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Electronic Health Records Interoperability Research Needs Assessment: A Systematic Review.

Introduction

Interoperability should be a key functionality of any health care ecosystem. In the simplest definition, interoperability is the capability of two computer systems, or providers, to jointly exchange and make use of information[1]. It is important to stress that interoperability requires an exchange of *information* to make the systems interoperable, and not simply the transfer of data. This delineation between data transfer and information exchange provides a platform for discussion into the challenges and opportunities for interoperability. This paper discusses interoperability in the context of how it pertains to the health care ecosystem and is centered on the electronic health record as well as how the research community consumes interoperability.

Health care data systems are generally considered to suffer from a lack of interoperability[2], which implies that systems are either missing interoperable functions or the needed functions do not exist. The efforts to resolve interoperable challenges are best described as piecemeal. The fragmentation of the health care ecosystem necessitates interoperability; however, fragmentation also contributes to the interoperable challenges.

In 2018, the Office of National Coordinator (ONC) published a report[3,4] describing the challenges and barriers to interoperability in six categories: technical, financial, and trust barriers; administrative and reporting requirements; and general IT usability. The ONC report calls out technical barriers as "limiting interoperability through — for example — a lack of standards development, data quality, and patient and healthcare provider data matching" and points out "the lack of sufficient incentives for sharing information between health care providers." Furthermore, the ONC stresses the need for enhanced business models for secondary uses of data. The ONC report claims that 48% of office-based physicians and 90% of non-federal acute care hospitals are exchanging patient information with other health care providers. However, only 31% of office-based physicians and 53% of non-federal acute care hospitals can integrate health information received electronically into the recipient health IT system[3]. The report indicates a deficiency in primary interoperable uses that deal with patient care but omits secondary uses for interoperability.

At the heart of interoperability is information exchange, and the automation of that information exchange through information technology presents both business opportunities for and barriers to interoperability. The global healthcare interoperability market is expected to hit $3.5 billion by 2025[5]. While that amount is a fraction of the United States' $3.5 trillion cost in 2017[6], the market growth represents the promise and necessity for achieving interoperable systems.

Finally, repurposing EHR data for secondary use beyond clinical care (e.g., the abstraction of data directly from EHR systems for research purposes) remains a challenge.[7] This paper aims to call out the barriers and needs of the research community for better approaches to interoperable solutions. The findings will be useful to researchers looking for interoperable solutions from EHR systems, identifying current gaps and pitfalls in interoperable solutions in research.

Background

Research Community

This paper is a needs assessment targeting persons, studies, or teams that utilize information flows from, or to, an electronic health record. This information flow is needed to realize secondary uses data such as analysis, recruitment, cohort identification, retrospective cohort studies, prospective cohort studies, data set linking, or the creation of registries.

Functionalities of Interoperability

According to the ONC, interoperability functions in the following four domains: find, send, receive, and integrate [8]. Each domain is a fundamental process that adds to the capabilities of an interoperable system, and each domain is independent and can be utilized by a system separately. For example, a lab system might only send a result, or a portal might only receive patient demographics. The ONC report measures interoperability based on the achievement of these capabilities for non-federal acute care hospitals. Overall, the ONC report indicates that only 41% of non-federal acute care hospitals met all four domains in 2017.[9]

Find

The 'find' domain can query outside of the healthcare system to discover patient health information. An example is querying if a patient existed in another hospital network. 61% of non-federal acute care hospitals achieved the 'find' domain in 2017.[9]

Send and Receive

The 'send' and 'receive' domains are the abilities to transmit patient health information to another health entity or accept other health care systems' patient health information. The 'send' and 'receive' domains are not dependent upon each other and can stand alone. An example is electronically transmitting a lab order and receiving the result (without manual entry). 88% of non-federal acute care hospitals achieved the sending domain, and 74% achieved the receiving domain in 2017.[9]

Integrate

The 'integrate' domain permits external clinical information to be included in the patient's health record. An example is converting scanned documents into discrete data elements is an integration[8]. Fifty-three percent of non-federal acute care hospitals achieved the integrate domain in 2017.[9]

Levels of Interoperability

Interoperability is a process. A system achieves different states of interoperability as described by the Levels of Conceptual Interoperability Model (LCIM).[2,10]

The LCIM levels range from 0 to 6, and Figure 1 shows an adaptation of Tolk, et. al,'s LCIM model[10]. The context of this paper and review of literature includes a discussion of syntactic (2), semantic (3), and pragmatic (4) levels.

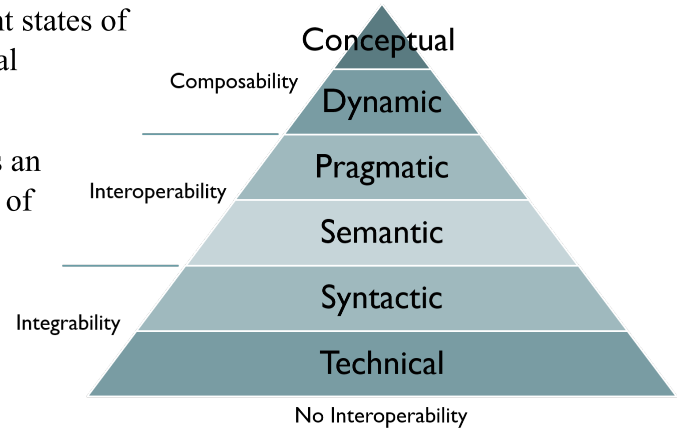

Figure 1: Levels of Conceptual Interoperability Model

Syntactic Interoperability

The syntactic interoperability layer is the base requirement for any interoperable system, acting as the syntax for the data transmission. The syntactic layer includes a data structure dictated by some common model or format such as XML, ANSI SQL, CDIST ODM, HL7 v2.x, or DICOM. "On the syntactic level, common protocols structure the data for use. The format of the information exchange is unambiguously defined[10]." The syntactic layer offers the capability for system processing based on this shared model but does not assume each system utilizes the same common model.

