The Journal of Systems and Software 215 (2024) 112093

Contents lists available at ScienceDirect

The Journal of Systems & Software

journal homepage: www.elsevier.com/locate/jss

Semantic interoperability for an AI-based applications platform for smart hospitals using HL7 FHIR☆

Emmanouil S. Rigas [a,b,*], Paris Lagakis [a], Makis Karadimas [c], Evangelos Logaras [a], Dimitra Latsou [d], Magda Hatzikou [d], Athanasios Poulakidas [c], Antonis Billis [a], Panagiotis D. Bamidis [a,b,1]

[a] Lab of Medical Physics and Digital Innovation, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece
[b] AHEPA University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece
[c] Netcompany - Intrasoft, Athens, Greece
[d] Pharmecons Easy Access, Athens, Greece

ARTICLE INFO

Keywords:
Semantic
Interoperability
FHIR
Smart hospital
Digital healthcare
Artificial intelligence
Application platform

ABSTRACT

The digitization of the healthcare domain has the potential to drastically improve healthcare services, reduce the time to diagnosis, and lower costs. However, digital applications for the healthcare domain need to be interoperable to maximize their potential. Additionally, with the rapid expansion of Artificial Intelligence (AI) and, specifically, Machine Learning (ML), large amounts of diverse types of data are being utilized. Thus, to achieve interoperability in such applications, the adoption of common semantic data models becomes imperative. In this paper, we describe the adoption of such a common semantic data model, using the well-known Health Level Seven Fast Health Interoperability Resources (HL7 FHIR) standard, in a platform that assists in the creation and storage of a plethora of AI-based applications for several medical conditions. The FHIR server's efficiency is being showcased by using it in an application predicting coronary artery stenosis as well as for managing the platform's key performance indicators.

1. Introduction

Interoperability in health-related digital applications holds the potential to revolutionize the healthcare landscape. This is so, as technology progresses and healthcare systems become increasingly digitized. In such an environment, the seamless exchange of information between different applications, platforms, and devices becomes ever more important (Iroju et al., 2013; Cardoso et al., 2018). Interoperability refers to the ability of these systems to communicate, share data, and work harmoniously together. The ultimate goal is to enhance patient care, improve clinical outcomes, and optimize healthcare workflows.

The need for interoperability is driven by the fragmented nature of healthcare data. Patient information is often spread across electronic health records (EHRs), medical devices, telehealth platforms etc, making it difficult for healthcare providers to create a comprehensive and accurate view of a patient's medical history (Olaronke and Oluwaseun, 2016). Interoperability reduces these difficulties, enabling healthcare providers and other parties to access, share, and update patient data seamlessly. This real-time accessibility can translate to faster and more informed decision-making, reduced medical errors, and improved patient safety. Furthermore, interoperability assists innovation (Hodapp and Hanelt, 2022; Lehne et al., 2019). When different health-related applications can exchange data effortlessly, developers and practitioners can create more robust and specialized solutions. For example, wearable devices can integrate with mobile or online platforms, or even EHR, allowing healthcare providers to monitor a patient's daily activity and health trends remotely (Baskar et al., 2020; Rubí and Gondim, 2020). This data fusion enables, amongst others, personalized treatment plans, early disease detection, and more effective chronic disease management.

The Health Level Seven International (HL7) Fast Healthcare Interoperability Resources (FHIR)[2] is designed to enable and support the electronic exchange of healthcare information across different systems, thereby streamlining the integration and interaction among diverse healthcare infrastructures. This standard facilitates the seamless sharing

☆ Editor: Laurence Duchien.

* Corresponding author at: Lab of Medical Physics and Digital Innovation, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece.
E-mail address: erigas@auth.gr (E.S. Rigas).

1 P. Bamidis and A. Billis share senior authorship of this paper.

2 https://www.fhir.org/.

https://doi.org/10.1016/j.jss.2024.112093
Received 17 August 2023; Received in revised form 11 May 2024; Accepted 14 May 2024
Available online 16 May 2024

of data among clinicians, researchers, and organizations, significantly enhancing the efficiency of healthcare delivery. FHIR structures data into resources,[3] which can be easily combined to address complex healthcare data management needs. These resources cover a broad spectrum of healthcare information, from patient details and care plans to observations and clinical findings, allowing for comprehensive and flexible data representation. The utilization of FHIR is rapidly expanding within the healthcare industry (Vorisek et al., 2022), underlined by its growing adoption rates. According to a recent study,[4] approximately 24% of healthcare companies have already integrated at-scale FHIR APIs into their operations, with an anticipated 67% of providers expecting to follow suit by 2023. This trend underscores the critical role of FHIR in advancing interoperability and the future outlook of healthcare technology, towards a more connected, efficient, and patient-centric healthcare ecosystem.

