European Journal of Clinical Microbiology & Infectious Diseases (2019) 38:1023–1034
https://doi.org/10.1007/s10096-019-03501-6

REVIEW

Semantic data interoperability, digital medicine, and e-health in infectious disease management: a review

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Received: 30 January 2019 / Accepted: 30 January 2019 / Published online: 15 February 2019

Abstract

Disease management requires the use of mixed languages when discussing etiology, diagnosis, treatment, and follow-up. All phases require data management, and, in the optimal case, such data are interdisciplinary and uniform and clear to all those involved. Such semantic data interoperability is one of the technical building blocks that support emerging digital medicine, e-health, and P4-medicine (predictive, preventive, personalized, and participatory). In a world where infectious diseases are on a trend to become hard-to-treat threats due to antimicrobial resistance, semantic data interoperability is part of the toolbox to fight more efficiently against those threats. In this review, we will introduce semantic data interoperability, summarize its added value, and analyze the technical foundation supporting the standardized healthcare system interoperability that will allow moving forward to e-health. We will also review current usage of those foundational standards and advocate for their uptake by all infectious disease-related actors.

Keywords Health information interoperability · Reference standards · Logical Observation Identifiers Names and Codes (LOINC) · The Unified Code for Units of Measure (UCUM) · Systematized Nomenclature of Medicine–Clinical Terms (SNOMED CT) · Health Level Seven (HL7)

Introduction

Antimicrobial resistance (AMR) is one of the major emerging infectious disease-related threats. Due to the loss of action of antibiotics, we face a huge burden of deaths related to AMR. AMR has the potential to transform common and relatively innocent infectious diseases into major threats causing losses worldwide. Consequently, there is a call for strong actions [1, 2] ranging from increasing scientific knowledge to development of rationalized antibiotic usage for both human and animals, more efficient antibiotic stewardship, introduction of e-health (including telemedicine), and improved data sharing to support secondary and integral usage of medical data [1, 3–6]. Clinical microbiology laboratories are a central element in the chain of data producers involved in the fight against infectious diseases and AMR [7]. Laboratories are facing a strong trend toward automation [8] and also experience a growing need for expert systems [9]. In parallel, we witness the emergence of the so-called P4-medicine (predictive, personalized, preventive, participatory) that started in the field of cancer-related needs and now also spans infectious disease management [10–12].

E-health development and implementation are key technical building blocks for P4-medicine. Two important e-health innovations are electronic health records (EHRs) and health information exchange (HIE) networks. EHRs refer to the collections of patient health information in a digital format (ideally the complete and longitudinal electronic records for a patient), and HIE describes networks that allow electronic sharing of clinical information among caregivers across organizational boundaries [13]. The ultimate aim of these tools is to increase the quality of individual patient care as well as providing detailed support for global epidemiological surveillance and research applications [13–15]. EHRs and HIE networks not only are a preoccupation of developed economies

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but also are under serious consideration and development for low to middle-income countries [16–18].

The most recent evolution of EHRs is their move from selectively provider-based data toward personal, mobile solutions initiated, for instance, by Apple through its "Health Records" app [19]. One can expect a movement toward patient empowerment relating to their personal medical data, which will also require special consideration of potential issues correlated with privacy of personal data. These trends are part of the global evolution of "digital Medicine" (DM) that is anticipated to impact all aspects of clinical intervention and care [20] (chronic pathology surveillance, infectious disease monitoring, telemedicine, etc.). Such an evolution is happening in all countries irrespective of their high/medium/low-income states [18, 19, 21–24].

One of the basic principles for current developments in DM and e-health is the sharing and exchanging of medical data records across medical systems to support immediate patient care as well as "secondary use" of data for medical and clinical research, epidemiological surveillance, patient care management across the hospital, general practitioner, nursing, and physiotherapy and more [25]. This basic principle of systems and data "interoperability" is further presented in Fig. 1. Medical system interoperability was recently documented as a significant and current blocking point to the sharing of medical data, to the point where procurement strategy templates targeting this need are now proposed by the US National Academy of Medicine [25, 26]. In health care, "interoperability" has been defined by the Healthcare Information and Management Systems Society (HIMSS) as "the ability of different information technology systems and software applications to communicate, exchange data, and use the information that has been exchanged" [27].

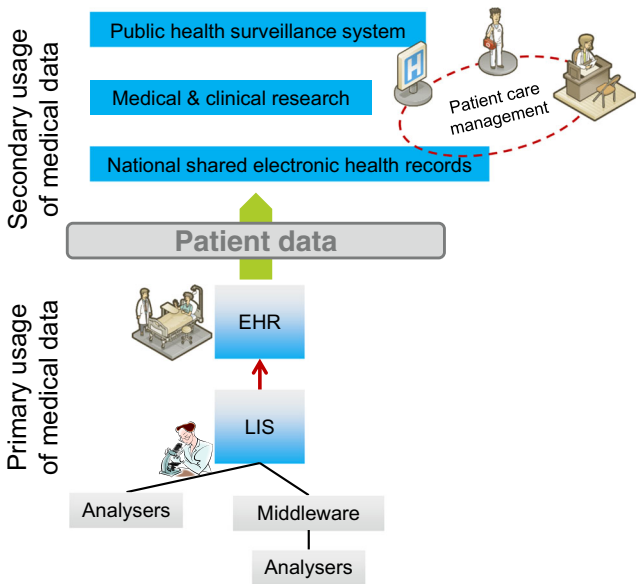

Fig. 1 Why do we need system and data interoperability? This figure illustrates that medical data originate from different sources (medical laboratory devices, medical reports, etc.) and flow up to the laboratory information system (LIS) and/or Electronic Health Records (EHR) to support immediate patient care. On top of that is the secondary usage of data to support medical and clinical research, epidemiological surveillance, patient care management (across the hospital, general practitioner, nursing, physiotherapy, etc.). Those different usages do rely on systems and data interoperability

