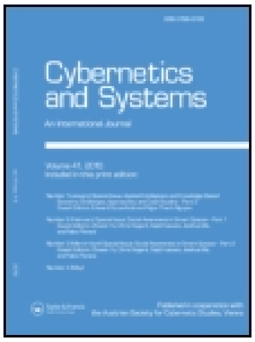

Cybernetics and Systems

An International Journal

ISSN: 0196-9722 (Print) 1087-6553 (Online) Journal homepage: http://www.tandfonline.com/loi/ucbs20

Experience-Based Electronic Health Records

Naiara Muro, Eider Sanchez, Carlos Toro, Eduardo Carrasco, Sebastián A. Ríos, Frank Guijarro & Manuel Graña

To cite this article: Naiara Muro, Eider Sanchez, Carlos Toro, Eduardo Carrasco, Sebastián A. Ríos, Frank Guijarro & Manuel Graña (2016) Experience-Based Electronic Health Records, Cybernetics and Systems, 47:1-2, 126-139

To link to this article: http://dx.doi.org/10.1080/01969722.2016.1128774

Published online: 09 Feb 2016.

CYBERNETICS AND SYSTEMS: AN INTERNATIONAL JOURNAL
2016, VOL. 47, NOS. 1–2, 126–139
http://dx.doi.org/10.1080/01969722.2016.1128774

Taylor & Francis
Taylor & Francis Group

Experience-Based Electronic Health Records

Naiara Muro[a,b], Eider Sanchez[a,c], Carlos Toro[a], Eduardo Carrasco[a,c], Sebastián A. Ríos[d], Frank Guijarro[e], and Manuel Graña[b,f]

[a]Vicomtech-IK4, Donostia-San Sebastian, Spain; [b]Computational Intelligence Group, University of The Basque Country UPV/EHU, San Sebastian, Spain; [c]Biodonostia Health Research Institute, San Sebastian, Spain; [d]Industrial Engineering Department, Business Intelligence Research Center, University of Chile, Santiago, Chile; [e]Bilbomatica, Bilbao, Spain; [f]ENGINE Centre, Wrocław University of Technology, Wrocław, Poland

ABSTRACT
Electronic Health Records are clinical information repositories that have been proposed primarily to provide access to all clinical data of a patient. They have been formally defined by a dual model composed of a reference model and an archetype model. Such dual approach allows semantic interoperability, thus making different systems understand each other. In this work we extend the current structure with a third Decisional Model that will allow reasoning over the embedded clinical contents. Such reasoning will be based on the reuse of the clinical experience gained by the corresponding clinical professionals during different decision procedures.

KEYWORDS
Clinical decision support system; electronic health record; knowledge extraction; semantic model; triple model methodology

Introduction

The use of Electronic Health Records (EHR) has been extended to many hospitals and medical centers during the last decade. EHR are proposed as clinical information repositories that make clinical records of individual patients accessible to practitioners taking care of those patients in a later stage (Kalra and Ingram 2006; Peixoto et al. 2010). Kalra and Blobel (2007) promote the semantic interoperability of EHR. Within their approach, they focus in the seamless and meaningful information and standardization of EHR. In order to achieve this goal, every record must be understandable by any EHR so that the information of a patient traveling throughout different health care systems can be reused and accessed (Bowman 2013; Kobayashi, Kume, and Yoshihara 2015; Moreno-Conde et al. 2015; Sun et al. 2015).

The aforementioned approach is aligned with the concept of semantic interoperability, which to some extent is already a reality. Dolin and Alschuler (2010) maintain that such aspect is still limited to a structural level. A consequence to this is that EHR cannot be used yet for automatic machine-driven reasoning processes (Fette et al. 2012). The automatic processing of clinical contents is relevant in the case that implicit knowledge contained in the

CONTACT Carlos Toro ctoro@vicomtech.org Vicomtech-IK4 - Visual Interaction, Communication Technologies, Mikeletegi Pasealekua 57, Parque Tecnológico, 20009 Donostia, San Sebastián, Spain.
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/ucbs.

EHR is prone to be analyzed (Kukafka et al. 2007; Seebode et al. 2013; Griffon, Charlet, and Darmoni 2014; Marco-Ruiz et al. 2015). As an example of the validity of implicit knowledge within this context, relevant conclusions could be acquired from the experience analysis. Even unsuccessful results after following protocol of a certain therapy in a group of patients will add to the embedded knowledge. Medical areas with demanding research needs, such as oncology and neurology, could benefit from such discovery of knowledge.

Due to the large number of patients' records stored in an EHR system, manually dealing with the analysis could be difficult (i.e., time and resources required are huge). Regarding the automatic analysis, there are still problems that have not been solved. One of these is the type of logical representation of the clinical data in current EHR (Martínez-Costa et al. 2009).

