Smart CDSS: Survey Report

Ubiquitous Computing Lab, Department of Computer Engineering, Kyung Hee University, Korea

Contents

Smart CDSS

The rise in living standards that has occurred with the advancement of new technology has increased the demand for sophisticated health-care applications and services. This has led to the emergence of information and communication technology (ICT)–based clinical decision support systems (CDSS) and online health-care (e-health) applications, systems, and services. To decrease their associated costs, the US federal government is investing $27 billion in health information technology (HIT) under the American Recovery and Reinvestment Act of 2009[Blumenthal2010]. This huge investment was targeted to adopt electronic health records (EHR) at each level of care with meaningful use of HIT—the "meaningful use" criteria of EHR. It has been revealed that health-care costs could be reduced if HIT reduces expensive adverse events [Evidence2008]. In recent studies, researchers have determined that CDSS support in EHR produces the best return on investment for providers, as most of the meaningful-use criteria target these functionalities [Kern2012]. Moreover, various experiments have shown that EHR can improve patient care, reduce errors, and reduce time, if properly equipped with clinical decision support services [Wright2009].

The clinical decision support system (CDSS) has a strong history, starting in 1960 with stand-alone environments. With the advancement of architectural approaches and new requirements, CDSS has evolved from a stand-alone to a service-oriented architecture (SOA) environment. Moreover, for seamless integration of CDSS with existing health-care systems (EHRs, EMRs, PHRs, and CPOEs) to allow sharing of medical knowledge, various standards have emerged to achieve the desired goals. The most prominent knowledge representation language in the clinical domain is HL7 Arden syntax. Therefore, we will discuss the CDSS supporting Arden syntax as the main standard for the knowledge base.

Thyrexpert, Toxopert, and Heaxpert are commercially developed systems that use HL7 Arden syntax for knowledge representations. Thyrexpert assists in thyroid hormone test results and triggers reminders for quality assurance of thyroid diagnoses. Toxopert helps in interpretation of time sequences of toxoplasmosis serology test results. Heaxpert is a web-based system that helps in interpretation and plausibility-checking of hepatitis A and B and serology test results. It includes one main MLM that evokes other MLMs: three MLMs containing decision-making and one MLM containing the template texts for outputs. Its authors state it is integrated with Siemen and with Orbis of Agfa, and they are planning for integration with iPhone and iPad [M. Samwald, 2012].

Moni-ICU detects and continuously monitors nosocomial(i.e., hospital-acquired) infections. Moni-ICU uses a distinct approach by invoking a number of MLMs and implementing different rules that are controlled from one central MLM. The Moni-ICU application works in the ICU connected to a microbiology lab and a patient management system. It monitors all patients on a daily basis in each of the normal intensive care units, which comprise around 100 beds in total [M. Samwald, 2012].

Arden2ByteCode, a newly developed open-source compiler, runs on Java virtual machines (JVM) and translates Arden syntax directly to Java bytecode (JBC) executable. This complier is integrated with SOA-based environments called open services gateway initiative (OSGi) platforms. The compiler has the capability to support all operators of Arden syntax and compile production Java bytecode in minimal time. Due to this direct bytecode, the execution time of MLM is considerably reduced [Gietzelt2011].

Arden/J is a Java-based MLM execution environment that provides integration with XML-based and EMR systems and produces recommendations by executing MLM compiled to Java code. Arden/J supports a runtime environment that allows integration with other systems by implementing mapper interfaces. The authors claim good performance of the compiler and have tested it with XML based EMR [Karadimas2002].

All these systems have potential usages in integrated environments but have failed to communicate with third party heterogeneous health-care systems. The most prominent problem is lack of standardized interfaces that allow an external system to interact with these systems for decision support. Moreover, these systems have lacks in combining multiple knowledge bases in the same domain and controlling knowledge evolution.

Arden Syntax provides standard base format that resembles natural language. The rules representation called MLM (Medical Logic Modules) is independent of any programming platform that makes it easily understandable by non-experts. Platform independence makes MLM based knowledge bases able to share across diverse organizations. Arden Syntax is widely used knowledge representation and it is considered suitable for CDS implementation in terms of;

readability of syntax, syntactic features such as flexible list handling and finally actively developed HL7 standard [M. Samwald, 2012].