This concept embeds [27, 28]:

- "Foundational" interoperability meaning that the receiving information technology system does not have to interpret the data again;
- "Use case" or "workflow" interoperability which, by constraining the sequence of messages exchanged, coordinates the work processes across healthcare systems (see Fig. 2 for further illustration of the "workflow interoperability");
- "Structural" (or syntactic) interoperability that defines the structure or format of data exchange (i.e., the message format standards). It ensures that data exchanges between information technology systems can be interpreted at the data field level (see Fig. 3 for further illustration of "syntactic interoperability");
- "Semantic" interoperability, which is the ability of two or more systems or elements to exchange information and to conveniently use the information that has been exchanged. It takes advantage of both the structuring of the data and proper encoding of the data including vocabularies so that the receiving information technology systems can interpret the data (see Fig. 4 for further illustration of the "semantic interoperability").

Analysis of the economic impact of interoperability is not trivial and is a still-open question with a large range of answers that are not always fully aligned [30–33]. Different economic indicators are defined, such as cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA). Applicability of those indicators to health is troublesome. Indeed, CBA implies to assign a monetary value to health outcome; CEA may be used to compare interventions for the same health problem, but it loses the side impact on other health-related aspects. CUA measures the "healthy years" through the quality-adjusted life years (QALY) and includes mortality and morbidity in one single measure.

It is very difficult to assess the so-called positive externality where impacts of a particular e-health intervention may go far beyond its primary action to affect other areas such as management of adverse treatment effects, reduction of redundant tests, reduction of time spent on manual information entry, or shortening length of hospital stay. Nevertheless, some works [32, 33] report national impacts that could range from 2 to 5% of total spending in health depending of the European country considered and, for the USA, up to 36 billion dollars/year by

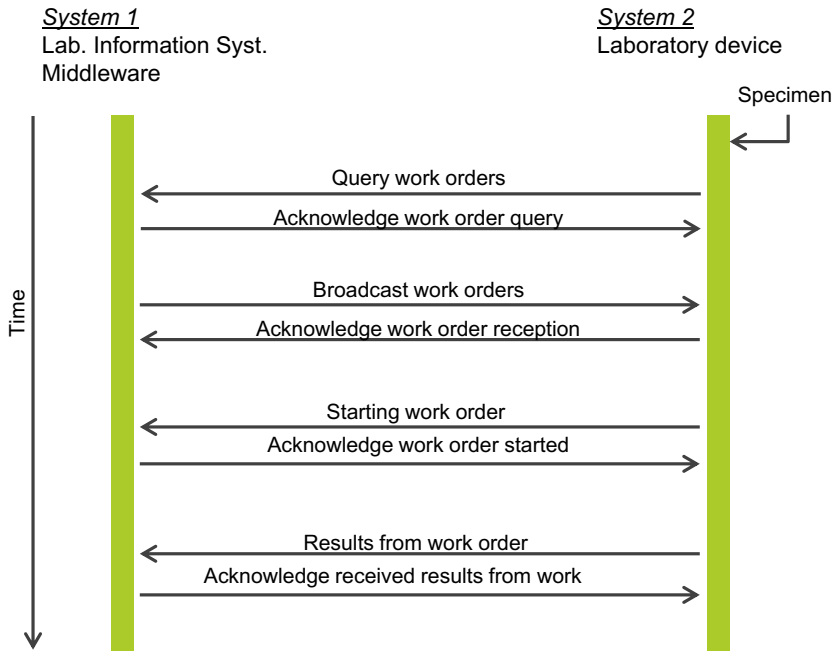

Fig. 2 Workflow interoperability concept. This illustrates the "workflow interoperability" section from the definition given for "interoperability." It is inspired by the HL7–IHE Laboratory Automation Workflow (LAW) profile [29] and presents an interaction between the laboratory information system (LIS) and a laboratory device. We see messages exchanged, where the IVD device recognized a specimen container and queries the LIS for a test order on that specimen. The LIS sends test to orders the IVD systems that acknowledge reception, start test, and sends results to the LIS

addressing only medical device interoperability. In the USA, where EHR are strongly adopted since the abovementioned HITECH act in 2009, it was shown that less than one third of the hospitals are able to electronically find, send, receive, and integrate patient information from another health provider [26].

Interoperability standards

Healthcare interoperability relies on health information technology (IT) standards that allow the different concepts of interoperability to be put in practice. Those health IT standards include:

- Integration of the Healthcare Enterprise (IHE) technical frameworks [29] that describe standardized use cases in healthcare such as the Laboratory Analytical Workflow (LAW). This means that IHE technical frameworks support the "workflow interoperability" aspects. Those frameworks explain how to use standards in the context of the different use cases;
- Application of Health Level 7 (HL7) [28] standards. HL7 mainly takes care of the syntax of the messages exchanged between healthcare systems and thus allows the "structural or syntactic interoperability" to happen;
- Support of the "semantic interoperability" aspects by clinical terminologies [34] such as the Logical Observation Identifiers Names and Codes (LOINC) [34–38], the Unified Code for Units of Measure (UCUM) [39], and the Systematized Nomenclature of Medicine–Clinical Term (SNOMED CT) [34, 40]. LOINC and SNOMED CT are well-known for their capabilities to encode microbiology and infectious diseases related data.