Semantic Interoperability

An evolution of the syntactic layer, the semantic interoperability layer adds system translatable meaning to the data. The semantic layer achieves this translation by compounding structure with the codification of the data that confers meaning. Standard coding system examples include, but are not limited to, ICD, CPT, SNOMED, MeSH, and LOINC. The addition of terminology to the syntactic layer allows the data to inherit meaning, thus, transforming data into information.

Furthermore, metadata can be interwoven with the data structures to provide additional meaning and context. The Fast Healthcare Interoperability Resources (FHIR) specification is an example of a semantic layer data structure. FHIR combines a common structure using XML or JSON with a common set of metadata to provide a standard semantic communication resource.

Pragmatic Interoperability

Pragmatic interoperability is the continued evolution of semantic interoperability in that the business meaning of the actual information is included. Pragmatic interoperability captures the intent of the information as disseminated by a user in the context of its application and as understood by the participating systems. The context of the information exchange must also be unambiguously defined.[10] An example of pragmatic interoperability is conferring the actual meaning or intended effect of a lab result, say a hemoglobin A1C value of 9.2 is indicative of a diabetes diagnosis. The semantic meaning is 9.2, however, one pragmatic meaning could be the diagnosis of diabetes.

Interoperability versus Transportability

A system configured to exchange information with another system does not imply that the system is universally interoperable, nor does it mean a system can scope to additional data concepts. A system can convey information to another specific system and be considered interoperable in accordance with ONC's interoperable functions. However, the interoperable configuration is often unique or custom to a particular pairing of systems, such as an EHR and a lab information system (LIS). One of the main challenges for achieving any level of interoperability is the technical and cultural effort required to replicate an interoperable solution with another system. For example, an electronic health record may receive lab results from system A, but each additional system that provides lab results requires unique configurations, mappings, or set-up.

Methods

Data Sources

Peer-reviewed literature from PubMed, Web of Science, and Embase were searched by title and abstract with specific terms related to interoperability and interoperable technologies such as HL7 and FHIR, the layers of interoperability, and electronic health records. (See **Appendix 1** for search queries and terminology)

Studies are eligible for inclusion for review if the literature was in English, published within the past five years (2014-2019), and matched the search queries terms.

Study Selection

All studies discovered in the data sources were processed using Mendeley reference software to remove duplicate studies. Afterward, we uploaded the studies to a web-based systematic review production tool called Covidence. The selection process then involved review of each study's title and abstract for inclusion or exclusion criteria. Studies that met inclusion criteria became eligible for a full-text review.

Studies were selected if we determined that the study had an interoperable *application or use*. This determination specifically intends for the study to utilize data over any interoperable layer with an electronic health record, and not with another system, including data warehouses or personal health records. Another criterion excludes studies that only compared or mapped ontologies, discussed infrastructure or frameworks, discussed data models, or evaluated interoperability methods. The aim is to identify the uses of interoperability and not the method of interoperability in order to determine the needs in interoperable technologies application.

Results

Searching the data sources of PubMed, Web of Science, and Embase, we discovered 803 items of literature. Deduplication within Mendelay citation software eliminated 190 duplicates, leaving 613 articles to import into the Covidence systematic review application. Covidence discovered another 13 duplicates reducing the total number of articles to be screened to 600. Initial screening deemed 183 studies irrelevant to the inclusion criteria. Typically, irrelevant studies did not pertain to electronic health records or had only a vague mention of interoperability. Next, 417 articles were then processed and categorized for inclusion in the review. Assessments were made of the literature to determine if the article had the following criteria: 1) interoperable use, 2) source or destination of an EHR system, 3) not an evaluation or program of a governing body, 4) not only methodological comparisons (i.e., openEHR archetype comparison to FHIR resources), 5) created or discussed ontology or terminology only, and 6) only indicated future interoperability intent or desire. Of the 417 articles, represented in Figure 2, exclusion criteria removes 378 papers, broken into the following categories:

- 118 Evaluations or Programs
- 80 No interoperable use
- 63 Method comparisons
- 60 No EHR source or destination
- 44 Terminologies or ontologies only
- 13 The paper only indicated a future need for interoperability.

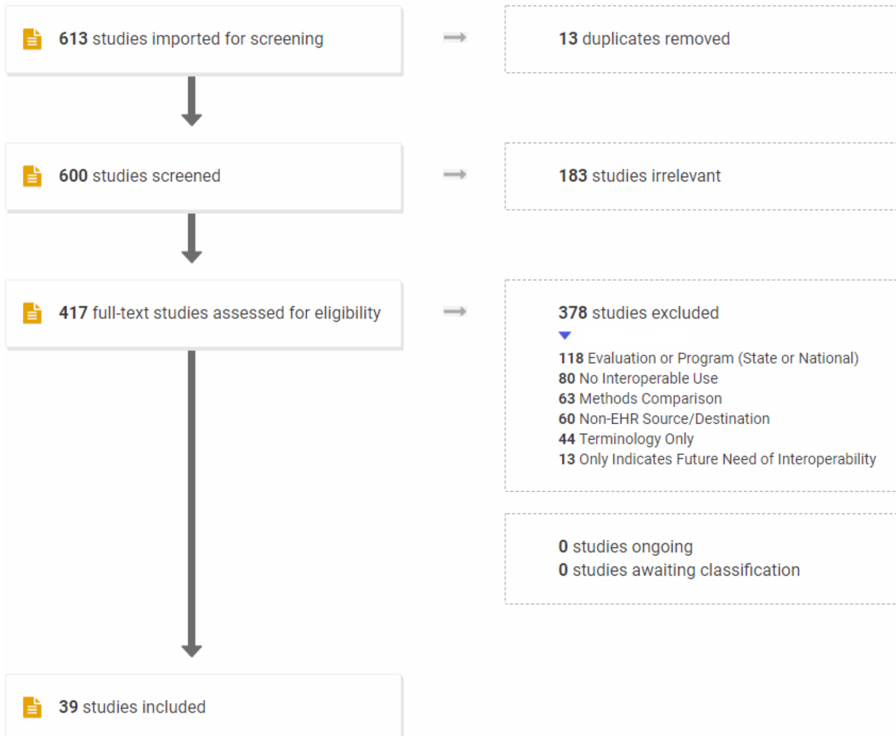

Figure 1: PRISMA diagram of study selection

The full-text review resulted in the final selection of 39 studies for inclusion in the review.