At the same time, Artificial Intelligence (AI)-based health applications have emerged as revolutionary forces at the connection of technology and healthcare, as highlighted by Secinaro et al. (2021). By harnessing sophisticated techniques such as machine learning, as discussed by Qayyum et al. (2020), these applications possess the potential to drastically change the medical field. They are capable of analyzing medical data with high precision, thereby assisting healthcare professionals in diagnosing conditions, forecasting disease trends, and customizing treatment plans for individual patients.

An important benefit of AI-based health applications is their ability to process and interpret extensive patient data, encompassing medical records, imaging scans, genetic profiles, and information from wearable devices amongst others. Furthermore, many of these applications are designed to continuously learn and improve from newly acquired data, thereby refining their diagnostic and predictive abilities over time. Nonetheless, the integration of AI into healthcare introduces significant challenges, including concerns over data privacy and access as outlined by Panch et al. (2019), the ethical management of patient information, and the imperative for thorough validation of AI algorithms to ensure their reliability and effectiveness, as Morley et al. (2020) suggest. Navigating these issues to find a balance between innovation and ethical practice is crucial for unlocking the full potential of AI-based health applications in enhancing patient care and advancing medical research.

In this work, we present a platform that supports the development and the storing of different AI-based applications for a plethora of medical conditions that can be used within a smart hospital domain. We focus on the interoperability of the applications platform giving emphasis on the common semantic data model that is adopted. Specifically, we select the HL7 FHIR standard and we expand its capabilities to support the demanding needs related to efficiency and security of the applications platform. We also assess its coherence with the FAIR principles (i.e., Findable, Accessible, Interoperable, Reusable) and we present example uses for one challenging medical scenario as well as for the management of several key performance indicators (KPIs) of the platform. In all cases, data are transformed into FHIR resources which act as the main artifacts in the decision making process of the applications.

The rest of the paper is structured as follows: Section 2 presents related work. Section 3 describes the architecture and the main components of the applications platform. Section 4 describes the HL7 FHIR implementation, its architecture, the assessment of its coherence to the FAIR principles and a FHIR resource validation tool. Section 5 presents two examples of using the FHIR server, the first being related to an application predicting stenosis of the coronary artery and the second being related to the monitoring of the platform's KPIs. Finally, Section 7 concludes the work and presents ideas for future expansions.

[3] https://build.fhir.org/resourcelist.html.

[4] https://healthtechresourcesinc.com/fhir-future-outlook-for-interoperability.

2. Related work

Considering that the majority of AI-based medical applications utilize machine learning, the necessity for large amounts of data to train and enhance the efficiency of the corresponding algorithms is imperative (Ngiam and Khor, 2019). When diverse applications, targeting the same or different diseases and conditions, are required to cooperate or at least coexist within a unified ecosystem, interoperability of these applications becomes critical. In situations where these applications are data-based or driven by data, establishing a common semantic data model is essential.