Segments #	Content
1	Observation ID
2	Type of value in 5th segment
3	Observation performed
4	Observation grouped by run
5	Observation results value
6	Unit of the observation
…	…

Fig. 3 Syntactic interoperability concept. As Fig. 2, it is inspired by the HL7–IHE LAW profile and presents the first data segments of the message used to transmit laboratory device tests results to the LIS (message OBX in HL7–IHE LAW). Segment n°3 and n°5 defines the laboratory test performed and its associated test result

Figure 5 is an evolved version of Fig. 1 now linking the different medical data formats to the HIMSS and HL7 interoperability principles and the health IT standards that are further described below.

IHE

The IHE initiative was born from a joint activity of HIMSS and the Radiological Society of North America (RSNA) [41]. It is now a worldwide initiative supported by a wide variety of healthcare and industry professionals aiming at improving the way healthcare systems share information. IHE promotes the coordinated use of established standards such as HL7, Digital Imaging and Communications in Medicine (DICOM), LOINC, and

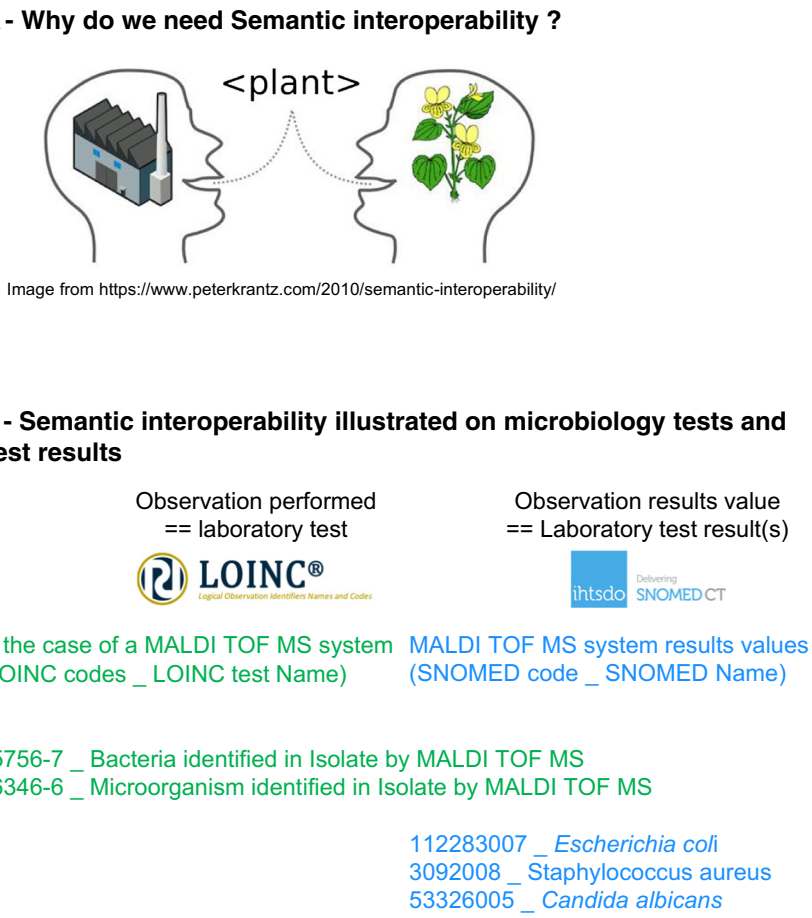

Fig. 4 Semantic interoperability concept. Part **a** presents the importance of agreed-upon vocabularies as associated semantic to describe an information. Here, the two distinct meanings of the word "plant" may generate misunderstandings between two individuals. Part **b** presents a device manufacturer-agnostic description of MALDI TOF MS identification test and associated test results using LOINC and SNOMED CT coding that are presented later in this document

SNOMED CT to support clinical needs for optimal patient care. It offers a framework of technical profiles split by clinical expertise (e.g., Pathology and Laboratory of Medicine, Radiology, Endoscopy, etc.), to support clinical integration needs. In the case of the "Pathology and Laboratory of Medicine" technical framework, IHE has developed profiles such as "Laboratory Device Automation"; "Laboratory Point of Care Testing"; and "Laboratory Analytic Workflow" (LAW). We reuse the LAW profile in this review to illustrate the integration of all the building blocks presented around laboratory-based microorganism identification and antibiotic susceptibility testing results. A comprehensive description of these profiles is beyond the scope of this review; interested readers will find extensive documentation about the IHE technical profiles on the IHE International web site (www.ihe.net).

HL7

Health Level 7 (HL7) is a standard development organization (SDO) [28] that creates specifications to structure, encodes and exchanges patient healthcare information and thus facilitates exchange between healthcare systems. The best-known standards developed by HL7 are:

- HL7 v2.x, text encoding of HL7 messages, to exchange messages between systems as depicted in Fig. 2;
- HL7 Clinical Document Architecture (CDA) as part of HL7 v3, to describe clinical documents;
- Fast Healthcare Interoperability Resources (FHIR), the new HL7 standard based on the latest web-technologies [28, 42].

