Interoperability Mechanisms of Clinical Decision Support Systems: A Systematic Review

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Abstract

The interoperability of Clinical Decision Support (CDS) systems is an important obstacle for their adoption. The lack of appropriate mechanisms to specify the semantics of their interfaces is a common barrier in their implementation. In this systematic review we aim to provide a clear insight into current approaches for the integration and semantic interoperability of CDS systems. Published conference papers, book chapters and journal papers from Pubmed, IEEE Xplore and Science Direct databases were searched from January 2007 until January 2016. Inclusion criteria was based on the approaches to enhance semantic interoperability of CDS systems. We selected 41 papers to include in the systematic review. Five main complementary mechanisms to enable CDS systems interoperability were found. 22% of the studies covered the application of medical logic and guidelines representation formalisms; 63% presented the use of clinical information standards; 32% made use of semantic web technologies such as ontologies; 46% covered the use of standard terminologies; and 32% proposed the use of web services for CDS encapsulation or new techniques for the discovery of systems. Information model standards, terminologies, ontologies, medical logic specification formalisms and web services are the main areas of work for semantic interoperability in CDS. Main barriers in the interoperability of CDS systems are related to the effort of standardization, the variety of terminologies available, vagueness of concepts in clinical guidelines, terminological expressions computation and definitions of reusable models.

Keywords:

Clinical Decision Support Systems; Semantic Interoperability; Terminologies; Clinical Models; Ontologies.

Introduction

Clinical Decision Support (CDS) systems are applications to assist users in health care decision making. They contribute to improve health care and reduce costs [1]. Current initiatives to power the adoption of health information standards are setting the basis for the general use of CDS systems. However interoperability to enable CDS systems smooth integration into clinical workflows and reuse across health care providers are considered as main barriers hindering CDS systems broad adoption [2–4]. New CDS specific standards such as the HL7 Virtual Medical Record (VMR) [5] are improving their modularity and interoperability. Nevertheless, the specification of precise semantics for the concepts used in CDS modules are hampering their successful adoption [3]. This has unveiled that advances in clinical information architecture standards are necessary but do not suffice to grant semantic interoperability (SIOp). Also, advances in other aspects of SIOp such as web services architectures that link information models, terminologies and knowledge models of CDS systems are needed [6].

This paper presents a systematic literature review of SIOp in CDS Systems that extends and includes the studies published since our previous work [7]. We have extended the publication period (adding the period from November 2014 to January 2016). We have modified the keywords in the search from our previous work in order to focus the discussion on the standards available to implement CDS systems attempting to provide a comparative overview of them. We answer the following research questions: which are the approaches and mechanisms currently available to enable SIOp of CDS Systems?; and, what is the coverage of each approach in the literature?

Materials and Methods

Three major research databases were searched for studies about SIOp in CDS. Pubmed, IEEE Xplore and Science Direct databases were queried using keywords ("clinical decision support" and "semantic interoperability"). Additionally studies from other sources considered relevant by the authors were included. Journal papers, book chapters and conference papers written in English since January 2007 to January 2016 were included for the first screening.

Inclusion criteria of papers were based on the following characterics: (a) The study described a CDS with some degree of SIOp with other systems; (b) the paper described mechanisms for the reuse of the CDS functionality across systems. Most papers included were related to medical use of decision support but papers from other areas such as decision support interoperability in industry were also considered if they provided new insights and directions for CDS SIOp.

Eligibility assessment was performed by a single reviewer mapping the identified publications into the aforementioned criteria. Titles and abstracts were first screened rejecting irrelevant papers. A second revision reviewed the studies in full-text selecting those compliant with the eligibility criteria.

No specific data collection form was used. Instead, for each included publication we extracted aspects related to mechanisms used to enable syntactic and semantic interoperability; and how these mechanisms (syntactic and semantic) are combined to grant SIOp. Special attention was paid in identifying barriers and advantages linked to the use of every approach.