Although MLM provides with rich set of metadata option which helps in management of large set of MLMs. However, as pointed out by [M. Samwald, 2012], Arden Syntax has some intrinsic limitations with respect to clear representations for different stakeholders; the knowledge creator and knowledge implementers. The main intent of Arden Syntax is to provide with knowledge representation scheme that is easily manageable for non-expert in computer science. In contrast, this facility comes with ignorance of knowledge implementer which is lacking of set of artifacts that can assure validation, verification and finally maintenance of growing knowledge base. CDSS knowledge implementer is needed to ensure knowledge consistency by incorporating proper verification and validation mechanism when new MLMs are added or existing MLMs are updated or aborted. Furthermore as Arden Syntax based systems enable composition of rules, i.e. invoking MLMs from another MLM which may reside in other knowledge base [Wright2008]. This feature of these systems makes it further complicate when MLMs are validated and verified across multiple chains of MLM calls.

Knowledge validation and verification is concerned about selection of correct clinical knowledge resources and then building the knowledge correctly for particular domain of interest. [Peleg2013] has summarized relevant approaches for clinical knowledge validation and verifications. Most of the research is focusing that clinical knowledge should be validated from domain expert by investigating all possible pathway of decision in clinical rule. However, these approaches failed as knowledge is growing for newly observed clinical outcomes of clinical research. Alternatively, the domain experts in collaboration with knowledge engineers validate the clinical rules by simulating its outcomes through patient sample data values. Moreover, knowledge verification investigates that the clinical rules are internally consistent and free of anomalies and finally the clinical rules satisfies a set of desired properties that intends during formal specification.

[Pérez2010] proposed framework which intends to provide authoring and verification for clinical interpretable guidelines. The proposed framework transform the clinical guideline rule into state chart and define various points in guidelines against which the internal consistency in rule is identified. The authors has verified various clinical rules with cross checking from IRC guideline specification and shows successful results for identifying internal anomalies of the clinical rules. The proposed approach has successes but it comes with few limitations. Firstly, the state chart representation is not supported for all clinical guideline tools. Secondly, the approach is targeting towards specific category of guidelines and variation cause failure to verification of this process.

[Duftschmid2002] proposed verification method for temporal constraints checking in execution of clinical guidelines. The method is based on calculating the minimal network of temporal constraints which tries to identify consistency in temporal scheduling constraints. Furthermore, it also suggests an equivalent non-minimal constraint which can be used by guideline interpreter to assemble feasible time interval of executable guidelines. A limitation of proposed approach is inability to fully verify temporal constraints on the execution of unordered sequential guideline activities.

In order to cater validation of the system, we are working with close collaboration of team of physicians from head and neck cancer department to develop clinical knowledge based on NCCN guidelines and use experiences in oncology of head and neck cancer diagnosis. For verification, we are proposing MLMbaseAugmentedCBR reasoner that uses (CBR) case base reasoning mechanism to verify the newly updated or created rules against available cases in case base. Each rule in clinical knowledge called MLM (Medical Logic Module) is associated with one or more cases from case base. These set of cases help in identification of duplicate rules and find out consistency among multiple clinical rules calling each other in chain. MLMbaseAugmentedCBR is using existing CBR framework from [Recio2014], which facilitates extension of the framework for MLMbase case management.

I-KAT (Intelligent Knowledge Authoring Tool)

There is substantial evidence that CDSSs are beneficial and assistant to clinicians in diagnosing and therapeutic decisions of patients. Shareable knowledge and integration with other healthcare system are important features of CDSS. Healthcare standards (HL7, SNOMED, vMR, Arden Syntax) play pivotal role in achieving these objectives. Several efforts have been made to adopt these standards for shareable knowledge. All these efforts have substantial success in development of shareable knowledge base, but lack facilitating the actual stakeholders (clinicians). Many existing approaches provide complex knowledge creation environment by involving clinicians too much in standard specifications related technical details. Our system provides a user friendly interface to physicians to acquire their knowledge into the knowledge base in easy way. System facilitates the physicians by Intelli-sense functionality that recalls all the related SNOMED CT concepts. System generates Medical Logic Module (MLM) using HL7 standard Arden Syntax that easily shareable with clinical communities. There are many existing systems in literature focusing on development of authoring tools in the area of CDSS. Following are some systems that are developed by different research groups.