In our work we suggest a new methodology that allows the exploitation of EHR and the use of its clinical contents by automatic reasoning tools. We propose to follow a new architecture for EHR that extends the current dual model based on a *reference model* and an *archetype model* into a *triple model architecture*. In our work the presented extension will be a *Decisional Model*. The dual model approach is based on the representation of the clinical information and follows a temporal order. Our proposed Decisional Model will represent information in terms of decisions made on patients by practitioners. It will allow the extraction of the experience generated during such decisions (e.g., a diagnosis, the prescription of a treatment, the follow-up of a therapy, etc.), based on the analysis of the context of the decisions and the measurements of the outcomes. Clinical Decision Support Systems (CDSS) could directly benefit from the knowledge extracted automatically from EHR. We assume that a decision could involve more than one clinical report of the dual model, and thus, the temporal sense in the Decisional Model could be reinterpreted in a different way. We present also a case study in which we applied our architecture in the breast cancer domain.

This article is arranged as follows: first we present some background concepts about EHR semantization and CDSS integration. Following, we propose our new triple model for EHR that extends the dual approach with a Decisional Model. A use case of such approach for breast cancer is also presented. Finally, conclusions and future work are discussed.

Background Concepts

In this section we introduce the most relevant concepts related to EHR systems and CDSS that would serve as a basis for our discourse.

Electronic Health Record (EHR) Semantization

Electronic Health Records (EHR) are systematic, nonredundant, ordered and complete information collections of digital health data about individual patients or populations (Fernandez-Breis et al. 2008). EHR's primary purpose is the support of efficient, high-quality, integrated health care, independent of the place and time of health care delivery (Hanzlíček, Přečková, and Zvárová 2007).

Current approaches on EHR are oriented toward a dual model (DMEHR) (Moner et al. 2006; Martínez-Costa, Menárguez-Tortosa, and Fernández-Breis 2009, 2010; Martínez-Costa 2010;). DMEHR is based on: (i) a reference model, in which the structure and the elements of the EHR are defined, and (ii) an archetype model, in which the clinical content is formally defined (Moner et al. 2006). The need of a dual model against the precursor single model was justified by Beale (2002). The main idea was to separate information from knowledge. The introduction of the archetype model aims to define domain concepts using restrictions of the structure instances imposed by the reference model. The work of Moner et al. (2006) justifies the use of archetypes, arguing that they provide standardization and an integration of the medical data, providing at the same time a semantic sense to them. Relevant works in this context were presented by Martínez-Costa, Menárguez-Tortosa, and Fernández-Breis (2009, 2010) who developed a new method for archetype transformation between ISO EN13606 and OpenEHR standards, based on Semantic Web Technologies. In such works they demonstrate its application and versatility in both standards thanks to the dual model approach. Furthermore, they also provide another extended transformation tool for the HL7 CDA standard, which permits the reuse of the archetypes described by other standards, even if they follow a different structure (Martínez-Costa, Menárguez-Tortosa, and Fernández-Breis 2011).

Nevertheless, some gaps have been identified around the EHR dual model when attempting to perform semantic activities: for instance, it is not possible to apply reasoning engines into the Archetype Description Language, by which archetypes are represented (Martínez-Costa et al. 2009). A solution combining the Semantic Web and model-driven engineering technologies is proposed for bridging such a problem (Martínez-Costa et al. 2009). The aforementioned approach could allow the extraction of the implicit knowledge recorded on the EHR for different uses, such as the generation of decision recommendations (Sanchez et al. 2014). As mentioned, in this article we propose a new approach that covers the current limitations of the EHR dual model and extends it toward a triple approach.

Clinical Decision Support Systems

CDSS are active, intelligent decision systems that provide specific recommendations for individual cases (Liu, Wyatt, and Altman 2006; Artetxe et al. 2013; Sanchez et al. 2014). Recent works focus on a knowledge-driven approach by which conclusions are obtained from an analysis of (i) patients' data,

(ii) preestablished decisional criteria, and (iii) prior knowledge about the mechanisms of the diseases involved in each case (Kalogeropoulos, Carson, and Collinson 2003; Berner and La Lande 2007). In the aforesaid approaches, the quality of the embedded knowledge in the CDSS determines the quality of the provided support, and thus, it is important to guarantee that it is always correct and up to date. The relevant challenge of maintaining and updating the knowledge of CDSS has been studied in the literature (Peleg and Tu 2006). In this sense, the exploitation of EHR has been identified as an interesting source of knowledge (Branescu, Purcarea, and Dobrescu 2014).