Results

Study Selection

The search of the three databases provided a total of 117 records after removing duplicates. Also 11 studies from other sources were considered for review. After screening by title and abstract 75 were discarded for not accomplishing criteria, 53 were selected as relevant for full text review. Of the 53 selected for full-text examination 41 remained to be included in the synthesis and 12 were discarded as they did not comply with the eligibility criteria. Figure 1 contains the workflow followed in the studies selection.
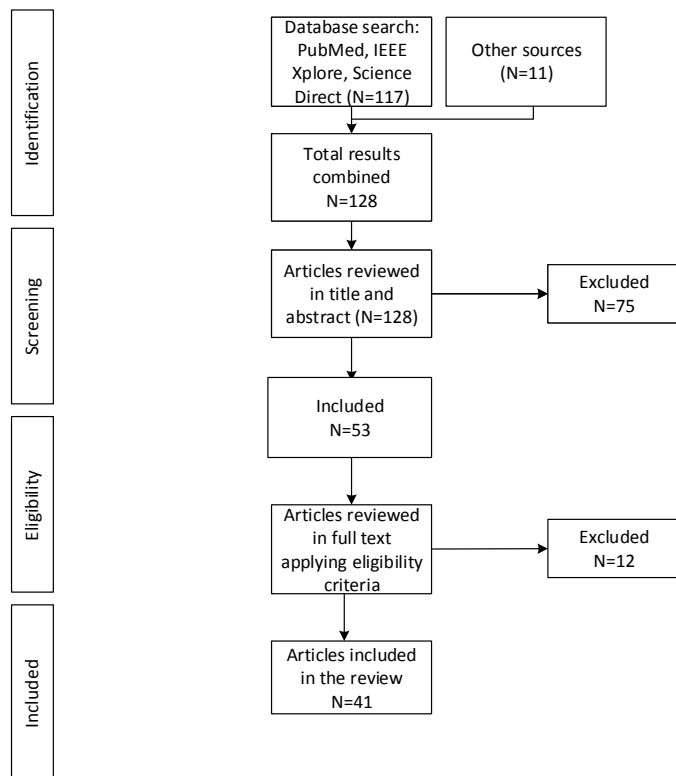

Figure 1 – Workflow followed in the review

Study Characteristics

Among the papers reviewed we identified five main mechanisms used to enable CDSS interoperability. Some provided features to enable syntactic interoperability while others enhanced those features to share information at a semantic level.

Of the 41 papers reviewed 22% (n=9) described the application of medical logic and guidelines representation standards (e.g. GLIF, Arden Syntax etc.); 63% (n=26) described the use of clinical information standards such as HL7 CDA, HL7 RIM, OpenEHR or HL7 VMR; 32% (n=13) employed semantic web technologies such as ontologies; 46% (n=19) outlined the use of standard terminologies; and 32% (n=13) reported the use of web services to offer CDS functionalities. Table 1 presents the mechanisms used to enable interoperability in the studies reviewed. It is important to notice that those categories are not disjoint but complementary. Thus a particular study may pertain to several of them.

Table 1 - Mechanisms used to enable SIOp

Category	Studies		
	Database search	Other resources	%
Use of Clinical Information Standards and Integration with the EHR	[8–27]	[4,28–32]	63 % (n=26)
Use of Terminologies	[3,8,33,12,13,6,16,17,19–21,24–27]	[28,31,34,35]	46 % (n=19)
Use of Semantic Web	[33,13,6,14,16,17,36,27]	[4,29,34,37,38]	32 % (n=13)
Use of Medical Logic Specification Standards	[13,20–22,39–41]	[4,32]	22 % (n=9)
Use of Web Services	[42,8,10,12,43,44,15,19,21,24,26,45]	[32]	32 % (n=13)
Others		[2]	2% (n=1)

Use of Clinical Information Standards and Integration with the EHR

Currently, several information architecture standards exist for the documentation and exchange of EHR extracts. Several works propose their use to specify the interface to interact with the CDS system. Thus, the logic references a standard information model rather than a proprietary data schema. This alleviates the 'curly braces' problem (queries to the EHR proprietary data schema from the MLM logic preventing decoupling

and reuse). Some of the reviewed works [4,12–14,24,25,32,45] propose the use of the HL7 RIM to create a VMR to feed the CDS system. This approach is followed by formalisms such as SAGE or the Arden Syntax [25,39].