[A. Soumeya et al. 2012] a research group at Department of Hospital Information, Henri Mondor Hospital, Creteil (France), presented a UMLS based knowledge acquisition tool for CDSS. The goal of this proposed system is to develop shareable and reusable knowledge base. The system generates the rules using two phases of process that perform by physicians. Firstly, the physicians select the domain ontology using UMLS browser. It also allows the user to add new concepts to domain ontology when it does not exist in UMLS ontology. Secondly, the physicians generate rules from selected domain ontology using condition-action template rule. This tool allows the clinical experts to build and maintain clinical knowledge base in systematic manner. Although the tool provides benefits to clinical experts but it is not an easy to use tool for the clinicians due to more focus on intermediate phases to create a single rule. The phases include clinicians to create domain ontology using UMLS browser initially, then selecting all related concepts for creating rule, and finally organizing an ascending order list to create actual rule. These phases put a lot of burden on the already burdened clinicians.

[R. Rachel 2009] proposed a clinical rule editor for EMR, developed for knowledge and rule management. Its purpose is to remove difficulty of editing hard coded rules. To create a single reminder needs more than one primitives, and the creation of these primitives are fully dependent on software and knowledge engineers. The system has no standard to create shareable knowledge.

[H. Nathan C, 2005] proposed an XML based flexible Knowledge Authoring Tool for physicians to acquire their knowledge into the knowledge base. The authors have used Clinical Document Architecture (CDA) standard for creating sharable and reusable clinical information documents. The complexity of the system is increased because the executable information is also embedded in CDA document. Relationship of multiple CDA for a single patient makes processing more complex. CDA is a standard format designed and recommended for sharing data only; it is not preferable choice to share rules. It is because the rules in CDA format are only shareable with CDA compliant organizations. The system does not use any standard terminology concepts in creating rules, avoiding the use of standard terminologies which decreases the level of interoperability.

[D. Dustin, 2008], developed a Knowledge Authoring Tool to enable clinicians to create knowledge rules without the help of knowledge engineers and programmers. The knowledge rules are creating by using a Pattern and Outcome approach. This authoring tool is used in CDSS for anesthesia but its scope is limited and difficult to extend to other diseases. The system creates java classes library of rules for sharing with other clinical organizations, but these are only works with java platform applications. To create rules first the system defines different patterns and outcomes as parameters. These parameters are stored in form of XML files. Therefore, the clinicians are directly involved to work in XML files, while clinicians are unaware with XML files. It requires some level of training to physicians and it is a tedious and time consuming task for them.

[J. Robert A, 2002] implemented standard based knowledge editor architecture which is used for knowledge dissemination and knowledge base sharing. The system uses vMR standard data model to create shareable knowledge. Understandability of the system is difficult for clinicians and common users due to selection of appropriate object from the vMR standard data model. The end user can only use the system if they have fair knowledge about vMR standard and MLM structure. But it is very tedious and time consuming task for physicians to get complete knowledge of vMR and to understand all the structure and syntax of Medical Logic Module (MLM).

[R. A. Jenders, 1996] proposed an easy to use tool for creation of MLMs. It provides three phases for development of single MLM. In first phase the system creates and composes the Library category of the MLM, it maintains the information about the author, specialist, MLM purpose and keywords. In second phase the user composes the logic part of the rule using controlled vocabulary and conditional operators. In third phase the user specifies the decision of the rule as output message. This system provides a systematic way to compose the MLM, but the controlled vocabulary and the structure of rules are limited to conditional operators only. The controlled vocabulary and support for limited set of operators narrows down the use of the system to a single organization.

[M. Samwald, 2012] presents the detailed implementation of Arden Syntax based clinical decision support system to handle a wide variety of clinical problem domains like hepatitis serology interpretation, monitoring nosocomial infections and melanoma patients. The authors explain development environment, compiler, rule engine and application server for Arden Syntax. The system used a standardized interface of vMR for integrating with external databases of medical information system. But the Arden Syntax IDE is used by the experts with localized terminologies to create MLM. The use of local terminologies instead of standard terminologies reduces the interoperability of the system and enhances the difficulties of integration of the system with other organizations.

