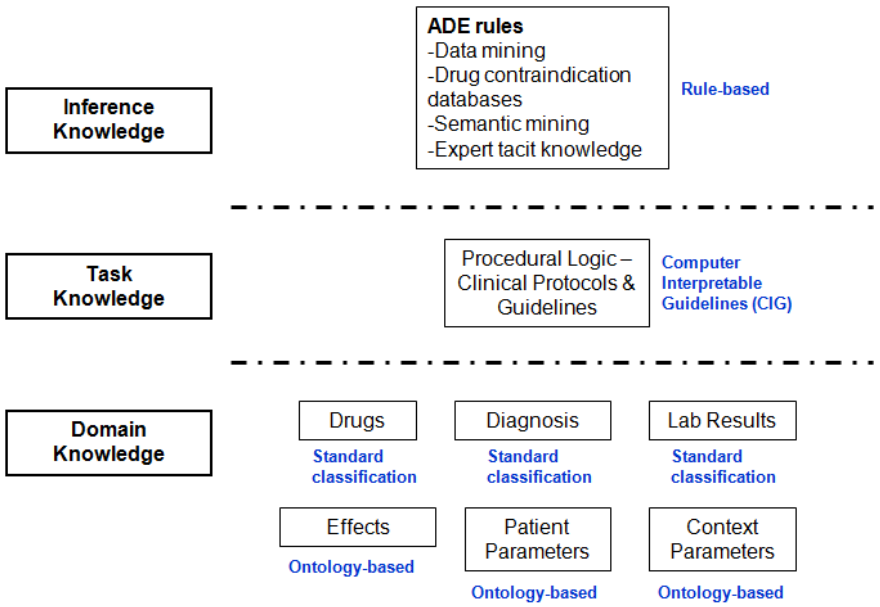

Figure 1. Knowledge model components in PSIP: discrimination among domain, task, and inference knowledge.

b) *Diagnosis*: Defines medical conditions to be used as input parameters for identifying possible ADEs based on the ICD-10 (International Classification of Diseases) standard classification.

c) *Lab results*: Defines the terminology for expressing lab results in the "conditions" part of ADE rules based on the C-NPU (Committee on Nomenclature, Properties and Units) standard classification of IUPAC (International Union of Pure and Applied Chemistry).

d) *Effects*: Ontology-based representation of the effects as entities based on attributes containing the recommendation, the level of severity, type of risk, etc.

e) *Patient parameters*: PSIP-specific ontology-based representation defining the terminology for expressing conditions of the ADE rules.

f) *Context parameters*: Set of context-related parameters defined to allow future contextualization for the CDSS modules.

g) *Procedural Logic – Clinical Protocols and Guidelines*: Description of clinical procedures, protocols and guidelines related to medication that aim to enable expressing knowledge related to human factors and complex ADE rules.

h) *ADE rules*: The core component encapsulating knowledge about potential ADEs in the form of rules associating a number of conditions to an effect.

According to the above, the PSIP knowledge model is defined as a set of ontology-based structures, either PSIP-specific or standard classifications to be used as terminology. In addition, a rule-based component is included that is defined via a set of classes and populated with rules. The ontology-based structures and the rule-based component constitute the fundamental elements to define complex procedural logic in terms of protocols and guidelines, following an electronic formalism, i.e., the guideline modeling component. This formalism enables the unification of the former knowledge components into one single source, so as to provide a knowledge framework based on which the CDSS platform will offer its services.

C. Implementation

Following the requirements and specifications of the knowledge sources, GASTON (http://www.medecs.nl/) was selected as the KBS/CDSS platform in the project. The core of GASTON consists of a guideline representation formalism [10], relying on a combination of knowledge representation approaches and concepts, i.e., primitives, problem-solving methods (PSMs), and ontologies. This formalism uses ontologies as an underlying mechanism to represent guidelines in terms of PSMs and primitives in a consistent way.

In the current development stage, rules generated from the knowledge discovery activities are implemented in the system, while standard and PSIP-specific terminologies have been incorporated and defined, respectively. Fig. 2 depicts the definition of the example rule "*IF DrugSuppr(proton pump inhibitor)=0 & Drug(proton pump inhibitor)=1 & Drug(glucid[nutrient])=0 & Drug(amox-clav[beta lactams antibiotic])=1 THEN Appearance of thrombopenia*" as guideline in GASTON. The rule combines several drug variables (denoted as Drug) that, subject to appropriate "true" (indicated with 1) or "false" (indicated with 0) values, result in the appearance of thrombopenia.

Aiming to avoid potential ambiguities in the description of terms/concepts contained in the discovered knowledge, an XML schema has been defined and agreed upon for knowledge exchange among the knowledge discovery teams and the knowledge authors participating in PSIP.

Due to the incremental knowledge model construction approach adopted in the project, several validation phases are planned throughout the entire lifecycle of the CDSS modules development, to assess their feasibility, technical efficiency, and ultimately their value in various clinical contexts.