Other clinical information standard used as data model for CDS systems is the HL7 Clinical Document Architecture (CDA). CDA is earning momentum as standard for clinical documents consumed by CDS systems as a consequence of the Meaningful Use initiatives [8–11,15,21,22,26,46]. An example of the use of CDA was found in Bouhaddou et al. [46]. They shared messages of patient information between the Department of Veterans and the Department of Defense to enable decision support for alerts and reminders such as drug-drug interactions, allergies or duplicative therapies.

Preparing the data specified in standards such as CDA or RIM to be used by the decision logic is challenging as a consequence of the impedance mismatch between the information model and the inference model. Works to map the RIM VMR to the guideline specification can be found in Peleg et al. [4]. Specifically, they use a mapping ontology (KDOM) to create the abstract concepts required by the logic from the fine grained information contained in the RIM-based VMR. To solve this problem in CDA-based VMRs, Saez et al. [22] proposed to use a wrapper in order to link CDA documents to the CDS rules. Although both RIM and CDA can be used as information models to build a VMR, they are complex and too detailed for the requirements of a CDS data schema. Kawamoto et al. studied the requirements to create a CDS specific information standard to build VMRs based on a simplification of RIM [30]. That work evolved into the current HL7 vMR CDS standard [11,19].

In the archetype-based standards milieu, Marcos et al. [20] and Fernandez-Breis et al. [29] proposed the use of openEHR archetypes. They relied on a VMR created reusing archetypes from the openEHR Clinical Knowledge Manager. As it occurred in the study of Peleg et al.[4], they needed to raise the level of abstraction of clinical concepts. This was accomplished by defining additional layers of archetypes over the VMR to finally provide the CDS with the high abstract concepts required. These layers are linked defining mappings between archetypes with LinkEHR [47].

Weather it is performed with ontologies or archetypes, the process of abstracting concepts from the VMR with mappings is complex and error-prone. In order to simplify it, Marco-Ruiz et al. presented an archetype data warehouse (DW) to execute queries in the Archetype Query Language to generate the concepts with the requested level of abstraction [18].

The choice of a particular information standard when developing CDS systems is not straightforward and has major implications for developers. Only one study was found comparing some of the available standards for implementing the CDS VMR. González-Ferrer and Peleg implemented several use cases to compare HL7 CDA, HL7 vMR and openEHR archetypes [11]. They concluded that HL7 vMR has the best learning curve and ease of implementation; whereas openEHR/ISO13606 archetypes are more powerful for extend-

ing and constraining the information model of the CDS system.

Table 2 presents the coverage of each standard in the studies reviewed. Among the 63% (n=26) of the studies covering the use of information model standards, HL7 CDA is the most spread, covered in 35% of the studies; it is followed by HL7 RIM-based VMR appearing in a 31%; and openEHR in 27% of the studies. 12% of the papers covered HL7 CDS VMR.

Table 2. Clinical information standards coverage

Information standard	Coverage in reviewed studies
HL7 CDA	35% (n=9)
HL7 RIM	31% (n=8)
openEHR	27% (n=7)
HL7 vMR	12% (n=3)

Use of Terminologies

The reviewed studies covered the need to adopt standard vocabularies to enable: (a) logic expressions to reference standard terms, (b) the mediation among systems, and (c) the annotation of the information model entities.