LOINC

LOINC is a terminology standard for identifying health measurements, observations, and documents that were first developed in 1994 at the Regenstrief Institute [37]. The overall scope of LOINC is "anything that can be tested, measured, or observed about a patient" [43]. LOINC divides its overall scope into two main divisions: laboratory and clinical. Here, we will concentrate only on the laboratory portion of LOINC as it directly relates to describing infectious disease and AMR patient data. The scope of the LOINC clinical part is much broader and only indirectly related to infectious disease and AMR.

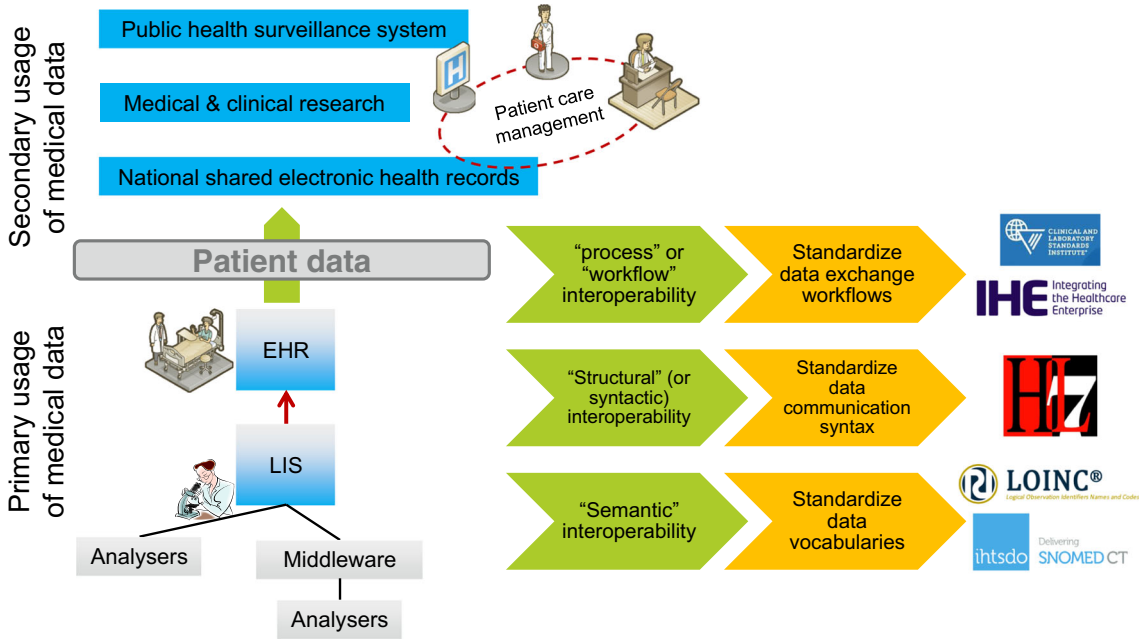

Fig. 5 Standards supporting healthcare interoperability. Laboratory data are sent to the laboratory information system (LIS) and then flow up to the EHR/EMR to support immediate patient care. On top of that are the secondary usage of data to support medical and clinical research, epidemiological surveillance, patient care management (across the hospital, general practitioner, nursing, physiotherapy, etc.). Those data usage depends on the three interoperability pillars on the right hand "process/workflow," "syntax," and "semantic" each of them being implemented by the internationally adopted standards mentioned

Essentially, a LOINC term represents the question asked by a laboratory test (aka. laboratory observation) and LOINC contains different codes for each test that have distinct clinical meanings or implications. It distinguishes an observation (test ordered/reported) across six dimensions called "parts" [44]:

- Component (analyte): the substance or entity being measured or observed;
- Property: distinguishes between different kinds of quantities relating to the analyte;
- Time: the interval of time over which an observation was made;
- System (specimen): the specimen for which the observation is made;
- Scale: how the observation value is expressed: qualitative, quantitative, using text or a name;
- Method: how the observation was made, which technique was used

To support the use of LOINC for infectious disease–related laboratory tests, LOINC published in August 2018 a guideline [45] with the aim "to help users select the most appropriate LOINC terms for clinical microbiology and infectious diseases laboratory tests."

The review recently published by Bodenreider et al. [34] will give interested readers more details on LOINC and related clinical terminologies. Example of LOINC codes can be found in Fig. 4.

UCUM

UCUM is a code system that provides a computable representation of units of measure. UCUM's scope includes domains across scientific, business, and engineering disciplines, and thus is broader than just health-related measurements [39, 46]. UCUM provides concise semantics to each defined unit, with the purpose "to facilitate unambiguous electronic communication of quantities together with their units." UCUM codes are intended for use in electronic communication (such as messages or documents in formats defined by HL7) and are often accompanied by other unit strings familiar to human interpretation.