Summarization of the 39 articles starts with stating the purpose of interoperable use. Then, each study receives a classification of the interoperable core domains (this is derived and interpreted from the purpose and methods). The target LCIM level(s) of interoperable achievement are analyzed as well as generalized data concepts. Next, we list any interoperable relevant technologies and terminologies used in the study. Finally, we note any barriers that are either explicitly stated or implied in the literature.

Table 1: Summary of Reviewed Literature

Study	Purpose	Functionality	Level	Data	Technologies & Terminologies	Barriers
Alterovitz 2015[11]	Create Genomics Resource for EHR consumption	Send	Semantic	Genomics	FHIR	Adoption of FHIR; Maturity of omics data structures
Bergquist 2017[12]	Embed Patient generated data into the EHR.	Receive Send Integrate	Semantic Pragmatic	Patient Generated Data	FHIR	Compliance; EHR Data Model non-conformance

Beyan 2014[13]	Integration of a single genomic result in the national health system.	Receive Send	Syntactic Semantic	Genomics	SNP; SNOMED; HL7; CBO	No standard translation between Genomic information and other terminologies. EHR data model maturity is lacking for genomics
Bush 2014[14]	Identify patient demographic variables predictive of patient no-show and automatic data collection for CER	Receive	Semantic Pragmatic	Patient EHR Record	standard automated electronic data extraction techniques	EHR implementation variance; Temporal Issues; Missing Data
Coon 2019[15]	iPhone App for achieving medication and vaccine portability	Receive Send	Semantic	Medications	FHIR	Adoption; Workflow Integration
Declerck 2015[16]	Enable secondary use of electronic health records (EHR) data for post-marketing drug surveillance. An important component of this toolkit is a drug-related adverse event (AE) reporting	Receive	Syntactic Semantic	Medications	HL7 CDA-CCD; ICD; LOINC; SNOMED-CT; MedDRA	Necessary data not available in EHR or free text
Delamarre 2015[17]	Transfer medication data from EHR to CDW from EHR data stream and appended with DKDB information	Find Receive	Syntactic Semantic	Medications	XML; ICD; LOINC, SNOMED; PN13/CIOsp	No international interoperability standard or terminology system
Dolin 2018[18]	Provide genetic information on medication order	Find Receive Send Integrate	Syntactic Semantic	Genomics	FHIR; GACS	Semantic gaps within the EHR system;

Estiri 2018[19]	Provide data quality checks on standard data models	Receive	Syntactic	Patient EHR Record	SQL; R	Data model-driven, meaning that it will have to be constantly updated once a new version of a CDM
Fisher 2018[20]	Developed a system for Prescription Management and General Inventory Control with data received from the EHR	Receive	Syntactic Semantic	Medications	HL7 v2; NDC; RxNorm	Terminal System
Frey 2015[21]	Create platform-independent virtualized secure web service for pediatric data transfer	Receive Send	Syntactic Semantic	Patient EHR Record	SQL; caGrid	Data malformations; Manual Curation
Gaebel 2016[22]	Create system-architecture for standardized access to patient-specific information for a CDSS for laryngeal cancer	Find Receive Send Integrate	Syntactic Semantic Pragmatic	Patient EHR Record	HL7; MLM; FHIR; MIMMS	Every alteration the corresponding MLMs and FHIR resources also need to be adjusted, or new ones need to be added
Gay 2015[23]	Culminate various data sources, including EHR, into myFitnessCompanion app.	Find Receive	Syntactic Semantic	Patient EHR Record	XML; JSON; HL7	Lack of Standards Utilization
Giordanengo 2018[24]	Integrate self-collected data into EHR	Receive Send Integrate	Semantic	Patient EHR Record Patient-Generated Data	FHIR	

Goldberg 2016[25]	CDS implementation for minor blunt head trauma within EHR	Receive Send	Syntactic Semantic	Patient EHR Record	XML; HL7 CCD; SNOMED	Standards too complex; Customized data schema
Gutteridge 2014[26]	Create real-time notification over multiple channels on admission events	Receive Send Integrate	Syntactic Semantic	Patient EHR Record	HL7 v2; HIE	Manual inclusion lists
He 2017[27]	Mobile app for patient surveillance and examination portal for post-hospitalization breast cancer patients	Receive Send Integrate	Syntactic Semantic	Patient-Generated Data	FHIR	Manual Entry of some elements
Kopanitsa 2018[28]	Implement a LIS via FHIR	Receive Send	Syntactic Semantic	Patient EHR Record	FHIR; LOINC	Standard Maturity and no backward compatibility
Laird-Maddox 2014[29]	Data Abstraction from EHR to research repurposing	Receive	Syntactic Semantic	Patient EHR Record	HL7 CCD; XML	Non-interoperable transformation; Missing data elements
Mahmoud 2017[30]	Combines both clinical (EHR) and self-reported information into a single event record in a data warehouse	Receive	Syntactic Semantic	Patient EHR Record Patient Generated Data	HL7 RIM; XML; SNOMED; KASPER; OpenEHR	Source Data variations, terminology compatibility
Marco-Ruiz 2015[31]	Create archetype-based data warehouse environment to enable the reuse of electronic health record data	Receive Send	Syntactic Semantic	LIS Data	openEHR; XML; SNOMED	Complex transformation rules