The most common use of terminologies in CDS is to provide a standard vocabulary for medical logic specification. This use has been studied by Ahmadian et al. [35] to identify the main barriers in specifying the concepts used in pre-operative assessment guidelines with SNOMED-CT. Although they successfully represented 71% of the 133 terms extracted from 6 guidelines, they found that 2 issues hampered the mapping of several concepts. First, 27 out of 39 non-matched concepts were terms specified in the guideline vaguely which violated the submission rules of those; i.e. they are not contained in SNOMED-CT and they cannot be considered for submission to it. Second, 12 of the non-matched concepts were valid and must be added to the terminology. In another review about use of terminologies in CDS systems [3] they point out that recent implementations of CDS systems are more likely to adopt international terminologies. They also report that the percentage of positive clinical performance is higher in systems using standard data (79% vs. 50%). That study identifies several barriers hindering the adoption and SIOp related to the use of terminologies: (a) the lack of standardized data is mentioned as a major obstacle by implementers of CDS systems (92% of the problems in CDS systems adoption are related to a lack of standardization); (b) despite the adoption of terminologies, their diversity is an obstacle for the interoperability of CDS systems; (c) despite the advances in international terminologies adoption, 42% of the systems still use local terminologies. To alleviate the problems derived from the diversity of terminologies they propose to adopt UMLS as integrator of different terminologies. In fact, The National Cancer Institute, provider of the UMLS, documents in their architecture caCore

[31] the improvement of their NCI Thesaurus terminology service to facilitate its use in CDS.

Terminologies are also found to play a role in mediation among systems. This is well documented by Bouhaddou et al. [46]. They present the use of several terminologies (RxNorm, UMLS and SNOMED-CT) to build a mediator providing SIOp between the Department of Veterans Affairs and the Department of Defense. Among other objectives, they aim to share patient summary information to apply CDS on allergies, drug-drug interactions and duplicative therapies. Their approach is to provide mediation terminologies and map the institutional terminologies to them. In specific, they used SNOMED-CT for allergy reactions, UMLS for drug allergies and RxNorm for medications. They report 92% successful mappings to terminologies. The mapping to pharmacology terms is reported as one of the main challenges.

Terminologies are also used to support knowledge modelling. Marco-Ruiz et al. [17] used SNOMED-CT to model respiratory symptoms and signs using archetypes and a ontology annotated with SNOMED-CT.

Overall 46% (n=19) of the studies covered use of terminologies. Table 3 shows how the most commonly used was SNOMED-CT reported in 63% of the studies; LOINC was used in 53% of the studies; RxNorm in 21% and ICD in 16%. Also the terminology integrator UMLS was used in 21% of the studies that covered terminologies.

Table 3. Terminologies coverage

Terminology	Coverage in reviewed studies
SNOMED-CT	63% (n=12)
LOINC	53% (n=10)
RxNorm	21% (n=4)
UMLS	21% (n=4)
ICD	16% (n=3)

Use of the Semantic Web

Ontologies have been extensively used in decision support due to their capabilities for knowledge representation and reasoning. Several works have been found in the review documenting their use for different purposes that cover from interoperability and knowledge representation to reasoning.

In knowledge representation we found studies such as the presented by Iqbal et al. [14]. They built an ontology extending the W3C Computer-based Patient Record (CPR) with the Western Health Infostructure Canada (WHIC) for chronic disease management. Of particular interest is the replacement of the CPR vocabulary with SNOMED-CT standard terms. They also map each of the concepts of the ontology to HL7 RIM classes to ensure that HL7 messages can be integrated with the ontology. For the HL7 RIM mapping a 100% successful mappings are reported; for properties, they report 8 out of 80 partial mappings and 10 out of 80 not possible mappings respectively. Another example is the aforementioned use of ontologies to represent symptoms and signs of respiratory diseases [17].