Current approaches mostly address solutions for natural language processing of the stored documents in EHR in order to provide some statistical results (Barrett and Weber-Jahnke 2009). Also, another trend is to provide high-level evaluation of results about certain clinical processes (Sockolow et al. 2012). A relevant work is IBM's WATSON, which focuses on the diagnosis and prescription of treatments in the field of oncology by the exploitation of the EHR and clinical documents (Castaneda et al. 2015). The main difference of our approach consists in the modeling of the knowledge, for which a decisional representation is followed. The proposed system architecture could allow the direct integration of EHR with CDSS.

Proposed EHR Model

In this section we present a new EHR model that allows a secondary usage of the information contained, as well as an architecture for EHR systems that follows the proposed approach. We link the new EHR methodology with its application on CDSS, which could benefit from (i) the extraction and analysis of the implicit knowledge embedded in EHR and (ii) the inclusion of such knowledge in the CDSS for the improvement of the conclusions obtained by them.

Triple Model Approach

Our approach extends the actual dual model into a triple model by adding a new Decisional Model, as depicted in Figure 1. The Decisional Model uses a knowledge structure that supports each decision as well as its context, allowing the reasoning over it. Each decisional event *Dn* is defined by (i) a set of parameters *Pi* involved in the decision-making process, (ii) a set of decision criteria *Cj* wherein such parameters have been analyzed, (iii) the objective *O* for which the decisional event *Dn* is made, (iv) a final decision value *V* that was assigned by the decision maker aiming *O*, and (v) the final result of the decision *R(t)* on the evolution of the patient measured in a future time *t* and measured based on the level of achievement of *O*. In particular, we propose the use of Decisional DNA and the set of experience knowledge structure (SOEKS) as a suitable knowledge structure for such aim, as defined in our previous works (Toro et al. 2012; Sanchez et al. 2014; Sanchez et al. 2015).

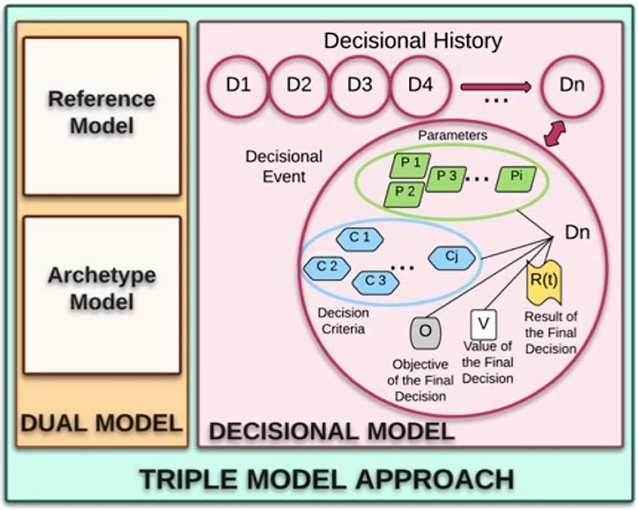

Figure 1. Structure of the presented triple model for EHR.

We assimilate a decision to an experience unit, because making decisions and analyzing the results (i.e., the success or failure associated to the interventions made on each one) provides valuable knowledge and promotes learning. Due to the fact that this learning process occurs everyday in the clinical routine, we propose to imitate such methodology automatically using reasoning tools. In order to do so, the proposed knowledge structure in the Decisional Model contains the whole decision history of the EHR (i.e., all decisions in all patients), which we assimilate to the clinical experience embedded in the EHR. Such decisional history will be generated by formalizing each decision and storing it into the Decisional Model.

Our approach aims to reuse the current EHR systems and extend them with new learning capabilities based on experience. We propose to formalize and acquire each decision from the different clinical events and documents that are already reported in the current EHR systems (see Figure 2). Some translation modules have to be implemented for each EHR system in order to extract the corresponding decisional events, formalize them, and add them to our Decisional Model.

Analyzing such experiences provides relevant conclusions that would lead to new knowledge discovery; for instance, on the mechanisms of a disease or the effectiveness of treatments on different types of patients. In this context, CDSS could play a relevant role, because they could be directly fed by the knowledge discovered from such analyses.

Experience-Based EHR Architecture

In this section we present our architecture for the development of experience-based semantically enhanced EHR (SEHR). Such architecture consists of four