In this area, a number of works exist in the literature (Duda et al., 2022). For example, Reda et al. (2019) introduce a semantic data framework capable of analyzing data extracted from unstructured sources, collaborating seamlessly with both generic and specialized datasets. The overarching objective is to harmonize these datasets within an interconnected data processing arena. This framework also empowers automated deductions and logical reasoning, substantially enhancing the recycling, utilization, and prospective enlargement of health-related data within the realm of the Internet of Things (IoT). Moreover, Kiourtis et al. (2019) put forth a methodology for fostering healthcare interoperability by converting healthcare data into the corresponding HL7 FHIR format. This method revolves around creating healthcare data ontologies, which are subsequently stored within a triplestore. For each of these developed ontologies, a determination is made regarding their syntactic and semantic resemblances to diverse HL7 FHIR resources. Once these outcomes are combined, the alignment with HL7 FHIR resources occurs, effectively translating healthcare data into a widely accepted medical standard. Additionally, Saripalle et al. (2019) delve into the Personal Health Record (PHR) concept, designed to enable patients to document and control their health information beyond what is available in Electronic Health Records (EHR), and ideally, to incorporate EHR data within the PHR. There is a consensus among specialists that allowing PHRs and EHRs to communicate in both directions significantly increases the efficiency and usefulness of PHRs for healthcare providers and patients alike. By facilitating the exchange of patient-entered data with EHR systems in near real-time, healthcare providers can make more informed clinical decisions, and patients are able to monitor any updates to their diagnostic or treatment plans. The study conducts a thorough examination and critique of HL7 FHIR in order to create and prototype a mobile PHR that is interoperable, aligns with the HL7 PHR Functional Model, and supports two-way communication with OpenEMR. Finally, Kush et al. (2020) investigate the factors contributing to the limited acceptance of common data elements (CDEs) and the ineffectiveness of CDEs or other standards in adequately addressing the widespread challenge of interoperability and data exchange. The authors provide suggestions for remedying this scenario to establish a foundation for responsible data sharing. Such an approach aligns with the FAIR principles and has the potential to cultivate learning health systems.

Apart from interoperability, the efficiency of AI-based medical applications hinges critically on the availability of data for training and validating machine learning models. This need underscores the significance of open science in facilitating access to a wide array of medical data. Open science (Nosek et al., 2015; Mirowski, 2018), as a movement, aims to make scientific research, data, and dissemination accessible to all levels of an inquiring society, amateur or professional. In the context of AI in healthcare, it promotes the sharing of not only raw data but also methodologies, software, and findings, thereby enhancing transparency, reproducibility (Collaboration, 2015), and trust in AI applications. The concept of open science, as discussed in the literature (Vicente-Saez and Martinez-Fuentes, 2018), is pivotal for overcoming barriers related to proprietary data sets and competitive interests that can impede the development of robust and effective AI tools in medicine. By advocating for open scientific practices, researchers and developers can leverage a broader pool of data, which is essential for the development of well-rounded and efficient machine learning models that can operate across diverse populations and conditions.

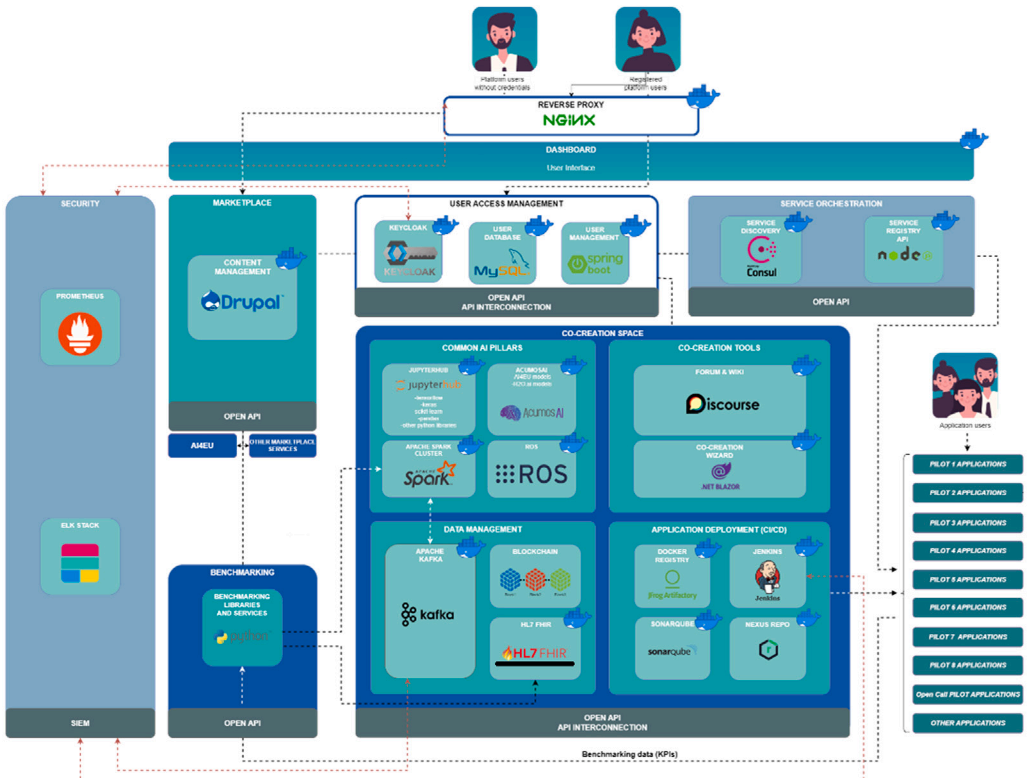

Fig. 1. HosmartAI reference architecture diagram.