Min 2018[32]	Add semantic interoperability to the clinical registry by converting data model to openEHR RM	Receive Send	Semantic	Patient EHR Record	openEHR;	Archetypes have finer granularity than corresponding EHR data elements, and the corresponding clinical data cannot be collected from the EHR system directly
Peters 2015[33]	Create a web-based game portal for the collection of patients reported data and combine with EHR data	Receive	Syntactic	Patient EHR Record Patient Generated Data	LOINC; HL7 v2, CDA;	Terminal System
Poulymenopoulou 2015[34]	Create a semantic ETL service that seeks to integrate and pre-process data from multiple sources to result in RDF documents	Receive	Syntactic Semantic	Patient EHR Record Social Media Sensor Data	HL7 CCD CDA	Vague ontology and semantic modeling
Rajkomar 2018[35]	Make predictions for an important clinical outcome (death), a standard measure of quality of care (readmissions), a measure of resource utilization (length of stay), and a measure of understanding of a patient's problems (diagnoses).	Receive	Syntactic Semantic	Patient EHR Record	FHIR	Terminal System

Ranade-Kharkar 2018[36]	Identify and assess a set of data standards to enable extraction of a patient's care team and related data from standards-based HIE	Receive Send	Semantic	Patient EHR Record	HL7 CDA; FHIR	gaps related to patients' non-clinical events and care team actions; CDA Extensibility
Schreiweis 2016[37]	Implement a regional personal cross-enterprise electronic health record and create a regional research platform for integration, consolidation, analysis, and evaluation of pseudonymized data	Receive Send	Semantic	Patient-Generated Data	XDS; HL7 CDA	Conflicting Standard Types
Sinaci 2015[38]	A Web-Based, Dynamic, and Interoperable System for Post-marketing Drug Surveillance Studies	Find Receive Send	Syntactic Semantic	Patient EHR Record	RDF; HL7 CCD; ISO13606; OMOP	Mapping Terminologies
Soguero-Ruiz 2018[39]	An interoperable system toward cardiac risk stratification from ECG monitoring	Receive Send	Syntactic Semantic	Patient EHR Record	HL7; CEN/ISO EN13606; SNOMED	Portability; Reproducibility (time and effort)
Song 2015[40]	Creating PHR that both EHR and PHR must be interoperable with each other via the compliance to all applicable medical standards	Find Receive Send	Syntactic Semantic	Patient EHR Record	HL7 CDA; CD-9-CM, SNOMED CT, LOINC,	Security; Adoption;

Spineth 2018[41]	Supplement CDS Hooks with Ardent to expand capabilities	Find Receive Send Integrate	Syntactic Semantic	Medications	FHIR; Ardent; JSON	Restriction to FHIR only
Torres 2016[42]	Create platform will be able to coordinate the clinical attention for ictus cases in the acute phase in different environments, counting on the real-time clinical advice of specialists	Find Receive Send	Syntactic Semantic	Patient EHR Record	XDS-b; CEN/ISO 13606; XML	Mobile Stability
Toubiana 2015[43]	Use an ontological approach to implement an information system for the French Fibromuscular Dysplasia Registry	Receive	Syntactic Semantic	Patient EHR Record	UML; MedDRA; HPO; ATC; ICD; CCAM	Mapping
Umberger 2019[7]	Automated EHR Data Capture and Early Identification of Sepsis	Receive	Syntactic	Patient EHR Record	HL7 v2; SQL	Barriers remain in seamlessly extracting data from the EHR in an analyzable format; Terminal system
Walinjkar 2017[44]	Use neural nets to classify ECG data to and transform to FHIR resource	Send	Syntactic Semantic	Sensor Data	FHIR; SNOMED	No production implementation
Walinjkar 2017-2[45]	Use neural nets to classify ECG data to and transform to FHIR resource	Send	Syntactic Semantic	Sensor Data	FHIR; SNOMED	No production implementation

Wei 2017[27]	Propose a new diabetes framework using the clinical data model (CDM) [7-10] and following health level 7 (HL7) standards, and integrating with data from third-party systems such as blood glucose, fundus image	Find Receive	Syntactic Semantic	Patient EHR Record	CDM, HL7 CDA; HL7 v2; openEHR	Mapping Terminologies
Williams 2018[46]	Create a patient-facing genomic test report with a companion provider report was configured for implementation within the EHR using a locally developed software platform	Find Receive Send Integrate	Syntactic Semantic	Patient EHR Record Genomics	SQL; XML; FHIR	Non-Standard Based approach
Wu 2018[47]	Developed a dynamic clinical data platform (CHCi) with high extensibility, accessibility, accountability, and interoperability	Receive	Syntactic Semantic	Patient EHR Record	XML; SQL; SNOMED; ICD	Local Terminology; Scalability

Summary of Interoperability Functionalities

Determining the interoperable core functionalities of each study included:

1) Find – if a study indicated a lookup or query could be performed internal or external to the studies system. For example, Dolin utilizes Find capability to determine if a patient exists in genetic data repository.[18]
2) Receive – if a study is a consumer of data or information at any level of interoperability.

3) Send – if a study is a provider of interoperable data at any level.
4) Integrate – if a study embeds data or information into the EHR workflow, such that the output is now interoperable in the source system.

Figure 3 illustrates the breakdown of functional classification; 25.6% of the reviewed studies achieved *Find* capabilities while the majority of studies are consumers of interoperable messages with *Receive* comprising of 93.3% of the studies. While 61.5% *Send* some interoperable information, the minority *Integrate* with only 4 (10.3%) studies indicating this function; this aligns with the expectations outlined by the ONC.