To achieve interoperability and provide ease of use for physicians in writing rules, the Rule Editor provides the facility of automatic and intelligent fetching of the SNOMED CT concepts according to vMR schema's selected class. SNOMED CT contains more than 0.3 million concepts, therefore searching and fetching the concepts from overall SNOMED CT ontology on base of vMR schema class will be very slow and deliberative task. However, each domain ontology contains 10 - 15% key concepts as well as relevant concepts of overall SNOMED CT concepts. Therefore, searching and fetching concepts from small ontologies is faster than large ontologies. I-KAT provides the intelli-sence facility from domain ontology instead of overall SNOMED CT ontology. Extraction of domain ontology is very tedious and time consuming task for ontology engineers. I-KAT overcomes this problem by providing automated extraction of domain ontology from SNOMED CT ontology. Following are some survey regarding domain ontology extraction.

[K. Milian, 2010] proposed a system to extract domain ontology; they have focused on breast cancer domain. This system extracts the domain ontology using two methods. Firstly, system extracts the key concepts of domain using seed query method. Secondly, they manually extract the concepts from existing guidelines provided by Dutch Institute for Healthcare Improvement. By using the first method, the system extracts only key concepts while the relevant concepts are omitted. The relevant concepts are extracted from guidelines and then mapped to SNOMED CT concepts manually. Manual extraction and mapping of concepts is time consuming and tedious task. The provided guidelines only cover the treatment; therefore the system only extracts the treatment related concepts while the diagnosis concepts are missing. Finally, the extracted disease-centric ontology contains only the concepts related to treatment of breast cancer disease. So this disease-centric ontology cannot cover the complete domain.

[J. L. I Allones, 2013] proposed a system to support semantic search across archetypes. The system provides an automated method based on SNOMED CT modularization to transform the clinical archetypes to SNOMED CT extracts. System is using different segmentation algorithms to automatically generate initial set of seed concepts from archetypes and then enhance the quality of extracted segments. The system performs graph traversal process on SNOMED CT ontology twice, once for mapping the seed concepts of archetype to SNOMED CT concepts and secondly, to extract the expected segment based on seed concepts. The system is using a virtuous approach of automated seed concepts to extract ontology segments but the scope of the extracted ontology is narrow to segments and the extracted segments may not cover the complete domain.

[M. Bhatt, 2004] introduced a system named, MOVE (Materialized Ontology View Extraction) to extract a subontology from the huge ontologies. MOVE system is using different optimization schemes to maintain the semantic completeness, well-formedness and to derive sub-ontology that is highly qualitative. MOVE system contains a user defined ontology labeling component that facilitates the manipulation during the extraction process. The labeling component allows the users to provide subjective information for included/excluded concepts and attributes in the targeted domain ontology. This is a standard way that the different components of the extraction process communicate with each other but it is a tedious task for users to identify both the selected and unselected concepts and relationships. This system may not handle those concepts that are not included in both sets of selected and unselected concepts but exists in the source ontology.

[J. Seidenberg, 2006] have provided a solution to extract customized segments to solve scaling problem of big ontologies. In this system the authors have proposed some algorithms that start the extraction process with one or more classes of user's choice and create an extract or segment around those related concepts. The system handles the supper class's hierarchy; sub classes hierarchy with the help of upward traversal and downward traversal respectively; while the sibling hierarchy is not included in the extract. It is assumed that the sibling concepts are not relevant enough to be included by default but users can explicitly select them for inclusion, if they are of interest. This system is using boundary classes to define the depth limit; this approach is very useful to minimize the depth of targeted ontology but system must be knows about the chain of links that creates a list of lasses to include in extract or segment.