3. Smart hospital applications platform architecture

As part of the HosmartAI[5] project, a platform to assist the creation of the AI-based applications on the one hand, and the hosting of these applications on the other hand has been developed. This platform consists of several components that will be briefly described in the rest of this section, while its architecture is depicted in Fig. 1.

The first layer is the Dashboard which provides an intuitive user interface for the users to use all the tools and applications that the platform provides. The user authentication is supported by Keycloack, the users are stored in a mySQL database and user management is supported by Spring Boot. Additionally, the traffic and the state of the platform is constantly being monitored to maximize the security of the platform, the applications and the data. The three main components of the HosmartAI platform are the co-creation space, the marketplace and the benchmarking tool.

The co-creation space supports the development of the medical applications and has four main components. These are (i) the common AI pillars that contain tools and applications to support the development and creation of AI-based applications; (ii) the co-creation tools that contain the platform's forum and wiki as well as a co-creation wizard; (iii) the data management that contain the Apache kafka, a blockchain and the HL7 FHIR server for the semantic interoperability of the tools and applications; and (iv) a set of tools for applications development and deployment supporting continuous integration (CI) and continuous delivery (CD).

The HosmartAI Marketplace is the place where the completed applications can be found and downloaded and/or used by interested parties. The marketplace includes the full description of all the applications, devices, services, data sources, etc. The project's marketplace also supports the services development processes end-to-end, through access to digital technologies, equipment and other related intellectual properties, but also through access to required complementary assets such as training, certification, technical support and consulting. Moreover, the Marketplace provides specific datasets for the proper execution of the algorithms, helping third party developers to deploy their AI-based solution. The HosmartAI marketplace is empowered by a unique multi-sided market platform that enables the participation of both supply-side and demand-side stakeholders.

Finally, the HosmartAI benchmarking tool is able to identify impacts of the actions and cost–benefit evidence. When a new Hospital or care Facility decides to improve their performance, data will be introduced in the Benchmarking tool, gaps will be identified and recommendations for improvements will be made. By bringing together all Health-related actors and sectors, different scales will be addressed.

The HosmartAI platform presently supports eight large-scale Pilots, which are executing and assessing enhancements in medical diagnosis, surgical procedures, disease prevention and treatment, as well as aiding rehabilitation and long-term care across various hospital and care environments. The pilots target different medical aspects or manifestations such as Cancer (Pilot 1, 2, and 8); Gastrointestinal (GI) disorders (Pilot 1); cardiovascular diseases (Pilot 1, 4, 5 and 7); Thoracic Disorders (Pilot 5); Neurological diseases (Pilot 3); Elderly Care and Neuropsychological Rehabilitation (Pilot 6); Prematurity and Fetal Growth Restriction (FGR) (Pilot 1). All pilots' applications utilize various types of data. To ensure semantic consistency, all variables have been mapped to FHIR resources. Additionally, some applications leverage HosmartAI's FHIR server for storing and managing their data. Lastly, all pilots store their KPIs in the FHIR server. A detailed description of HosmartAI's FHIR server can be found in the following section.

4. FHIR server for semantic interoperability

Given the complexity and plethora of components the HosmartAI platform has, and the demanding needs of the pilots, the use of common

[5] https://www.hosmartai.eu/.

data models that contribute to the semantic interoperability is highly important. In this section, the deployment of the FHIR server, the extra security barriers, its coherence to the FAIR principles and a FHIR resource validation tool are presented.

4.1. FHIR server

As mentioned earlier, FHIR is a standard framework created by HL7. Applications and solutions that are based on FHIR are built from a set of modular components called resources. These resources can be easily assembled into working systems that are able to solve real-world problems both clinical and administrative. Additionally, FHIR defines a simple framework to extend existing resources through the use of profiles. All systems can read all resources, but applications can add more control and meaning using profiles. Furthermore, each resource includes a human-readable text depiction using HTML. This holds particular significance for intricate clinical data, as numerous systems adopt a straightforward textual or document-oriented approach.