Ye et al. [38] present a pure semantic web-based approach. They defined the Clinical Pathway Ontology (CPO) for the specification of clinical pathways. The ontology is implemented as a combination of a new defined model, the process ontology specified in OWL-S and an entry ontology of time. They rely on their CPO rather than other formalisms as they consider: (a) CPO to be more accurate to specify pathways were multidisciplinary teams interact; (b) CPO to be more adequate to manage knowledge documentation and evolution. For temporal rules specification they used the Semantic Web Rule Language (SWRL) which guarantees a seamless integration with the OWL-based model. In their case study they use their framework to specify Cesarean guidelines. Another example of semantic web technologies used for CDS implementation is presented by Zhang et al. [27]. They implemented a CDS for diabetes management over a RIM-based information model using OWL for knowledge specification, SPARQL for queries definition and Jena rules for specifying decision logic.

Ontologies have also been used for integration of heterogeneous data models in several studies. For example, the project Advancing Clinico-genomic Trials on Cancer – Open Grid Services for Improving Medical Knowledge Discovery (ACGT) describes a complete framework where the ACGT master ontology is used to integrate heterogeneous distributed databases and clinical genomic data [34]. The project defines the model and the integration mechanisms to map ontology elements to data access service schemas. Next version is expected to exploit the model for decision support in assessment and management of clinical trials. Already mentioned, is the use by Peleg et al. [4] of the mapping ontology KDOM to map the HL7 RIM VMR to the clinical guideline by mapping ontology concepts from more basic (and close to the EHR) to more abstract (and close to the guideline).

Also, ontologies have been used for inferences. Fernández-Breis et al. [29] used OWL DL reasoning for clinical trials eligibility. They used archetype layers to raise the level of abstraction from the EHR to populate their ontology. The ontology was used to classify cohorts of colorectal cancer patients.

The combination of ontologies and archetypes is of special interest as enables reasoning over clinical data stored as archetype instances. Lezcano et al. [16] transformed archetypes into OWL and enabled decision support defining SWRL rules over the OWL representation. The work of Lezcano et al. annotates the ontology concepts with SNOMED-CT allowing the application of SWRL over standard terms.

The use of semantic web technologies appeared in 32% of the studies (n=13). Table 4 shows the field of application of semantic web technologies. 69% (n=9) of studies used ontologies to represent the conceptual models of the knowledge base; 38% (n=5) used ontologies to integrate different conceptual models or to overcome the impedance mismatch between the EHR and the CDS logic. Regarding inferences, OWL reasoning or SWRL were used in 31% of the studies (n=4).

Table 4. *Areas of aplication of Semantic Web*

Type of use of semantic web technologies	Coverage in reviewed studies
Knowledge representation	69% (n=9)
Integration and mapping	38% (n=5)
Rules specification	31% (n=4)

Use of Medical Logic Specification Standards

Several works used medical logic specification standards. One of them was the Arden syntax. It was one of the first formalisms designed to specify medical logic. Its main innovation was the capability to encapsulate CDS in sets related to one decision support functionality called Medical Logic Modules (MLM) which gradually evolved into HL7 standard. Samwald et al. [39] present the use of the Arden syntax to implement diverse MLMs in hepatology, rheumatology, oncology and Intensive Care Unit monitoring among others. They found that the reusability of the MLM was compromised by the well-known 'curly braces' problem. To overcome this issue they propose the integration of Arden with GELLO to take advantage of GELLO's object-based expression language and rely on the VMR as standard interface for data access. GELLO is currently another HL7 standard which data model is a simplified view of HL7 RIM [48].