Knowledge Button

Evidence based systems have long been used in clinical domain for clinical efficacy. In [Sackett, 1996], authors described that good doctors use individual clinical expertise and the best available external evidence in combination, and neither alone is enough. The efficacy studies of clinical practice that form the basis for evidence-based medicine constitutes only a small fraction of the total research literature [Haynes, 1993]. The full promise of clinical decision support systems (CDSSs) for facilitating evidence based medicine will occur only when CDSSs can "keep up" with the literature [Sim, 2001]. It is not surprising that most clinicians consider the research literature to be unmanageable [Sackett, 1996] and of limited applicability to their own clinical practices [McAlister, 1999]. In presence of a sheer amount of literature available online, it is required to reach to relevant information in less possible time with a coherent integration infrastructure of practice based evidence and research based evidence.

[Sim, 2001] provided the idea of evidence-adaptive CDSS; a subclass of CDSSs that are evidence-adaptive, in which the clinical knowledge base of the CDSS is derived from and continually reflects the most upto-date evidence from the research literature and practice-based sources. Evidence-adaptive CDSS is different from conventional evidence-based CDSS that alerts clinicians to a known drug–drug interaction and its clinical knowledge base is derived from scientific evidence, but no mechanisms are in place to incorporate new research findings. Among recommendations, [Sim, 2001] recommended for clinical and informatics researchers to define and build standard interfaces among the repositories (shareable, machine-readable repositories of executable guidelines), to allow evidence to be linked automatically among systems for systematic reviewing, decision modeling, and guideline creation and maintenance.

For any evidence based system to efficiently work in a domain, the context of that domain plays a critical role. Context provide the features for query generation in order to approach for relevant information. The source and format of data are crucial to consider for automatic or semi-automatic query generation.

[Cimino1, 2007] presented the idea of "Infobuttons" and "Infobutton Manager" (IM) that attempts to determine the information need based on the context of what the user is doing. Infobuttons are mainly topic specific with a question facility for the users to tune the query more towards the context. The redesigned of Columbia Infobutton Manager improved the performance by reducing the "perusal time" (time between evocation of the IM and selecting a topic) from 11.13 to 5.92 seconds [Cimino2, 2007]. The main focus of Infobuttons approach is to establish context-specific links to health information resources. It is based on simple topic based linkage to the resource from within the context of EMR/EHR and is not suitable to develop complex queries.

CDAPubMed [Perez-Rey, 2012] is a browser extension aiming to provide a tool to semi-automatically build complex quires. It provides additional information to the contents of EHR for improving and personalizing biomedical literature searches. HL7 Clinical Document Architecture (CDA) is used as a main source to extract clinical terms for query generation. It loads the patient clinical documents (CDA documents), identifies relevant terms for scientific search, and generates and launch literature search queries to a major search engine i.e. PubMed, to retrieve citations related to the HER under examination.

[Chuang, 2003] introduces automatic query taxonomy generation, which attempts to organize user's queries into hierarchical structure of topic classes. This approach consists of two computational processes: hierarchical query clustering and query categorization. The information source for the target queries is Web search results returned by real world search engines.

MCRDR (Multiple Classification Ripple-Down Rules) [Kang, 1995] knowledge base is used to generate queries to fetch information from MSN web search service [Kim, 2008]. MCRDR is a document classification system which employed knowledge acquisition method. The knowledge base of MCRDR document classification consists of rule tree, category tree, and cornerstone cases. Its automatically generate query in multiple ways including category based, rule based, category-rule combined and case based. The claim is to replace domain expert with simulated expert in order to avoid knowledge engineering work.

Without an established infrastructure it is very hard to integrate the relevant research evidence to the local knowledge base of CDSS which is mainly driven by practice based evidences. We propose a comprehensive model called KnowledgeButton that exhibits the properties of evidence adaption from credible knowledge sources. This covers both input request manipulation (query generation) and output response handling ranging from information retrieval to knowledge creation. The ultimate goal of this approach is to evolve the knowledge base of a

CDSS system with new research evidences in the domain. As a complimentary part of Smart CDSS [Maqbool et al. 2012], KnowledgeButton fulfills two objectives; to keep the KB upto-date with newly research evidences and to provide environment for clinical researchers to formulate search queries in easy to use interface. It provides an integrated view of knowledge rules in the KB and linked evidences to clinical decision made by the system.