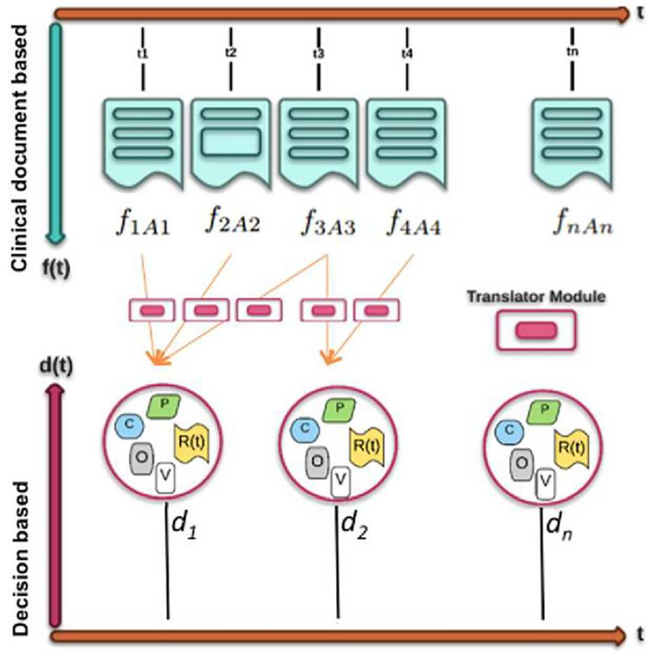

Figure 2. Relation of time-based dual approach and the decision-based triple approach.

layers, as depicted in Figure 3: (i) an integration layer, (ii) a structuration layer, (iii) an exploitation layer, and (iv) an application layer.

Integration Layer

The integration layer allows the translation of any type of EHR (e.g., ISO EN13606, HL7 CDA or OpenEHR) into the SEHR. This is achieved thanks to the development of specific translator modules that extract the corresponding EHR entries from the information about each decision that was made with regard to a patient (possibly coming from different clinical documents or reports). The information with regard to a decisional event will cover the involved parameters, decision criteria with which such parameters were analyzed, the objective of the decision, the decision value, and the outcomes of the decision on the evolution of the patient (level of accomplishment of objectives). Depending on the type of EHR, some natural language processing tools and algorithms might need to be developed in order to extract the relevant decisional information from plain text.

Structuration Layer

The structuration layer is in charge of the formalization of the Decisional Model. The different decisional events will be generated based on the information extracted in the integration layer and following the scheme depicted in Figure 1. Apart from the conceptual level within this layer, decisional events will be serialized and stored in an experience repository, where the full

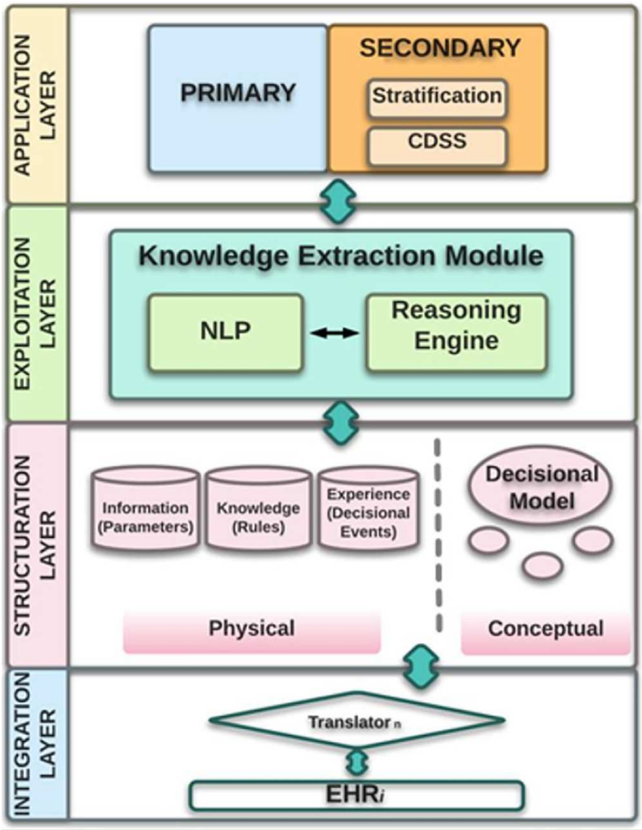

Figure 3. Layer-by-layer description of the new structural triple approach for EHR.

decisional history will be contained. A data repository storing the different patient data and a knowledge repository containing rules and decision criteria will be stored as well.

Exploitation Layer

The exploitation layer is composed of a set of tools allowing the analysis of the decisional events of the Decision Model. Tools centered on different approaches will be covered by this layer, each one focusing on different type of results:

- Semantic reasoning tools: we propose the use of production rules provided by domain experts for the modeling of the contents of EHR. This semantic reasoner divides data to be computer interpretable into three elements: data values, data structure, and terminology-related semantics.
- Natural language processing: This approach addresses the automatic computer interpretation of data contained in narrative text or plain text requiring a specific structure for processing it.
- Machine learning: statistical-based machine learning algorithms can predict some future situations from a selected data structure within EHR for further inputs of the selected group of records.

- Similarity analysis: based on the previous patient records saved on the system, some similarity metrics could be developed to improve the specificity of our system by classifying patients in groups that share common properties.

Application Layer

The application layer is in charge of the interpretation and visualization of the SEHR, as well as the knowledge discovered on them. Depending on the final application domain, different tools and approaches will be followed for such tasks. There are two main application domains: (i) a primary use of the EHR, in which the target is to access patient data and the different decisions and visualize them; and (ii) a secondary use of the EHR, in which the target is the set of conclusions obtained from the analysis of such data and decisions. The next section describes different application cases of secondary use of SEHR.