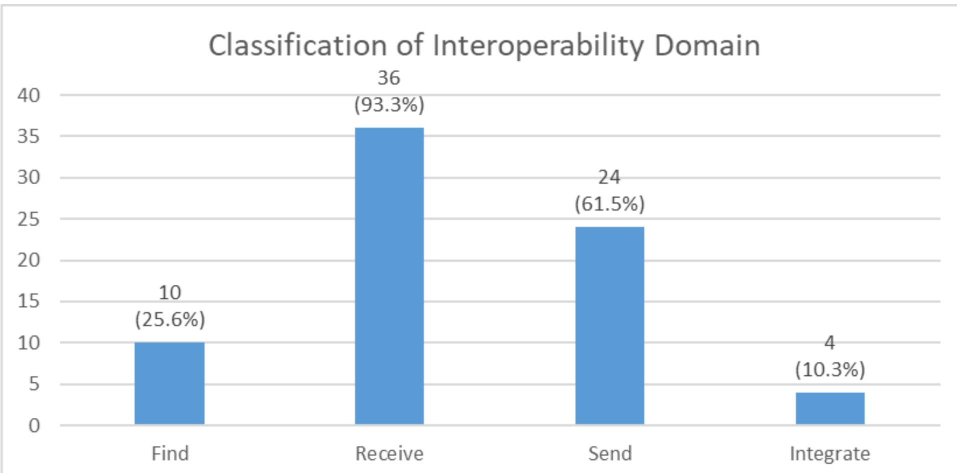

Figure 2: Summary of Interoperability Functionality Classification

Of the four functionalities (shown in Figure 4), 16 studies utilized single function (*Receive* [12], Send [3], *Integrate* [1]), 13 studies utilized two functions (*Find/Receive*[3], *Receive/Send*[10]), only 3 studies utilized 3 functions (*Receive/Send/Integrate*), and 4 achieved all 4 functions.

Note that *Find* was never solely utilized and was always coupled with *Receive.* Additionally, *Integrate* always had a *Receive* and *Send* functionality paired with it.

Core Domain	# Studies
Send	3
Receive	12
FindReceive	3
ReceiveSend	10
FindReceiveSend	3
ReceiveSendIntegrate	4
FindReceiveSendIntegrate	4
Grand Total	**39**

The summary indicates that most secondary systems interact using a unidirectional or bidirectional mechanism instead of integrative methods. The literature also indicates that there is not a strong need for the *Find* function, or at least *Find* is not a focal point of interoperability use.

Summary of Interoperability Levels

Overwhelmingly, studies focus on the semantic level of interoperability (92%). In general, syntactic interoperable (79%) was described or resolved as a means to semantic interoperability. Only three studies (8%) discussed only syntactic interoperability.[7,19,33] Additionally, three studies eluded to pragmatic interoperability[12,14,22], albeit none stated this explicitly. This is evidence of the continuing challenges of obtaining semantic interoperability in a generalizable fashion for the consumption of health care information.

Summary of Data Concepts

Data concepts were categorized into the following generalized areas:

- Genomics – Any genetic sequencing or variant information.
- Medications – Specifically only drug-related data and information, including dosing, adverse events, prescribing, or administration.
- Patient EHR Record – Information from an electronic health record encompassing multiple sub-concepts such as diagnosis, provider information, demographics, labs, medications, or observations.
- Patient-Generated Data – The patient creates the data by completing forms or other reporting, including questionnaires, surveys, exercise or nutritional logs.
- Laboratory Data – Specifically only laboratory tests and results from a laboratory information system.
- Social Media – Data from social media platforms, including but not limited to Facebook, Twitter, Instagram, or LinkedIn.
- Sensor Data – Data from wearables (Fitbit, Apple Watch), smart health devices (scales, glucometers) or other instrument devices (EKG, telemetry).

Figure 5 displays the breakdown of the study by data concept. Patient EHR Records make up 64% of the data concepts used within the studies, followed by Patient-Generated Data and Medications at 15% and 13%, followed by Genomics data at 10%, respectively.

Figure 5: Summary of Data Concepts

Summary of Technologies and Terminologies

There are 36 distinct technologies or terminologies that were recorded as part of the review and listed in Appendix 2. Of these studies, FHIR was used in 36% of the reviewed literature, with HL7 v2 used in 23%, and HL7 technologies used in 90%. SNOMED is the most commonly used terminology and was represented in 28% of the literature followed by LOINC and ICD codes, with each represented in 13% of the studies.

Discussion

The main objective of this paper is to extract information related to the '*interoperable use*' of systems from a research perspective. Gay described HL7 compliance in the development of their myFitnessCompanion application:

> "Unfortunately, not a single server used an official standard for health data exchange. Without exception, each server defined its specific data format. All the efforts made by the Health Level Seven (HL7) standardization group seem to be ignored and not taken

> into account. The consequence was that each server-specific software had to be written to interpret the data."[23]

This quote epitomizes the struggle with interoperability. Often, a new system seeks out interoperable systems to achieve its goals of information transfer only to discover some variance or a proprietary alteration of the standard. Laird-Maddox, et al., offers an example in their study implementing "a script of code transforms the Continuity of Care Document into a format that can be used by the research system."[29] Laird-Maddox's study's transformation effectively diminishes the interoperability of the system. The study's system becomes a *terminal system* (see below) and unless the system performs another transformation, the information is not interpretable to another system due to the proprietary format which is used.

A terminal system is a system that only utilizes the *Receive* interoperable domain. Terminal systems often are proprietary or closed systems. These studies[20 29 33 7 48] each operate only in the *Receiving* domain and express no output of interoperable messages and, thus, rely solely upon internal analysis of the data.