In the context of the HosmartAI project, FHIR was selected to be the means that support the semantic interoperability of the plethora of different types of data that are being used. For the development of the HosmartAI FHIR server, the well-known HAPI FHIR[6] implementation was used. HAPI FHIR is a complete implementation of the HL7 FHIR standard for healthcare interoperability in Java. The server is deployed on a virtual machine in the HosmartAI platform. Dockerized containers and OAuth 2.0 protocol are being used. According to HL7, a production FHIR system will need some kind of security sub-system that administers users, user authentication, and user authorization. In the context of the HosmartAI FHIR server, these recommendations have been considered and covered. Specifically: (1) The communication with the FHIR server is done over https. (2) User authentication is achieved using Keycloak.[7] (3) Tenants are being used, where each user is assigned to a specific tenant, and in this way each user is authorized to have access to the resources created by his/her tenant only. A detailed description of how tenants are created and used can be found in the HosmartAI Forum.[8] (4) HAPI FHIR is licensed under the business-friendly Apache Software License 2.0. and is a product of Smile CDR. HAPI FHIR is running for 18 years and is the most widely used implementation of FHIR. The conceptual architecture of the HosmartAI FHIR server is depicted in Fig. 2.

Users can access the FHIR server to create or view resources in two ways: (1) Using the visualization tool (see Figs. 3 and 4) that has been developed and is accessible through the HosmartAI platform[9] using the single sign-on (SSO) option. (2) Programmatically using the endpoint where detailed instructions for this option can be found under the HosmartAI Wiki.[10]

4.2. HosmartAI FHIR server and FAIR principles

The FHIR for FAIR - FHIR Implementation Guide[11] aims to develop best practices for implementing the FAIR principles when HL7 FHIR resources are used to represent the data. For each principle, a summary recommendation can be found in the previous link, and in the rest of this subsection we discuss if and how each principle is covered by the HosmartAI's FHIR server. The results are summarized in Table 1.

Findability: Findability refers to the ease with which information contained in the FHIR server can be found.

F1: (Meta)data are assigned a globally unique and persistent identifier.

- HosmartAI deployment: This requirement is covered as each resource has a unique URL in the form: "http://hapifhir.hhub.hosmartai.eu/fhir/<resource>/<id>"

F2: Data are described with rich metadata.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

F3: Metadata clearly and explicitly include the identifier of the data they describe.

- HosmartAI deployment: HAPI FHIR satisfies this recommendation by design.

F4: (Meta)data are registered or indexed in a searchable resource.

- HosmartAI deployment: HAPI FHIR satisfies this recommendation by design as, through its RESTful API, a user can search the data using query parameters as filters/search terms.

Accessibility: Once the user finds the required resources, they need to know how they can be accessed.

A1: Metadata and data are retrievable by each of their identifiers using a standardized communication protocol.

- HosmartAI deployment: Our deployment is RESTful, so this requirement is covered.

A1.1: The protocol is open, free and universally implementable.

- HosmartAI deployment: By default, this requirement is covered.

A1.2: The protocol allows for an authentication and authorization, where necessary.

- HosmartAI deployment: An authentication and authorization component is already developed.

A2: Metadata should be accessible even when the data is no longer available.

- HosmartAI deployment: In the HL7 FHIR space this requirement is fulfilled as far as metadata and data can be represented with distinct resources (see also Metadata and data page) and the used identifiers comply with FAIR principle, F1. Thus, this requirement is covered.

Interoperability: The resources usually need to be integrated with other resources. In addition, the resources need to interoperate with applications or workflows for analysis, storage, and processing.

I1: Metadata and data use a formal, accessible, shared, and broadly applicable language for knowledge representation.

- HosmartAI deployment: Covered by default through the mapping of all variables to existing FHIR resources.

I2: Metadata and data use vocabularies that follow the FAIR principles.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

I3: Metadata and data include qualified references to other metadata and data.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

Reusability: The ultimate goal of FAIR is to optimize the reuse of data. To achieve this, metadata and data should be well-described so that they can be replicated and/or combined in different settings.