SNOMED CT

SNOMED CT "provides a standardized way to represent clinical phrases captured by the clinician and enables automatic interpretation of these" [47]. It started in 1965 with the Systematized Nomenclature of Pathology (SNOP), published by the College of American Pathologists (CAP) that evolved to give the SNOMED Reference Terminology (SNOMED RT). The current SNOMED CT was created from a merger of SNOMED RT and the Clinical Terms Version 3 (CTV3) (also known as the Read codes), developed by the National Health Service of the United Kingdom [48]. SNOMED CT is a multi-axial onto-terminology containing more than 341,000

concepts (e.g., clinical information bullets) and 1,000,000 relationships (e.g., mechanism to describe relations between concepts) with a global scope covering a wide range of clinical specialties and disciplines. It is used to encode patient electronic health records (potentially using synonyms that suit local preferences while recording the information in a consistent and comparable form). Among the SNOMED CT use cases are the description of microbiology and infectious disease information, thus allowing secondary use of the data [6, 35] (e.g., data analytics at a local, regional, or national level).

This microbiology and infectious disease use case is supported, for example, by the SNOMED CT "Organism," "Clinical findings," and "Substance" hierarchies of concepts. It must be noted that the SDO's developing LOINC and SNOMED CT do collaborate together and that many users implement both coding systems together. The review recently published by Bodenreider et al. [34] will give the interested reader more details on SNOMED CT and related clinical terminologies. Examples of SNOMED CT codes can be found in Fig. 4.

Putting it all together

We illustrate in Fig. 6 how the HL7 IHE-LAW message structure, LOINC, encoded tests description, UCUM units, and SNOMED encoded result values can be used to transport and describe the test results and test result values of an automated identification and antibiotic susceptibility testing (ID & AST) laboratory system into the laboratory information system (LIS). Those correspond to the workflow depicted in Fig. 2. In order to simplify the figure, this example omits detailed workflow aspects and simplifies most of the HL7 message structure. The HL7 IHE-LAW message transmits the code of the feature (test performed or test result value) that is described as well as the identity of the coding system. From this point, the receiver's LIS then owns all information needed to "understand" the test result. It stores standard-encoded data for primary and secondary use [6, 35] and can translate them into the local terminology needed by a human reader [49] or aggregation terminologies for statistical analysis such as those defined by the World Health Organization "International Classification of Diseases" revision 10th or 11th [50] or research-oriented ontologies such as the Disease Ontology [51].

Encouraging the use of standards for microbiology and infectious diseases in the laboratory domain

Recording and transmitting laboratory data without consideration of systems and data interoperability, harmonization, and standardization places a strong burden on the primary and secondary users of data [6, 52]. Without such standards, it is difficult and often inefficient to aggregate and understand data from different sources. These barriers hinder our capability to fight antimicrobial resistance [6]. Although retrospective standardization of clinical laboratory data was proven to be

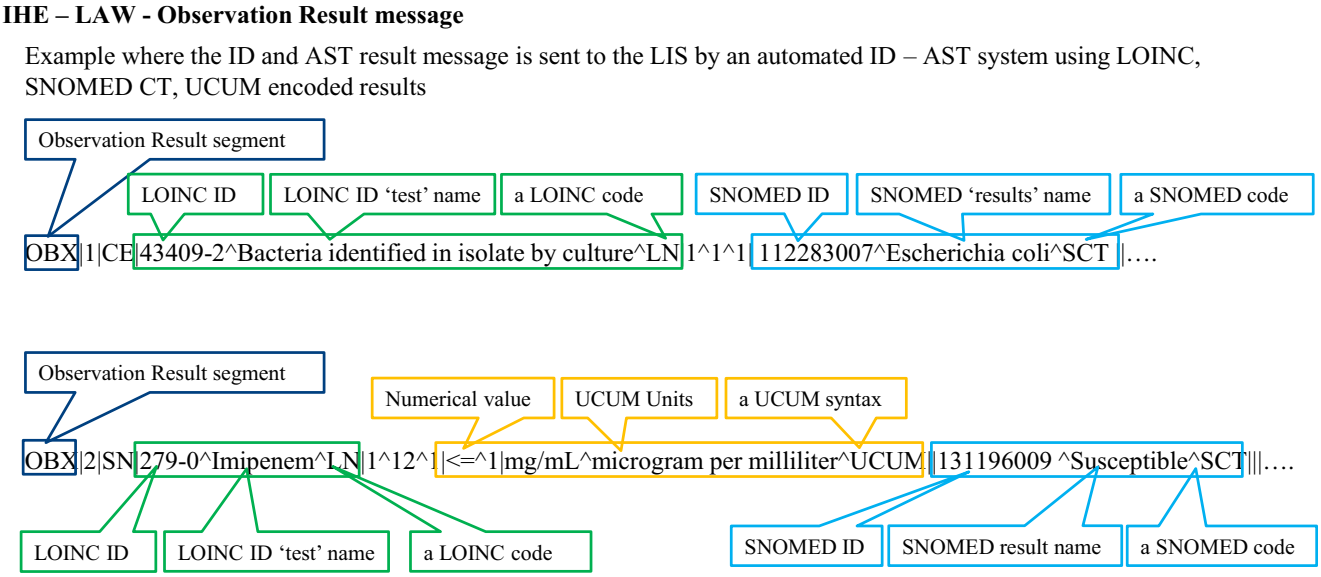

Fig. 6 Example of HL7 IHE-LAW test reporting results using LOINC, UCUM, and SNOMED CT. This example reuses HL7–IHE LAW message OBX (i.e., observation results message) introduced in Fig. 3. It shows part of the message sent by a laboratory device system to the LIS describing the identification and antibiotic susceptibility testing (ID and AST) tests performed as LOINC codes and tests results values (1) being the microorganism identified as a SNOMED CT code, (2) the MIC as a numerical value with UCUM units as well as (3) the MIC interpretation as a SNOMED CT code

achievable with excellent results using [35] or not [53] the health data standards we present in this review, it also proved to be difficult, and labor and maintenance intense. Those studies concluded that this process would have benefitted from explicit lab data standardization [35, 53, 54]. Such explicit medical and laboratory data harmonization and standardization not only facilitates and enhance future data integration, data analytics, and medical and clinical research [15] but is one of the keys to digital medicine [21, 55]. In line with that, such data standards are being pushed by actors on different sides, each of them for different but consistent diagnostic and clinical reasons.