Another issue is the alteration of interoperable messages by extensibility, where other systems are unaware of the extensions. Again Laird-Maddox, et al., notes that CCD data is "limited to demographics, vital signs, adverse events (problems, diagnoses, and allergies), and medications." However, the studies necessitate "additional structured information that was in the EHR but not in [the CCD]," and "extended the categories of data available [by] embedded database queries and aliases to match data from one system to the other,"[29] constraining due to the use of a terminal system.

One of the four studies achieving all core interoperability functionalities, Williams, et al., describes custom extensibility by "utilizing custom and standard data extractions that interface with Epic." They created a custom parser to account for the customization of the data structure.[46] While the study achieves all four functionalities and can declare semantic interoperability, the portability of the technology is unlikely.

On the other hand, it is often the case when a 'Standard' (being a generalized, reusable construct) is too specific or robust for interoperable consumption. Goldberg, creating a CDSS for children, deems that "the CCD was too complex for the limited amount of data; " Additionally, the study states, "other [models] were underspecified for structured data interchange [and] therefore the study created a custom data exchange model defined by an XML schema."[25] The same study provides an example of the transition from a possible 'Standard' to a custom format, thus, impeding interoperability.

Mapping

Data mapping may be the single largest barrier to interoperable implementation in any system. The following is a simple example that defines data mapping: A source has 'x,' and the destination knows 'y'; therefore, some conversion or transformation must occur to allow 'x' to act as 'y.' These mappings are the crux of semantic interoperability, and even systems that implore terminology or ontology standards may have varying implementations that impose barriers (e.g., ICD9 versus ICD10, outdated RxNorm releases). Goldberg, et al., found that semantics align well with only some possible mappings. In general, mappings became more general than the original concept but are still considered to be appropriate matches to each other. Only two concepts, because they are unmappable, lead to local extensions to the SNOMED CT terminology.[25] These exceptions, similar to technological extensions, result in a diminishing in the reusability of that data, although SNOMED CT does offer a more graceful method of terminology extensions.[49]

The process of mapping is arduous, taking considerable time and knowledge to correlate one concept to another, validating whether the mapping is equivalent, broader, or narrower in meaning; therefore, each item must be explained in context and adapted by aligning local terminologies with reference terminologies[43] to solve term definition ambiguities.[27]

A pivotal example of mapping creating interoperable conflict is the clinical data capture platform created by Wu and his team; they produced "a special diagnostic code table" where "users can create a temporary code if they feel the current codebook is lacking, [and] using locally agreed terms by clinicians to facilitate clinical data entry, rather than using standardized terminologies such as SNOMED CT or ICD9 codes. [The terms] can be later converted to standardized terminology."[47] This process sacrifices interoperability standards (particularly semantics) and preserves local uniformity.

Conclusion

Current and recent literature demonstrate that there are a multitude of barriers to achieving interoperability. The interoperability landscape is complex, fragmented, and decentralized. The complexity stems from the multiple requirements of data, and the meaning and interpretation of that data—this is a challenge of semantic versus pragmatic levels of interoperability. Fragmentation stems from many available solutions, terminologies, and specificity of interoperable needs, such as having ICD codes, CPT codes, and SNOMED codes to choose and convert to, and from. While standards are in the process of being created, many institutions and corporations interpret these standards differently and implement them on different timelines or with additional features. We suggest efforts should utilize current standards and harmonize existing technologies and standards into *source* and *destination* systems. Movement away from 'middleware' technologies and painstaking terminology mappings would promote faster implementations, less ambiguity, and greater maturity of interoperability levels.

I propose an interoperability educational framework that collects the multitude of interoperability solutions and components, such as ontologies, coding systems, and protocols, and subsequently visualizes the technologies as a network. This framework will allow researchers to view and explore existing interoperability means and methods and relate them to their research data needs. The aim of this framework is to centralize knowledge related to interoperability, thereby reducing the complexity and guesswork of what data is readily available in interoperable systems (EHRs), the methods in which those data can transmit (HL7, FHIR, CCD), and terminology systems used in those methods (SNOMED, ICD, CPT). Coalescing the available interoperability information will reduce the need for creating new systems and ontologies for research purposes by permitting researchers to readily identify past interoperable works and solutions. An example of this would be a use case of transmitting research consent information using FHIR. The researcher could use this framework to quickly see the maturity level of that FHIR resource and that it is only in trial use, as well as other research pertaining to consent information in interoperable solutions.