Secondary Use of EHR

Our approach provides an adequate framework for reasoning over the gathered experience on previous records and the generation of conclusions that could drive a continuous learning right from the EHR. Three different kinds of applications are considered:

- CDSS: we propose SEHR systems as the knowledge repositories of CDSS, in which clinical experience gathered from the decisions applied to patients by physicians is represented in a model that makes it exploitable and reusable. Such methodology allows CDSS to learn from previous decision outcomes (i.e., success and failure) and become more accurate, thus generating new knowledge as well as more adequate decision recommendations.
- Clinical knowledge discovery: Extracting information from biomedical literature supports clinicians' information needs. Thanks to different standards and frameworks, interoperability is enabled, so that discovered knowledge can be easily shared. This improves existing processes for concept identification, treatment effectiveness, evaluation, and disease normalization.
- Patient stratification and population management systems: Different types of patients are grouped and analyzed in order to obtain some relevant results by some parameters of interest for each illness. These studies are related to the different decisions that were taken between patients with similar characteristics, the different treatments that were prescribed, and their effect evaluation or their recuperation time rate, among others.

Case Study on Breast Cancer

We have applied our model in a case study related to breast cancer. We have based our work on the information system developed under the Spanish project LIFE (LIFE Consortium 2015), in which Breast Functional Units (BFU) are provided with a web-based health record. Such record is specifically oriented to breast cancer and implements different archetypes, e.g., a general surgery exploration archetype and an anatomical pathology report archetype, among others. The specification of the breast cancer health record was very structured and contains several categorized parameters and very little free text. Figure 4 shows an example user interface of the breast cancer health record for anatomical pathology.

We generated the archetype for the anatomical pathology report compliant with OpenEHR (see Figure 5 partially depicting a caption of the archetype). The composition class *anatomical pathology* contains three section classes (i) General Section, with the entry *inflammatory carcinoma*, (ii) Surgical Piece, with the entries *size* and *number of lymph nodes*, and (iii) Core Needle Biopsy, with the entry *molecular subtype*.

For the decision of the radiotherapy protocol for a breast cancer patient, data coming from different clinical documents (which are based on different archetypes) will be analyzed by the radiation oncologist. In order to generate the decisional event model for such decision, the translator module will extract the following parameters from each clinical document and store them in the information repository: (i) the age obtained from the patients general information sheet, (ii) the existence of inflammatory carcinoma, the size of the surgical piece, the number of lymph nodes, and the molecular subtype from the anatomical pathology report, (iii) the Breast Imaging Report and Database System (BIRADS) of each lesion from the radio diagnosis report, (iv) the intervention type from the general surgery report, and (v) the breast size and the existence of hypersensitivity from the radiotherapy report. During this process, as shown in Figure 4, the user interfaces of our breast cancer health record store a majority of parameters already categorized, and

Figure 4. Example user interface of the breast cancer health record for anatomical pathology.

```
EVENT[at0002] occurrences matches {0..1} matches {  -- CoreNeedleBiosy
    data matches {
        ITEM_TREE[at0003] matches { -- Tree
            items cardinality matches {0..*; unordered} matches {
                ELEMENT[at0032] occurrences matches {0..1} matches {*}
                CLUSTER[at0004] occurrences matches {0..*} matches {    -- String
                    items cardinality matches {0..*; unordered} matches {
                        ELEMENT[at0006] occurrences matches {0..*} matches {
                        -- PathologicAnatomy_CoreNeedleBiosy_MolecularSubtype
                        whit Internal codes value matches {
                                DV_CODED_TEXT matches {
                                    defining_code matches {
                                        [local::
                                        at0007,     -- Luminal_A
                                        at0008,     -- Luminal_B
                                        at0009,     -- Triple-
                                        at0010] -- HER-2
                                    }
```

Figure 5. Breast cancer anatomical pathology report archetype caption.

thus, there is no need to extract them from a free text box with the use of natural language processing tools. Nevertheless, in other health records some natural language processing could be needed during this step.

Such parameters are analyzed by the radiation oncologist following some criteria, which in our system are modeled as a set of production rules (shown in Figure 6) and stored in the knowledge repository.