Other publications focus on guidelines and workflow specification. Peleg and Gonzalez-Ferrer [32] reviewed several guideline specification languages based in Task-Network Models. The most prominent are EON, GLIF, GELLO, New Guide, PROforma, GLARE and GASTON. A full evaluation of them is out of the scope of this paper but examples of PROforma and GLIF-3 use can be found in Marcos et al. [20] and Peleg et al. [4] respectively. A relevant work which evolved many of the features presented in those formalisms and deployed them in a standards oriented environment is the Standard-Based Active Guideline Environment (SAGE). Tu et al. [25] presented a SAGE overview describing the use of different standards for CDS in the project. It relies both in standard information models and terminologies as, for example, SNOMED-CT. It evolves concepts as the VMR of EON or the GLIF decision models. It also uses previously defined languages to specify data access and computation such as GELLO. A difference of SAGE with respect to other guideline formalisms is that it relies in an event-driven architecture so as not to interfere with the host system's workflow. Other example of the SAGE architecture applied to CDS for immunization is described by Hrabak et al. [13].

More oriented to knowledge management of CDS modules, Sordo and Boxwala [23] present the Grouped Knowledge Elements (GKE). The GKEs are artifacts which contain: (a) structured templates to specify the patient data to feed the CDS and (b) an order set which contains the set of actions to be applied under certain circumstances. This way a GKE links the specification that the patient data should comply with and the

medical logic to process it. HL7 has published the HL7 CDS Knowledge Artifacts (KA) [49] for the specification of GKEs using Event-Condition-Action (ECA) rules and an harmonized data set of several existing CDS data schemas. We found that 22% (n=9) of the studies covered medical logic specification formalisms. Table 5 shows the coverage of each logic formalism. SAGE was covered in 33% (n=3) of studies; the Arden Syntax, GLIF, PROforma, were covered in a 22% (n=2) of the studies each. Other standards for logic specification and knowledge management were mentioned less commonly, Jess and the HL7 KA 11% (n=1) each.

Table 5. *Logic specification formalisms coverage*

Logic specification formalism	Coverage in reviewed studies
SAGE	33% (n=3)
Arden syntax	22% (n=2)
GLIF	22% (n=2)
PROforma	22% (n=2)
Others (e.g. Jess, KA)	11% (n=1)

Use of Web Services

With regards to Web Services, 32% (n=13) of the studies covered their use to interoperate with CDS systems. Web services can play an important role in the modularization and interoperability of CDS systems. One of the pioneer works that proposed to take advantage of the Service Oriented Architecture (SOA) for CDS is the presented by Kawamoto et al. [43]. Recently, Dixon et al. [8] and Wright et al. [26] performed a pilot to study the challenges in offering a CDS system in the cloud to several independent health organizations. Among the lessons learned they reported that the main challenges were the difficulties in the negotiation of the legal framework, concerns of clinicians about lack of control over the CDS rules hosted in other organization and the high cost in implementing SIOp. Regarding the cost of SIOp the following are pointed out as main barriers: (a) mapping of local terminologies to SNOMED-CT; and (b) use different terms of the same vocabularies for same entities in each of the organizations.

Discussion

The reviewed publications show that five main fields of work are opened in SIOp for CDS systems: information standards, terminologies, medical logic specification formalisms, semantic web and web services. Most studies covered the use of some information model standard to provide the information interface to represent data. Standard terminologies are used to annotate data instances and integrate different vocabularies. The review shows that they are being increasingly adopted. Ontologies are suggested to provide knowledge domains specification, conceptual models integration and reasoning. Medical logic formalisms are proposed to specify the reasoning logic and allow the reuse of medical procedural knowledge. Web

services are proposed as a tool to offer CDS across organization boundaries.

Different information standards are used to define the VMR data schema. These standards allow decision logic to reference standard information entities of the VMR instead of the EHR avoiding dependencies on proprietary DB schemas. HL7 CDA is the most spread information standard. HL7 CDA is not only used to define the VMR but also to define messages that travel across organizations as SOA payloads [8,46]. Although HL7 CDA is the most adopted standard, HL7 RIM is still significantly used to define VMRs [4,13,14,24,25,39,45]. Regarding openEHR, the studies covering it exploit its archetype model as a scalable method to define the VMR with several layers that gradually increase the level of abstraction of the concepts in the VMR to define aggregations that feed decision logic [20,29]. Also the use of AQL to abstract information using queries over archetypes has been proposed to reduce the amount of mappings needed [18]. Less spread is the use CDS specific information standard HL7 VMR. Nevertheless some evaluations have recognized HL7 vMR as the standard with the best learning curve for developers [11].