Interoperability Adapter

Legacy systems can benefit from decision support system only when standards are followed. Standards are divided into different categories based on their objectives. Although some standards have same objectives but different approaches based on information models having semantic differences. Health Information System's (HIS) compliant to these heterogeneous standards can enable communication or exchange of information when these semantic differences are resolved. Health Level 7 Clinical Document Architecture (HL7 CDA) and openEHR are two standards that resembles in managing and storing, retrieval and exchanging health data as Electronic Health Records (EHR). The objective is the same but semantic differences exist due to differences in the information models. The interoperability challenges exists in various terminologies standards as well like LOINC and SNOMED CT. LOINC medical terminologies information is only related to laboratory domain but that can still be mapped to the laboratory related information of SNOMED CT. Therefore the problem occurs when healthcare systems compliant to these heterogeneous health-care standards want to communicate with each other. Resolving these semantic differences results in achieving the objective of semantic data interoperability. There exists literature related achieving interoperability objective using these standards.

Jini Health Interoperability Framework (HIF-J) [Ducrou2009] uses Jini technology which is based on SOA. The main purpose of HIF-J is to exchange semantically interoperable messages. It provides translation services, which behaves as a mediator between standards. These translation services convert message instances HL7 V2 and V3 and also HL7 and openEHR message instances. It is based on XSLT transformations between message instances of different standards. Since standards are growing with new domains, so managing XSLT becomes very difficult. Moreover, XSLT is just transforming syntactic structure and semantic transformation is not achieved.

Artemis [Dogac2006] project is based on achieving semantic interoperability between healthcare systems by using semantic web services. It also uses the concept of semantic mediation which focuses on resolving the heterogeneities between different standards. It mainly focuses on resolving the heterogeneities between HL7 V2 and V3 standards. Artemis uses OWLmt tool, an ontology mapping tool providing a graphical user interface to define the mappings between two ontology schemas. It is limited only to conversion between HL7 V2 and V3 standards.

PPEPR [Sahay2008] project is an integration platform that focuses on resolving the heterogeneity problem between two version of the same standard HL7 (V2 and V3). It is based on semantic SOA concepts and solves the problem of interoperability at the semantic level. It used Web Service Modeling Ontology (WSMO) approach unlike Artemis which uses OWL-S. It mainly focuses on integration of Electronic Patient Records and conversion between HL7 V2 and V3 is specified. The scope is only limited to transformations between standards that comes under the umbrella of HL7.

Ortho-EPR [Magni2008] standard is a proposed standard that is based on the integration of HL7 and DICOM standards for electronic orthodontic patient records. The main purpose of this standard is storage and communication of orthodontic patient records. The message part is handled by HL7 while imaging is handled by DICOM and there integration results in Ortho-EPR standard. Its main purpose is the integration of two standards and not interoperability between standards.

A data aggregation platform [Pieterjan2012] for decision support is proposed to achieve interoperability among health care systems. Semantic web technologies are used for aggregation of multiple sources to enable interoperable communication among healthcare organizations.

Conclusion

Smart CDSS is project is providing set of tools for facilitating clinical recommendation. Smart CDSS knowledge base comprises of MLM supported reasoner with philosophy of case base reasoning that support validation and verification of clinical rules developed by the clinicians. Moreover, the physicians are provided with set of authoring tools called I-KAT which facilitates knowledge creation using easy to use interfaces with support of integrated clinical vocabulary. KnowledgButton is additional tool which provides with facility of incorporating evidences to clinical knowledge. The tool also provides to retrieve all relevant research of interest and associate with existing knowledge as clinical evidence.

References

[A. Soumeya et al. 2012] A.Soumeya, D.Michel, R.Claire, B.Philippe and L.Eric. "A UMLS based knowledge acquisition tool for rule-based clinical decision support system development." Journal of the American Medical Informatics Association , vol 8, no. 4, pp. 351-360, 2012.

[R. Rachel 2009] R. Rachel, G. Rupali and R. Roberto A, "A Clinical Rule Editor in an Electronic Medical Record setting: Development, Design, and Implementation", Proceedings of the AMIA Annual Symposium. American Medical Informatics Association, pp. 537–541, 2009.