Once a final decision on the radiotherapy protocol for a patient is made, a decisional event is generated by the system and stored in the experience repository. Such decisional event links (i) the extracted parameters and values, (ii) the set of rules related to the radiotherapy protocol election, (iii) the final value decided, (iv) the objective of the decision, and (v) the parameter by

```
<?xml version="1.0" encoding="UTF-8"?>
<Rules>
        <LoadRule>
                <KeyLoadRule>1</KeyLoadRule>
                <RuleID>RT0001</RuleID>
                <Rule>If (( CLASS PathologicAnatomy with the PROPERTY
                PathologicAnatomy_SurgicalPiece_Size EQUALS TO T0 ) OR ( CLASS
                PathologicAnatomy with the PROPERTY
                PathologicAnatomy_SurgicalPiece_Size EQUALS TO T1mic ) OR ( CLASS
                PathologicAnatomy with the PROPERTY
                PathologicAnatomy_SurgicalPiece_Size EQUALS TO T1a ) OR ( CLASS
                PathologicAnatomy with the PROPERTY
                PathologicAnatomy_SurgicalPiece_Size EQUALS TO T1b ) AND ( CLASS
                GeneralSurgery with the PROPERTY GeneralSurgery_InterventionType
                EQUALS TO Conservative ) AND ( CLASS Radiotherapy with the PROPERTY
                Radiotherapy_hypersensitivity EQUALS TO Yes ) AND ( CLASS
                PathologicAnatomy with the PROPERTY
                PathologicAnatomy_SurgicalPiece_LymphNodes EQUALS TO 0 )) then (
                CLASS Radiotherapy with the PROPERTY Radiotherapy_ProtocolName
                EQUALS TO MAMA-50 ) </Rule>
                <Weight>100</Weight>
                <AccordingTo>Regla proporcionada por médicos del Servicio de
                Oncología Radioterápica del Hospital General Universitario de
                Valencia</AccordingTo>
        </LoadRule>
        …
…
```

Figure 6. Example production rule for radiotherapy protocol selection.

which the accomplishment of such objective will be measured. The radiation oncologist introduces the last two in the system manually while the final decision value is selected. For each type of decision, there will be a general objective shared by most of the individual decision instances (set default for each decision type), and in only a minor number of cases the objective will be set different (manually introduced to override the default value). In the current example case of the selection of the most adequate radiotherapy protocol for a patient, the main objective will be the total removal of the tumor from the patient, and the accomplishment degree will be measured by analyzing the size and number parameters of tumors in the mammography report.

In order to show the experience-based learning process, we have implemented an example algorithm (see pseudocode Algorithm 1) that calculates the accomplishment degree associated to each rule. In particular, an outcome rate *U* is calculated for each rule, which measures the number of times that an objective has been achieved (Boolean) for a rule that was followed during decision making and that recommended the final decision value. Rules for which *U* is lower than a set threshold should be revised by decision makers, because the recommendation provided by them does not achieve target objectives.

Pseudocode Algorithm 1: Calculation of the Accomplishment Degree Associated to a Rule

```
initialize accomplishment[k]
initialize rulerecommendationapplied[k]
for n=1 to Number of decisional events in decisional history
     for k=1 to Number of rules
            if value recommended by rule_k equals final decision value
                   rulerecommendationapplied[k]=rulerecommendationapplied[k]+1
                   measure the value of result.parameter
                   if rule objective is accomplished analysing result.parameter
                          accomplishment[k]=accomplishment[k]+1
                   end
            end
     end
end
for k=1 to number of rules
     U[k]= accomplishment[k]/rulerecommendationapplied[k]
     if U[k] < threshold
            Recommend revision of rule
     end
end
```

Conclusions and Future Work

In this article we have proposed to extend the current dual model into a triple model that considers a new representation of the information in the EHR based on the different decisions made about patients. Our new approach allows the explicitation of the experience generated during such decisions, based on the analysis of the context and the outcomes of each decision. Such approach could lead to the discovery of new relevant conclusions about a disease, its mechanisms, or the effectiveness of certain treatments applied to a certain type of patients.

Our approach is based on the extension of the current model and, thus, considers the reuse of current EHR systems, as well as of the tools that have been developed for their use. Such tools are mainly focused on a primary use of EHR in which patient data is made accessible. Our approach is focused on extending such functionalities for a secondary use of EHR in which knowledge is generated from the data stored for all patients.

CDSS have been identified as a target application domain in which such approach could provide a direct benefit. The knowledge discovered could be directly inputted to CDSS, facilitating the maintenance of their knowledge bases and supporting them to be up to date with the same experience that the clinical team has learned during real praxis.

As future work we will focus on the generation of predictive models based on the registered experience in the Decisional Model. Additionally, the automatic generation and update of clinical guidelines based on the extracted experience is another target of research work. We will also focus on the tracking of medical decisions and attribution of effects to each decision for legal liability or medical protocol improvements.

Acknowledgment

We would like to express our gratitude to ERESA and the rest of the members of the LIFE project.

Funding

This research was partially funded by the Centre for the Development of Industrial Technology (CDTI) of the Ministry of Economy and Competitiveness of Spain under the grant IPT-20111027 (part of the INNPRONTA program). Some authors received support by EC under FP7, Coordination and Support Action, Grant Agreement Number 316097, ENGINE European Research Centre of Network Intelligence Innovation Enhancement.