Terminologies provide standard vocabularies that are used to identify the concepts referenced from the CDS logic, integrate disparate systems using the terminology as a concept mediator and annotate information models. The use of standard terminologies is becoming more common in new implementations of CDS systems [3]. However, the lack of standardized data and the high diversity in existing terminologies is still a barrier for CDS SIOp [3]. Terminologies also play an important role when systems from different organizations need to be integrated. They provide the common vocabulary that the different organizations will need to map their concepts to [8,46]. Main challenges found in the adoption of terminologies are: (a) the effort of standardization [3]; (b) the linkage of local terms to standard terminologies [35,46]; (c) the diversity of available terminologies; (d) the need to transform iso-semantic models [3,6]; (e) the annotation of information model entities [6]; and (f) the limitation to process pre- and post-coordinated expressions [6,20].

Semantic web technologies acquire a transversal role in CDS implementations. They have been used to cover areas where information standards, terminologies or logic specification do not suffice; or areas where advanced semantic interoperability features such as reasoning are desired [14,38,45]. The most relevant use of Semantic Web technologies is the definition of ontologies for knowledge specification. Some studies use semantic rules systems for logic specification [16,38,45]. Semantic web technologies also play a role in heterogeneous data models integration by defining a common ontology as mediator [34]. Other use as integrator is the use of mapping ontologies to overcome the impedance mismatch between the EHR/VMR and the CDS logic [4].

There is a high diversity of formalisms to specify decision logic. The Arden Syntax was the first presented to encapsulate CDS artifacts and it is still broadly used. Nowadays its 'curly braces' problem can be alleviated using a VMR and languages to define restrictions and mappings such as GELLO [39].

Some of these logic definition formalisms are ontology based running over reasoners providing a good integration between terminologies, ontology concepts and decision algorithms [25]. Other formalisms lack of mechanisms to manage the data model and mappings. Archetypes [20] or ontology [4] mapping frameworks can be a good complement for them.

With regards to Web Services, the definition of SOA principles is a constant. CDS web services are proposed as a solution to encapsulate the CDS into a web service decoupling it from the EHR. Also, SOAs are proposed to create national frameworks to share CDS systems to allow their broad adoption [43]. UDDI registers to enable their discovery can be useful for this as proposed by Nee et al. [21]. Specific projects to study CDS services (HSSP) architectures have led to the HL7 DSS Implementation Guideline that leverages the use of CDS web services with the HL7 vMR and terminologies [50].

Finally, knowledge management of CDS modules is a topic only covered in one study. Rocha et al. covered this topic and presented the HL7 standard for Knowledge Assets specification [23]. It defines a complete set of metadata for knowledge management and a new information model harmonizing other existing information schemas such as GELLO or the HL7 CDS VMR.

Conclusion

Five main complementary mechanisms are currently used to grant SIOp of CDSS. Clinical information standards are used to define standard data models to interoperate at a syntactic level. Semantic Web technologies are used to define conceptual models of knowledge bases, integrate them, and, in some cases, specify procedural knowledge (decision rules). Logic specification formalisms aim to define shareable algorithms among systems. Terminologies provide a standard language to attach accurate terms descriptions to data and conceptual models. SOA is used as architectural paradigm to encapsulate the CDS and allow several clients to reuse its functionality. The mechanisms presented have effectively helped to decouple CDSS from the EHR and advanced in their interoperability capabilities. Nevertheless, challenges implementing SIOp to share CDS across organizational boundaries are still present [8,26].

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