[H. Nathan C, 2005] H. Nathan C, R. Roberto A, F. Guilherme Del, B. RICHARD L, H. Timothy P and R. Lorrie K, " KAT: A Flexible XML-based Knowledge Authoring Environment", Journal of the American Medical Informatics Association, vol 12, no. 4, pp. 418-430, 2005.

[D. Dustin, 2008] D. Dustin, D. Jemery, B. Christopher, F. Simon and A. J. Mark. "A Knowledge Authoring Tool for Clinical Decision Support" Journal of Clinical Monitoring and Computing, vol 22, no. 3, pp. 189-198, 2008

[J. Robert A, 2002] J. Robert A and D. Balendu, "Challenges in Implementing a Knowledge Editor for the Arden Syntax: Knowledge Base Maintenance and Standardization of Database Linkages", Proceedings of the AMIA Symposium. American Medical Informatics Association, pp. 355–359, 2002

[R. A. Jenders, 1996] R. A. Jenders, and B. Dasgupta. "Assessment of a knowledge-acquisition tool for writing Medical Logic Modules in the Arden Syntax." Proceedings of the AMIA Annual Fall Symposium. American Medical Informatics Association, 1996

[M. Samwald, 2012] M. Samwald, K. Fehre, J. De Bruin, and K. P. Adlassnig. "The Arden Syntax standard for clinical decision support: Experiences and directions." Journal of biomedical informatics 45.4 (2012): 711-718

[K. Milian, 2010] Milian, K., Aleksovski, Z., Vdovjak, R., ten Teije, A., & van Harmelen, F. 2010. Identifying disease-centric subdomains in very large medical ontologies: a case-study on breast cancer concepts in SNOMED CT. Or: finding 2500 Out of 300.000. In Knowledge Representation for Health-Care. Data, Processes and Guidelines pp. 50-63 (2010). Springer Berlin Heidelberg

[J. L. I Allones, 2013] Allones, J. L. I., Taboada, M., Martinez, D., Lozano, R., & Sobrido, M. J. 2013. SNOMED CT module-driven clinical archetype management. Journal of biomedical informatics, 46, 3 (2013), 388-400.

[M. Bhatt, 2004] Bhatt, M., Flahive, A., Wouters, C., Rahayu, W., Taniar, D., & Dillon, T. 2004. A distributed approach to sub-ontology extraction. In Advanced Information

Networking and Applications, 2004. AINA 2004. 18th International Conference on (Vol. 1, pp. 636-641). IEEE.

[J. Seidenberg, 2006] Seidenberg, J., & Rector, A. 2006. Web ontology segmentation: analysis, classification and use. In Proceedings of the 15th international conference on World Wide Web pp. 13-22 (May 2006). ACM.

[Blumenthal2010] Blumenthal D, Tavenner M. The “meaningful use” regulation for electronic health records. N Engl J Med. 2010; 363(6):501–4.

[Evidence2008] Evidence on the costs and benefits of health information technology; 2008. Publication No. 2976. http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/91xx/doc9168/05-20-healthit.pdf, Accessed:September 23, 2012.

[Kern2012] Kern LM, Wilcox A, Shapiro J, Dhopeshwarkar RV, Kaushal R. Which components of health information technology will drive financial value? Am J Manage Care. 2012; 18(8):438–48.

[Wright2009] Wright A, SittigDF, Ash JS, Sharma S, Pang JE,Middleton B. Clinical decision support capabilities of commercially-available clinical information systems. J Am Med Inform Assoc. 2009; 16(5):437–644.

[Gietzelt2011] Gietzelt M, Goltz U, Grunwald D, Lochau M, Marschollek M, Song B, et al. Arden2ByteCode: a one-pass Arden syntax compiler for service-oriented decision support systems based on the OSGi platform. Comput Methods Prog Biomed. 2011.

[Karadimas2002] Karadimas HC, Chailloleau C, Hemery F, Simonnet J, Lepage E. Arden/J: an architecture for MLM execution on the Java platform. J Am Med Inform Assoc. 2002; 9(4):359–68.