Push for data standards by regulatory authorities

Regulatory authorities from many different countries do advocate, recommend, or push for the uptake of health data standards as an aid to implement global epidemiological surveillance, to sustain the fight against AMR and to control and reduce costs to the health system. This is a global trend; we will here focus on a limited set of examples from both low and high-income countries.

Nigeria recently published a "National Health ICT (Information and Communication Technology) strategic framework _ 2015-2020" [18] which states that "by 2020, health ICT will help enable and deliver universal health coverage in Nigeria." This strategic vision explicitly recommends the use of LOINC and SNOMED in the terminology service part of the framework.

France published a legal text in 2016 [56] stating that electronic lab reports should be structured according to a national interoperability referential explicitly requiring the use of LOINC codes to describe laboratory tests (France also has an ongoing analysis toward SNOMED CT, but no conclusions have been published as yet). This same text also reuses HL7–CDA R2 (Clinical Document Architecture) standard to structure laboratory reports. In the field of laboratory accreditation, the French guidance document SH GTA 02 [57] relates to information system evaluation in the scope of laboratory accreditation according to ISO 15189, ISO 22870, and the French SH REF 02 [58]. This guidance document also explicitly recommends usage of IHE–HL7 profiles and LOINC laboratory test encoding. In September 2018, the French Ministry of Health published its national health strategy [59] that calls, between many other items, for an enhanced usage of e-health and the development of health system interoperability. The associated technical report [60] clearly indicated the need for referential including HL7, IHE, and LOINC.

The United Kingdom, maintaining a leadership position on medical terminologies with the CTV3/Read code classification that constituted one of SNOMED's roots, is currently hosting the SNOMED international headquarters. The British National Health System (NHS) published "Personalized Health and Care 2020" document in 2015 [61] which states that it "(…) endorses the move to adopt a single clinical terminology – SNOMED CT – to support direct management of care, and will actively collaborate to ensure that all primary care systems adopt SNOMED CT by the end of December 2016; the entire health system should adopt SNOMED CT by April 2020."

In the USA, the HITECH act was voted for a decade ago [62] and had a profound impact on health IT by pushing forward meaningful use of EHR. Its impacts are clear, but this is certainly not the end of the road [63, 64]. Through private–public partnership under the MDIC (Medical Device Innovation Consortium) umbrella, US Federal agencies (Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), National Library of Medicine (NLM), National Institute of Health NIH)) do stimulate a shared effort with laboratory representatives CAP (College of American Pathologists), APHL (Association of Public Health Laboratories), ACLA (American Clinical Laboratory Association), and industries (IVD Industry Connectivity Consortium, IICC) to push forward the healthcare data standard presented above [65]. The first output of this work was the LIVD (LOINC for IVD) specification published by the IICC (see below) and the recent FDA guidance on "LOINC for In Vitro Diagnostic Test" [66]. This work is only a part of the many initiatives in the USA [26]. Others include, and this is not an exhaustive list, the publication by the CDC-NHSN (National Healthcare Safety Network) of a list of SNOMED CT codes for reportable organisms, the publication by the FDA of a set of guidelines related to "Real World Evidence" and interoperable medical devices [67,

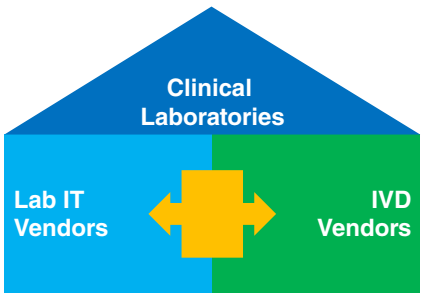

Fig. 7 IVD Industry Connectivity Consortium (IICC). This figure presents the IVD Industry Connectivity Consortium (IICC) and its missions toward laboratory device connectivity. IICC has members from both Laboratory IT vendors field and IVD vendors fields working together. To achieve its missions, IICC is committed to create and ensure adoption of an interoperable connectivity paradigm to reduce the complexity and variability of data exchange between IVD testing systems and healthcare informatics systems. IICC members vendors are Abbott Laboratories, A&T, Beckman Coulter, BecktonDickinson, bioMérieux, Data Innovations, Hitachi, IZASA SA, Orchard Software, Ortho Clinical Diagnostics, Roche Diagnostics, Samsung, Siemens Healthcare Diagnostics, Sunquest Information Systems, and Systelab Technologies SA. This figure is adapted from a slide present on the IICC website at https://ivdconnectivity.org/?ddownload=858

68], or the yearly publication by the Office of the National Coordinator for Health Information Technology of its assessment of the health IT standards landscape known as the "Interoperability Standards Advisory" [69]. All those are moving forward in the same direction toward a strong promotion of the standards mentioned in this review paper in the in vitro diagnostic field.