References

Artetxe, A., E. Sanchez, C. Toro, C. Sanin, E. Szczerbick, M. Graña, and J. Posada. 2013. Impact of reflexive ontologies in semantic clinical decision support systems. *Cybernetics and Systems* 44 (2–3):187–203. doi:10.1080/01969722.2013.762256.

Barrett, N., and J. H. Weber-Jahnke. 2009. Applying natural language processing toolkits to electronic health records - An experience report. *Studies in Health Technology and Informatics* 143:441–446.

Beale, T. 2002. Archetypes: Constraint-based domain models for future-proof information systems. Paper presented at Proceedings of the OOPSLA 2002 workshop on behavioural semantics, Seattle, WA, USA, November 4–6.

Berner, E. S., and T. J. La Lande. 2007. Clinical decision support systems, theory and practice. In *Chapter overview of clinical decision support systems, Number 1*, ed. by E. S. Berner, 2nd ed., XIV, 270. New York: Springer.

Bowman, S. 2013. Impact of electronic health record systems on information integrity: Quality and safety implications. *Perspectives in Health Information Management* 10:1c.

Branescu, I., V. L. Purcarea, and R. Dobrescu. 2014. Solutions for medical databases optimal exploitation. *Journal of Medicine and Life* 7 (1):109–118.

Castaneda, C., K. Nalley, C. Mannion, P. Bhattacharyya, P. Blake, A. Pecora, A. Goy, and K. S. Suh. 2015. Clinical decision support systems for improving diagnostic accuracy and achieving precision medicine. *Journal of Clinical Bioinformatics* 5:4. doi:10.1186/s13336-015-0019-3.

Dolin, R. H., and L. Alschuler. 2010. Approaching semantic interoperability in health level seven. *Journal of the American Medical Informatics Association* 18:99–103. doi:10.1136/jamia.2010.007864.

Fernandez-Breis, J. T., M. Menarguez-Tortosa, C. Martínez-Costa, E. Fernandez-Breis, J. Herrero-Sempere, D. Moner, J. Sanchez, R. Valencia-Garcia, and M. Robles. 2008. A semantic web-based system for managing clinical archetypes. Paper presented at the 30th Annual International IEEE EMBS Conference, Vancouver, British Columbia, Canada, August 20–24.

Fette, G., M. Ertl, A. Wörner, P. Klügl, S. Störk, and F. Puppe. 2012. Information extraction from unstructured electronic health records and integration into a data warehouse. *GI-Jahrestagung* 208 of LNI, 1237–1251.

Griffon, N., J. Charlet, and S. J. Darmoni. 2014. Managing free text for secondary use of health data. *IMIA Yearbook of Medical Informatics* 9:167–169. doi:10.15265/iy-2014-0037.

Hanzlíček, P., P. Přečková, and J. Zvárová. 2007. Semantic interoperability in the structured electronic health record. *ERCIM News* 69:52–53.

Kalogeropoulos, D. A., E. R. Carson, and P. O. Collinson. 2003. Towards knowledge-based systems in clinical practice: Development of an integrated clinical information and knowledge management support system. *Computer Methods and Programs in Biomedicine* 72 (1):65–80.

Kalra, D., and B. G. Blobel. 2007. Semantic interoperability of EHR systems. *Studies in Health Technology and Informatics* 127:231–245.

Kalra, D., and D. Ingram. 2006. Electronic health records. *In Information technology solutions for healthcare*, ed. K. Zieliński, M. Duplaga, and D. Ingram, 135–181. New York: Springer.

Kobayashi, S., N. Kume, and H. Yoshihara. 2015. Restructuring an EHR system and the medical markup language (MML) standard to improve interoperability by archetype technology. *Studies in Health Technology and Informatics* 216:881.

Kukafka, R., J. S. Ancker, C. Chan, J. Chelico, S. Khan, S. Mortoti, K. Natarajan, K. Presley, and S. Kayann. 2007. Redesigning electronic health record systems to support public health. *Journal of Biomedical Informatics* 40:398–409. doi:10.1016/j.jbi.2007.07.001.

Life Consortium. 2015. Home page of the LIFE project (only Spanish). http://www.proyectolife.es (accessed November 23, 2015).

Liu, J., J. C. Wyatt, and D. G. Altman. 2006. Decision tools in health care: Focus on the problem, not the solution. *BMC Medical Informatics and Decision Making* 6:4.

Marco-Ruiz, L., J. A. Maldonado, R. Karlsen, and J. G. Bellika. 2015. Multidisciplinary modelling of symptoms and signs with archetypes and SNOMED-CT for clinical decision support. *Studies in Health Technology and Informatics* 210:125–129.