[Wright2008] Wright, A., and Sittig, D.F. A framework and model for evaluating clinical decision support architectures. Journal of biomedical informatics. 41, 6 (March. 2008), 982-990

[Peleg2013] Peleg, M. Computer-interpretable clinical guidelines: A methodological review. Journal of biomedical informatics. 46, 4 (June. 2013), 744-763.

[Pérez2010] Pérez, B., and Porres, IAuthoring and verification of clinical guidelines: a model driven approach. Journal of biomedical informatics. 43, 4 (March. 2010), 520-536.

[Duftschmid2002] Duftschmid, Georg, Silvia Miksch, and Walter Gall. "Verification of temporal scheduling constraints in clinical practice guidelines." Artificial intelligence in medicine 25.2 (2002): 9

[Recio2014] Recio-García, Juan A., Pedro A. González-Calero, and Belén Díaz-Agudo. "jcolibri2: A framework for building Case-based reasoning systems." Science of Computer Programming 79 (2014): 126-145.3-121.

[Sackett, 1996] Sackett, David L., et al. "Evidence based medicine: what it is and what it isn't." BMJ: British Medical Journal 312.7023 (1996): 71.

[Haynes, 1993] Haynes, R. Brian. "Where's the meat in clinical journals." ACP Journal club119.3 (1993): A22-A23.

[Sim, 2001] Sim, Ida, et al. "Clinical decision support systems for the practice of evidence-based medicine." Journal of the American Medical Informatics Association 8.6 (2001): 527-534.

[McAlister, 1999] McAlister, Finlay A., et al. "Evidence- Based Medicine and the Practicing Clinician." Journal of General Internal Medicine 14.4 (1999): 236-242.

[Cimino1, 2007] Cimino, James J. "An integrated approach to computer-based decision support at the point of care." Transactions of the American Clinical and Climatological Association 118 (2007): 273.

[Perez-Rey, 2012] Perez-Rey, David, et al. "CDAPubMed: a browser extension to retrieve EHR-based biomedical literature." BMC medical informatics and decision making12.1 (2012): 29.

[Chuang, 2003] Chuang, Shui-Lung, and Lee-Feng Chien. "Automatic query taxonomy generation for information retrieval applications." Online Information Review 27.4 (2003): 243-255.

[Cimino2, 2007] Comino, James J., et al. "Redesign of the Columbia University infobutton manager." AMIA Annual Symposium Proceedings. Vol. 2007. American Medical Informatics Association, 2007.

[Kim, 2008] Kim, Yang Sok, and Byeong Ho Kang. "Search query generation with mcrdr document classification knowledge." Knowledge Engineering: Practice and Patterns. Springer Berlin Heidelberg, 2008. 292-301.

[Kang, 1995] Kang, B., Paul Compton, and Phillip Preston. "Multiple classification ripple down rules: Evaluation and possibilities." The 9th knowledge acquisition for knowledge based systems workshop. 1995.

[Maqbool et al. 2012] Maqbool Hussain, Wajahat Ali Khan, Muhammad Afzal, Sungyoung Lee, "Smart CDSS for Smart Homes", 10th International Conference On Smart homes and health Telematics(ICOST 2012), Artimino, Italy, June 12-15, 2012.

[Ducrou2009] A. Ducrou. Complete interoperability in healthcare: technical, semantic and process interoperability through ontology mapping and distributed enterprise integration techniques. Doctor of Philosophy Thesis, 2009.

[Sahay2008] R. Sahay, W. Akhtar, and R. Fox. Ppepr: plug and play electronic patient records. In Proceedings of the 2008 ACM symposium on Applied computing, pages 2298-2304. ACM, 2008.

[Magni2008] A. Magni, R. de Oliveira Albuquerque, R. de Sousa Jr, M. Hans, and F. Magni. Solving incompatibilities between electronic records for orthodontic patients. American Journal of Orthodontics and Dentofacial Orthopedics 32(1):116-121, 2007.

[Pieterjan2012] Pieterjan De Potter, Hans Cools, Kristof Depraetere, Giovanni Mels, Pedro Debevere, Jos De Roo, Csaba Huszka, Dirk Colaert, Erik Mannens, and Rik Van de Walle. Semantic patient information aggregation and medicinal decision support. Computer methods and programs in biomedicine, 108(2):724{735, 2012.