Endorsing data standards by industries

The IICC is "a global, non-profit organization dedicated to creating and encouraging adoption of a unified connectivity standard to reduce the cost and variability of data exchange between IVD devices and healthcare informatics" [70]. As presented in Fig. 7, IICC is composed of some of the major IVD vendor companies and LIS companies located on both sides of the Atlantic. Its missions are to modernize connections between LIS and analyzers as well as to enable clinical laboratories to achieve more and spend less.

In these objectives, IICC co-authored [71] the IHE-LAW (Laboratory Analytic Workflow) profile that is now being submitted to become a Clinical and Laboratory Standards Institute (CLSI) standard. This future CLSI Auto16 standard is aimed at replacing the current ASTM standard. The LAW profile "standardizes the data flow of IVD patient and QC analytical work order steps and test results between instruments, middleware and LIS systems" [72]. IICC, answering US-FDA incitation for laboratory data standards mentioned above, also authored the LIVD data format [71], together with CLSI, HL7, APHL, IHE, MDIC, FDA, CDC, Regenstrief Institute, and NIH. LIVD "defines the digital publication of LOINC using vendor defined IVD tests associated with a set of predefined LOINC codes. LIVD assures that laboratory personnel select the appropriate LOINC codes for IVD test used by their laboratory. It also allows LIS systems to automatically map the correct IVD vendor test result to a LOINC code." [73].

At present, we can find LOINC codes assigned by manufacturers to their products made available to their customers in the form of LIVD files. Usually, this is done through service documentation. We also start to find systems supporting HL7 IHE-LAW and LOINC code connections, together with legacy connections, as presented on the IICC website [74].

Implementation in laboratories, hospitals, and national health surveillance organizations

As shown before, the use of healthcare data standards can be powerful in reconciling disparate laboratory data. We present below a partial selection of implementations of those standards gathered from different countries. Some of those implementations are directly related to infectious diseases and AMR management.

In Europe, although mandated by French law, it appears that the HL7–CDA R2 is implemented on a limited scale only [75]. On the semantic side, LOINC has been made available by the Paris Hospital Organization (for the biology part) through a searchable website (www.bioLoinc.fr). White papers (co-authored by representatives from French medical organizations, authorities, and industries), presenting data sets supporting medical microbiological laboratory data encoding, were made available through the Interop'Santé association [76, 77]. On their side, French regional health authorities (Alsace–eSanté for example) demonstrated the added values of HL7 and LOINC–encoded data in pilot implementations [78] to support e-health.

In the UK, the NHS–Wales showed the added value of SNOMED CT for the neurological electronic patient record system that inventories diagnostic, treatment, and interventional information in a database underpinned by SNOMED CT [79]. In the UK, SNOMED CT is now being implemented actively in general practice starting from April 2018 [80].

In The Netherlands, the health authorities defined HL7- and FHIR-based infrastructure using LOINC and SNOMED CT–encoded data to enable data flow between medical laboratories and to national surveillance agency [81]. A reference list of reportable microorganisms using SNOMED CT codes was defined as well [82]. Based on those, the National Institute for Public Health and the Environment (RIVM, Rijks Instituut voor Volksgezondheid en Milieu) established a network of laboratories to monitor infectious diseases and antimicrobial resistance (ISIS-AR, Infectieziekten Surveillance Informatie Systeem-Antibiotica Resistentie). In this network, laboratory data are described, aggregated, and analyzed via HL7 connections using LOINC and SNOMED CT encoding.

In Turkey, LOINC is being requested by health authorities from in vitro diagnostics companies and laboratories. The Turkish health authorities made available to medical laboratories a website allowing to find the correspondence between LOINC codes and Turkish billing codes known as SUT codes (http://loinc.saglik.gov.tr).

Australian authorities do deploy important efforts to establish the infrastructure supporting nationwide patient health records. Use of HL7, LOINC, and SNOMED CT is supported by the Australian Digital Health Agency and the CSIRO (Commonwealth Scientific and Industrial Research Organisation). Among many other aspects, this pushes medical laboratories (including some microbiology laboratory) to use LOINC and SNOMED CT–encoded data as well as national patient electronic records (called "My Health Record") being deployed nationally along 2019 [83]. It is worth noting that "My Health Record" also uses SNOMED CT–encoded patient data [84].

In the USA, as in the other countries mentioned, implementation is progressing [1, 53]. In addition to the public–private partnerships mentioned in a previous section, and to help

enforce the use of data standards in the country, the US-FDA, US-CDC, NLM, LOINC, and IICC were present at the April 2018 US Clinical Laboratory Improvement Advisory Committee (CLIAC) where a full working session on "laboratory semantic interoperability" took place. Interestingly, CLIAC recommends (1) that an official interoperability implementation guideline for IVD device–Lab IS interaction specifying the standards be used (IHE-LAW and LOINC/LIVD) and (2) that qualitative (barriers for adoption) and quantitative analysis (ROI, cost of not implementing, etc.) of interoperability be issued [85]. It has to be noted that live and de novo implementation of the health data standards proved their added value; this is, for example, the case for combined use of LOINC and SNOMED CT for colorectal and breast cancer synoptic worksheets [86]. It is also worth mentioning the CDC–National Notifiable Diseases Surveillance System (NNDSS) [87] uses the same HL7, LOINC, and SNOMED CT terminologies on a national scale. Last but not the least, we mention the HL7 FHIR Argonaut project [88]. This project aims at developing a FHIR-based application programming interface supporting information sharing of electronic health records between different data providers (i.e., hospitals) and users (i.e., health records applications). The Argonaut project makes extensive use of HL7 FHIR as well as LOINC and SNOMED CT to encode data. A well-known usage of the Argonaut project is the Apple Health Record application that we mentioned earlier [19, 89].