Marco-Ruiz, L., D. Moner, J. A. Maldonado, N. Kolstrup, and J. G. Bellika. 2015. Archetype-based data warehouse environment to enable the reuse of electronic health record data. *International Journal of Medical Informatics* 84 (9):702–714. doi:10.1016/j.ijmedinf.2015.05.016.

Martínez-Costa, C. 2010. Semantic interoperability of dual-model EHR clinical standards. Paper presented at the Scientific Meeting of the University of Murcia, TICBioMed Doctoral Symposium, Murcia, Spain, June 15–16.

Martínez-Costa, C., M. Menárguez-Tortosa, and J. T. Fernández-Breis. 2009. Towards ISO 13606 and openEHR archetype-based semantic interoperability. Paper presented at Proceedings of MIE 2009, Medical Informatics in a United and Healthy Europe, Sarajevo, Bosnia and Herzegovina, August 30–September 2.

Martínez-Costa, C., M. Menárguez-Tortosa, and J. T. Fernández-Breis. 2010. An approach for the semantic interoperability of ISO EN 13606 and OpenEHR archetypes. *Journal of Biomedical Informatics* 43:736–746. doi:10.1016/j.jbi.2010.05.013.

Martínez-Costa, C., M. Menárguez-Tortosa, and J. T. Fernández-Breis. 2011. Clinical data interoperability based on archetype transformation. *Journal of Biomedical Informatics* 44:869–880. doi:10.1016/j.jbi.2011.05.006.

Martínez-Costa, C., M. Menárguez-Tortosa, J. T. Fernández-Breis, and J. A. Maldonado. 2009. A model-driven approach for representing clinical archetypes for Semantic Web environments. *Journal of Biomedical Informatics* 42:150–164. doi:10.1016/j.jbi.2008.05.005.

Moner, D., J. A. Maldonado, D. Bosca, J. T. Fernández, C. Angulo, P. Crespo, P. J. Vivancos, and M. Robles. 2006. Archetype-based semantic integration and standardization of clinical data. Paper presented at Proceedings of the 28th IEEE EMBS Annual International Conference, New York City, USA, August 30–September 3.

Moreno-Conde, A., D. Moner, W. D. Cruz, M. R. Santos, J. A. Maldonado, M. Robles, and D. Kalra. 2015. Clinical information modeling processes for semantic interoperability of electronic health records: Systematic review and inductive analysis. *Journal of the American Medical Informatics Association* 22 (4):925–934. doi:10.1093/jamia/ocv008.

Peixoto, H., J. Machado, J. Neves, and A. Ablha. 2010. *Semantic interoperability and health records. E-Health. IFIP*, Advances in Information and Communication Technology, 335, 236–237. Brisbane, Australia: Springer.

Peleg, M., and S. Tu. 2006. Decision support, knowledge representation and management in medicine. *IMIA Yearbook of Medical Informatics* 45:72–80.

Sanchez, E., W. Peng, C. Toro, C. Sanin, M. Graña, E. Szczerbicki, E. Carrasco, F. Guijarro, and L. Brualla. 2014. Decisional DNA for modeling and reuse of experiential clinical assessments in breast cancer diagnosis and treatment. *Neurocomputing* 146 (25):308–318. doi:10.1016/j.neucom.2014.06.032.

Sanchez, E., C. Toro, M. Graña, C. Sanin, and E. Szczerbicki. 2015. Extended reflexive ontologies for the generation of clinical recommendations. *Cyberntetics and Systems* 46 (1–2):4–18. doi:10.1080/01969722.2015.1007723.

Seebode, C., M. Trautwein, M. Ort, and J. M. Lehmann. 2013. A clinical information management platform for semantic exploitation of clinical data. Paper presented at International multiconference of engineers and computer scientists, Hong Kong, China, March 13–15.

Sockolow, P. S., C. Liao, J. L. Chittams, and K. H. Bowles. 2012. Evaluating the impact of electronic health records on nurse clinical process at two community health sites. Paper presented at Proceedings of the 11th International Congress on Nursing Informatics, Montreal, Canada, June 23–27.

Sun, H., K. Depraetere, J. Roo, G. Mels, B. Vloed, M. Twagirumukiza, and D. Colaert. 2015. Semantic processing of EHR data for clinical research. *Journal of Biomedical Informatics* 58:247–259. doi:10.1016/j.jbi.2015.10.009.

Toro, C., E. Sanchez, E. Carrasco, L. Mancilla-Amaya, C. Sanín, E. Szczerbicki, M. Graña, P. Bonachela, C. Parra, G. Bueno, and F. Guijarro. 2012. Using set of experience knowledge structure to extend a rule set of clinical decision support system for Alzheimer's disease diagnosis. *Cybernetics and Systems* 43 (2):81–95. doi:10.1080/01969722.2012.654070.