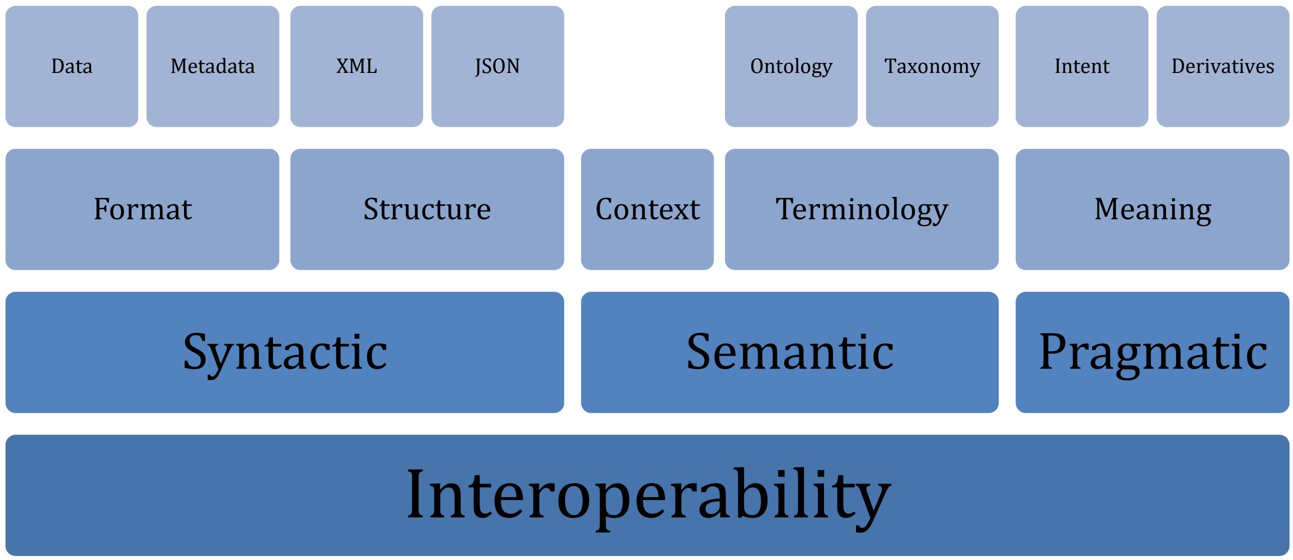

Figure 3: Concepts of Interoperability Framework

The main component of this framework will be a network visualization of interoperability information, including news, publications, and industry changes to the interoperable landscape. This visualization aims to address the interoperability fragmentation and decentralization that exists in the health care and research sectors as indicated in this paper.

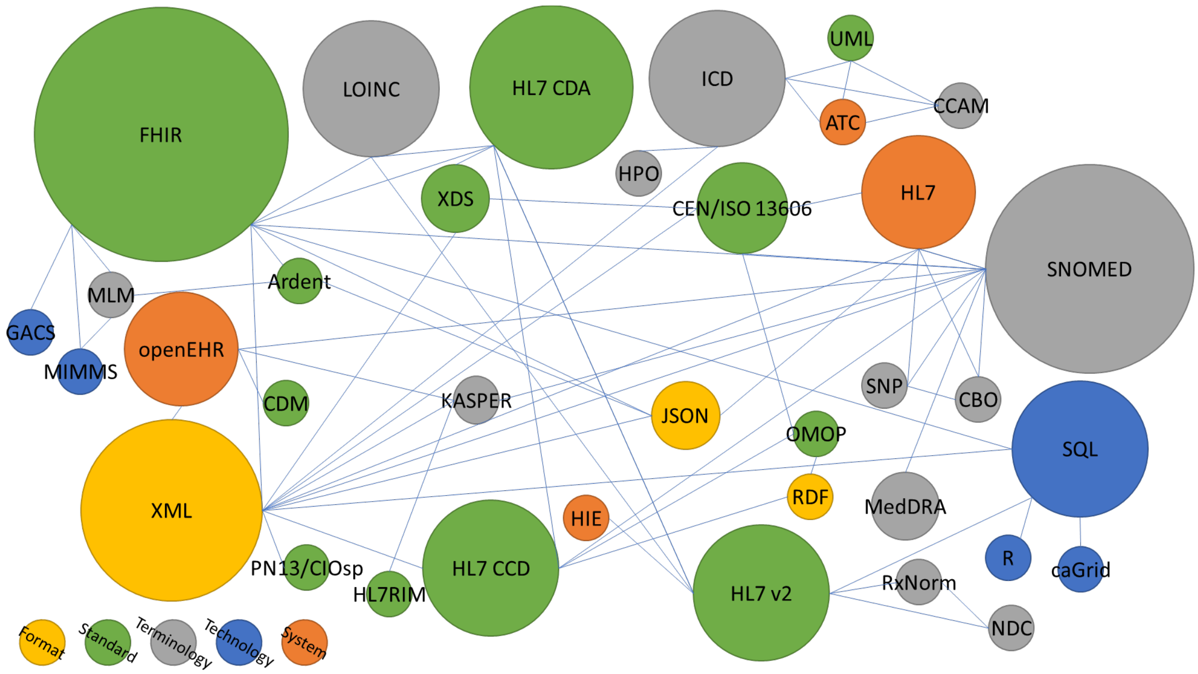

Figure 4: Network Model of Interoperability Components

Lastly, this framework and visualization will be accessible as a publicly available, web-based tool. The research and health informatics community can use this tool to learn, explore, and assist in the development of interoperable solutions for data-driven projects. These tools will permit researchers to identify state-of-art uses and identify trends and changes in health care interoperability ecosystem and assist in staying current with evolving technologies and practices.

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Appendix 1: Database Search Criteria

PubMed

((((((((((((((interoperable[Title/Abstract]) OR interoperability[Title/Abstract])) OR fhir) OR ((HL7[Title/Abstract]) AND interface[Title/Abstract])) OR ((interconnect[Title/Abstract]) AND interoperability[Title/Abstract]))) OR "semantic interoperability"[Title/Abstract]) OR "syntactic interoperability"[Title/Abstract]) OR "pragmatic interoperability"[Title/Abstract]))) AND "electronic health record") AND "last 5 years"[PDat]))

Web of Science

(TS=(interoperable) OR TS=(interoperability) OR TS=(fhir) OR (TS=(HL7) AND TS=(interface)) OR (TS=(interconnect) AND TS=(interoperability)) OR TS=("semantic interoperability") OR TS=("syntactic interoperability") OR TS=("pragmatic interoperability"))AND TS=("electronic health record")

Embase

(interoperable:ti,ab OR interoperability:ti,ab OR fhir:ti,ab OR 'pragmatic interoperability':ti,ab OR 'semantic interoperability':ti,ab OR 'syntactic interoperability':ti,ab OR (hl7:ti,ab AND interface:ti,ab) OR (interconnect:ti,ab AND interoperability:ti,ab)) AND ('electronic health record'/exp OR 'electronic health record') AND (2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py)

Appendix 2: Abstracted Technologies

Abbreviation	Name	Description
Arden	Arden	Standard, formal procedural language that represents medical algorithms in clinical information systems as knowledge modules.
ATC	ATC Medical	ATC Medical is an internet-enabled, multi-channel distributor of medical, surgical and therapy supplies and equipment
caGrid	caGrid	Services oriented Grid software infrastructure, building on the Grid Services architecture for the use of discovery, integrated and large-scale data analysis and coordinated research in the cancer field
CBO	clinical bioinformatics ontology	The CBO is a curated semantic network trying to combine a variety of clinical vocabularies, e.g. SNOMED and LOINC.
CCAM	Classification Commune des Actes Médicaux	Used in France for DRG databases and fee for services payment.
CDM	Common Data Model	Generic term for leveraging a structured data repository for adoption. Examples include OMOP and PCORnet.