IV. CONCLUSIONS

Identification of ADEs constitutes a very challenging problem, considering the complexity of medical information that has to be processed to generate ADE signals, as well as the validation of these signals with respect to their medical/clinical soundness. PSIP employs a systematic approach towards the identification, validation, and efficient representation of ADE-related knowledge exploring, besides patient data, human factors involved in medication errors. The ultimate goal of this analysis is to develop contextualized CDSS modules for preventing ADEs in the entire PDAC medication chain. The decision support services are envisaged to become available to clinical IT systems via a highly interoperable, scalable, and robust platform that will provide the appropriate connectivity mechanisms enabling systems such as CPOE to access and integrate the relevant knowledge and functionality in their local context. Currently, population of the knowledge model is performed, in order to construct an operational KB, while niches of the CDSS modules are also produced for testing and verification. The major challenges faced in the current stage include the incorporation of more complex knowledge sources in the KB, i.e., knowledge related to human factors and tacit knowledge, avoiding over-alerting via contextualization of the KB, as well as validation of the CDSS modules.

ACKNOWLEDGMENT

The research leading to these results has received funding from the European Community's Seventh Framework Program (FP7/2007-2013) under Grant Agreement n° 216130 – the PSIP project (http://www.psip-project.eu/), and has been performed by the PSIP Consortium.

REFERENCES

[1] L. T. Kohn, J. Corrigan, and M. S. Donaldson, "To err is human: Building a safer health system", National Academy Press, 2000.

[2] D. W. Bates, R. S. Evans, H. Murff, P. D. Stetson, L. Pizziferri, and G. Hripcsak, "Detecting adverse events using Information Technology", J Am Med Inform Assoc., vol. 10, no. 2, 2003, pp. 115–128.

[3] E. Chazard, B. Merlin, G. Ficheur, J. C. Sarfati, and R. Beuscart, "Detection of adverse drug events: Proposal of a data model", Studies in Health Technologies and Informatics, vol. 148, IOS Press, pp. 63–74, 2009.

[4] E. Chazard, G. Ficheur, B. Merlin, M. Genin, C. Preda, and R. Beuscart, "Detection of adverse drug events: Data aggregation and data mining", Studies in Health Technologies and Informatics, vol. 148, IOS Press, pp. 75–84, 2009.

[5] N. Leroy, B. Bjørn, A. Baceanu, and M. C. Beuscart-Zephir, "Human factors methods to support the experts' review of automatically detected adverse drug events", Studies in Health Technologies and Informatics, vol. 150, IOS Press, pp. 542–546, 2009.

[6] A. Gómez-Pérez, M. Fernández-López, and O. Corcho, "Ontological Engineering", Springer-Verlag, 2004.

[7] A. Ligêza, "Logical Foundations for Rule-Based Systems", Studies in Computational Intelligence, vol. 11, 2nd Ed., Springer-Verlag Berlin Heidelberg, 2006.

[8] P. A. de Clercq, J. A. Blom, H. H. M. Korsten, and A. Hasman, "Approaches for creating computer-interpretable guidelines that facilitate decision support", Artif Intell Med., vol. 31, no. 1, 2004, pp. 1–27.

[9] M. A. Musen, Y. Shahar, and E. H. Shortliffe, "Clinical Decision-Support Systems", In: E.H. Shortliffe (Ed.). Biomedical Informatics: Computer Applications in Health Care and Biomedicine, Springer-Verlag, 2006, pp. 698–736.

[10] P. A. de Clercq, A. Hasman, J. A. Blom, and H. H. M. Korsten, "Design and implementation of a framework to support the development of clinical guidelines", Int J Med Inform., vol. 64, no. 2–3, 2001, pp. 285–318.

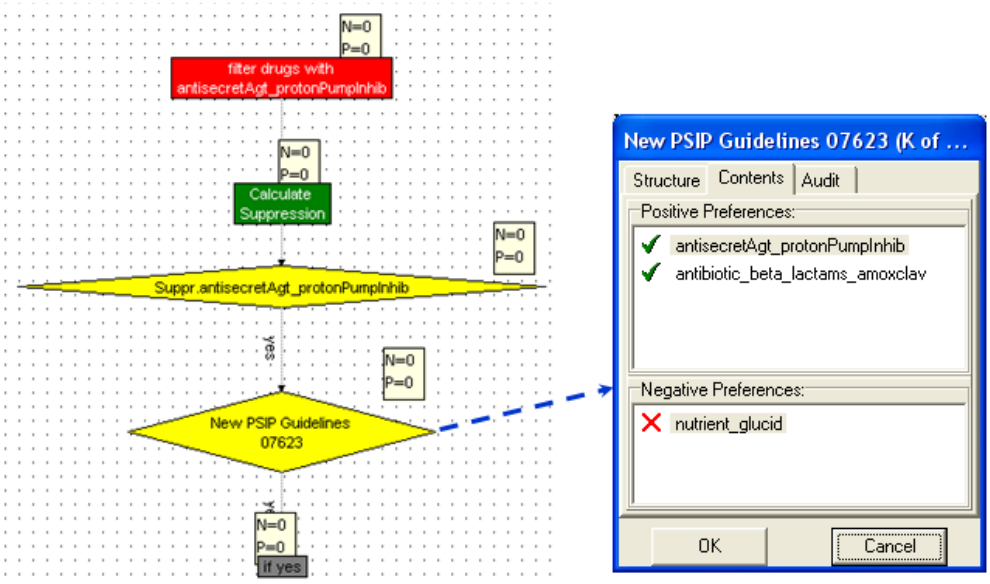

Figure 2. Example rule implementation as guideline (left side: flowchart corresponding to the entire rule implementation, right side: illustration of positive and negative preferences corresponding to rule conditions in a specific guideline decision step).