In Canada, Health Infoway/Inforoute Santé acts as the national release center for both LOINC and SNOMED International and manages the creation of the pan-Canadian LOINC Observation Code Database (pCLOCD). It appears that most laboratories have mapped their local test catalogs to the pCLOCD/LOINC and that, in their HL7 v2.x messages, they send the local code and the corresponding LOINC code (L. Carey, Infoway, personal communication). Most provinces have created a laboratory repository, which contains a large portion of the provinces laboratory test results. The repository is possible because each laboratory that contributes uses LOINC. The recent presentation on implementation of SNOMED CT in the hospital information system at the York General Hospital in Toronto [90] has shown a gain both at the level of budget and the number of human lives saved.

Table 1 Foreseen impacts of semantic data interoperability

Direct impacts		Primary stakeholders' benefits			
		Care providers	Care payers	Patients	Device manufacturers
Impact due to lack to medical device interoperability	Adverse events from drug errors, misdiagnosis, and failure to prevent harm	X	X	X	
	Redundant testing resulting from inaccessible information	X	X	X	
	Clinician time spent manually entering information	X			
	Increased length of stay from delays in information transfer	X			
Lack of commonly adopted standards for interoperability	Device testing and development costs				X
	Provider costs to integrate devices with EHRs	X			
Indirect impacts		**Primary stakeholders' benefits**			
		Care providers	Care payers	Patients	Device manufacturers
Impact due to lack to medical device interoperability	Limited ability to collect and leverage data analytics to improve clinical decision support	X	X	X	
	Sub-optimal care driven by limited adoption and efficacy of remote patient monitoring		X	X	
	Limited ability for operational maintenance and optimization of utilization/inventory management	X			
Lack of commonly adopted standards for interoperability	Limited device choice, innovation and competition due to switching costs	X			X

This table is adapted from the work of the Westhealth Institute [33]. It presents the area of direct and indirect impacts to medical device interoperability on two dimensions (medical device interoperability and standards for interoperability) for the four stakeholders that are care providers, care payers, patients, and device manufacturers

If countrywide initiatives are implementing semantic data interoperability technologies and demonstrating their added value, this helps promote similar initiatives in daily medical laboratory practice. Semantic laboratory data interoperability implementation in those facilities faces both a change and a live cycle management issue linked to the validation and accreditation of laboratory IT infrastructures. This translates, as Jonnaert S. and Heierman E [71] show, into "most laboratories that are installing new instruments follow specifications from guidance documents that are now more than 20 years old and no longer meet the data interoperability and security needs of contemporary laboratories."

We can safely hypothesize that with (1) an enhanced awareness of semantic medical data interoperability impacts and advantages (see Table 1, adapted from [33]) and (2) LIS turnover (e.g., new infrastructure replacing legacy ones), optimized technical principles and solutions will continue to emerge. Additionally interoperability procurement specification strategies are now proposed by the US National Academy of Medicine [26]. We acknowledge that extensive quantitative analysis of the impact of implementation of the presented standards is still lacking, which limits adoption. Nevertheless, it has to be noted that quantification of the impact is a significant subject for several groups setting up demonstration projects.

Conclusions

Healthcare data interoperability is one of the key technical building blocks to support digital medicine and e-health. Interoperability should be distinct in our toolbox and be implemented to improve the fight against infectious diseases and antimicrobial resistance. It is key that all actors in the healthcare chain ensure that the standards presented here are duly considered and implemented, thus ensuring fluent data flow and sharing without loss of time, effort, and money for reconciling disparately described patient data. We no longer inhabit a world of data silos, but we reside in a world of free data exchange and no "big data" analytics will happen without optimized data sharing and reuse.

Acknowledgments The authors acknowledge the critical reading of this manuscript by Laurent Lardin, Sergyl Lafont, and Julien Textoris (bioMérieux); Lina Soualmia (University of Rouen, France); and Daniel Vreeman and Swapna Abhyankar (LOINC, Regenstrief Institute). They also acknowledge key input from Pim Volkert regarding the situation in The Netherlands and Lorie Carey regarding the situation in Canada.

Funding information Work by Xavier Gansel and Alex van Belkum was entirely funded by bioMérieux, but the company had no influence on the design of the current analyses. Work of Melissa Mary was supported by a CIFRE grant no. 2014/0341 from the French Ministère de la Recherche et de l'Enseignement Supérieur.

Compliance with ethical standards

Conflict of interest Xavier Gansel is a bioMérieux employee. He represents bioMérieux in the LOINC Laboratory Committee meeting, takes part in SNOMED CT projects and is involved in the MDIC/NESTcc SHIELD project. Alex van Belkum is a bioMérieux employee. He is also the Editor in Chief of the European Journal of Clinical Microbiology & Infectious Diseases. Apart from the above, the authors declare that they have no conflict of interest.

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