CEN/ISO 13606	European Committee for Standardization/International Standards Organization 13606	European Committee for Standardization specifies the communication of part or all of the electronic health record (EHR) of a single identified subject of care between EHR systems, or between EHR systems and a centralized EHR data repository.
FHIR	Fast Healthcare Interoperable Resource	FHIR is a new specification based on emerging industry approaches, but informed by years of lessons around requirements, successes and challenges gained through defining and implementing HL7 v2, HL7 v3 and the RIM, and CDA. FHIR can be used as a stand-alone data exchange standard, but can and will also be used in partnership with existing widely used standards.
GACS	Genomic Archiving and Communication System	Used to store, share and query genomic information. Similar conceptually to a Picture Archiving and Communication System (PACS).
HIE	Health Information Exchange	The mobilization of health care information electronically across organizations within a region, community or hospital system. In practice the term HIE may also refer to the organization that facilitates the exchange.
HL7	Health Level Seven	Health Level Seven International (HL7) is a not-for-profit, ANSI-accredited standards developing organization. This term often represents both the organization and the commonly used version 2 standard. When a document refers to 'using' HL7 it is often implied as to the HL7 v2 standard.
HL7 CCD	HL7 Continuity of Care Document	The Continuity of Care Document (CCD) is built using the HL7 Clinical Document Architecture (CDA) elements and contains data that is defined by the ASTM Continuity of Care Record (CCR). It is used to share summary information about the patient within the broader context of the personal health record. A Continuity of Care Document is represented in XML.
HL7 CDA	HL7 Clinical Document Architecture	CDA is an XML-based, electronic standard used for clinical document exchange that was developed by Health Level Seven. CDA conforms to the HL7 V3 Implementation Technology Specification (ITS), is based on the HL7 Reference Information Model (RIM) and uses HL7 V3 data types.
HL7 RIM	HL7 Reference Information Model	An object model created as part of the Version 3 methodology, the RIM is a large, pictorial representation of the HL7 clinical data (domains) and identifies the life cycle that a message or group of related messages will carry.
HL7 v2	HL7 version 2	A highly adopted health care standard for the communication of information.

HPO	Human Phenotype Ontology	Standardized vocabulary of phenotypic abnormalities encountered in human disease.
ICD	International Classification of Diseases	A medical classification list by the World Health Organization (WHO). It contains codes for diseases, signs and symptoms, abnormal findings, complaints, social circumstances, and external causes of injury or diseases.
JSON	JavaScript Object Notation	A lightweight data-interchange format
KASPER	King's Auxiliary System for Provisionally Encoding Records	Concept terminology system for survey responses.
LOINC	Logical Observation Identifiers Names and Codes	A common language (set of identifiers, names, and codes) for identifying health measurements, observations, and documents.
MedDRA	Medical Dictionary for Regulatory Activities	Standardized Medical terminology. MedDRA was based on a terminology belonging to the Medicines and Healthcare products Regulatory Agency (MHRA) of UK
MIMMS	Medical Information and Model Management System	Architecture for separation of modeling tools and processing from actual data sources.
MLM	Medical Logic Module	An independent unit in a healthcare knowledge base that represents the knowledge published on a requirement for treating a patient according to a single medical decision. Component of the Arden Syntax.
NDC	National Drug Code	It is a universal product identifier for human drugs in the United States.
OMOP	Observational Medical Outcomes Partnership	The OMOP Common Data Model allows for the systematic analysis of disparate observational databases. The concept behind this approach is to transform data contained within those databases into a common format (data model) as well as a common representation (terminologies, vocabularies, coding schemes), and then perform systematic analyses using a library of standard analytic routines that have been written based on the common format.
openEHR	Open Electronic Health Record	name of a technology for e-health, consisting of open specifications, clinical models and software that can be used to create standards, and build information and interoperability solutions for healthcare.
PN13/CIOsp	PN13/CIOsp	French standard developed by Phast for syntactical transmission of health data, particularly prescribing information. This is coupled with a semantic resource for the content that is CIOsp.
RDF	Resource Description Framework	Standard model for data interchange on the Web

RxNorm	RxNorm	A normalized naming system for generic and branded drugs; and a tool for supporting semantic interoperation between drug terminologies and pharmacy knowledge base systems
SNOMED-CT	Systematized Nomenclature of Medicine -- Clinical Terms	Standardized, multilingual vocabulary of clinical terminology
SNP	Single nucleotide polymorphisms	A genetic variation commonly targeted in Ontology development.
SQL	Structured Query Language	The domain-specific language used in programming and designed for managing data held in a relational database management system.
UML	Unified Modeling Language	Standardized modeling language consisting of an integrated set of diagrams
XDS	Cross-enterprise Document Sharing	Provides a standards-based specification for managing the sharing of documents between any healthcare enterprise
XDS-b	Cross-enterprise Document Sharing version b	Implementation profile for cross-enterprise document share sponsored by IHE (Integrating the Healthcare Enterprise)
XML	eXtensible Markup Language	Markup language designed to store, transport data, and to be self-descriptive.