R1: Metadata and data are richly described with a plurality of accurate and relevant attributes.

[6] https://hapifhir.io/.
[7] https://www.keycloak.org/.
[8] https://forum.hhub.hosmartai.eu/t/hosmartai-fhir-server-documentation/20.
[9] https://hapifhir.hhub.hosmartai.eu.
[10] https://forum.hhub.hosmartai.eu/t/hosmartai-fhir-server-documentation/20.
[11] http://build.fhir.org/ig/HL7/fhir-for-fair/FHIRandFAIR.html.

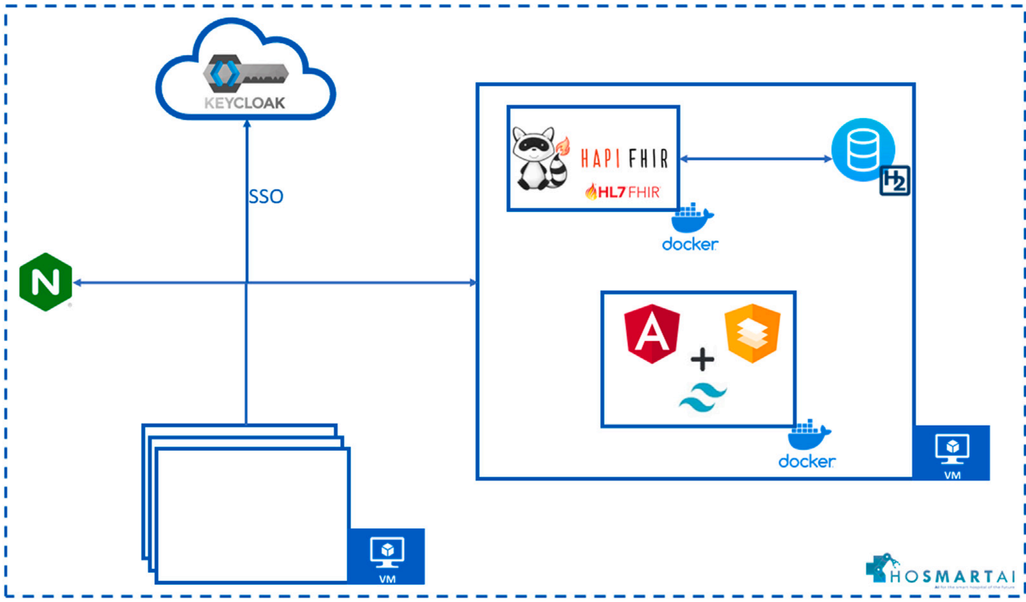

Fig. 2. HosmartAI FHIR server architecture.

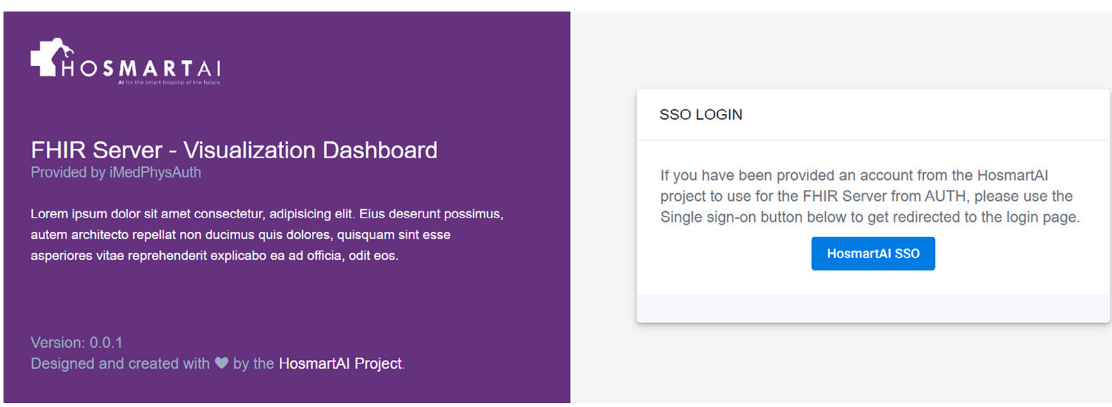

Fig. 3. HosmartAI FHIR server visualization tool — login page.

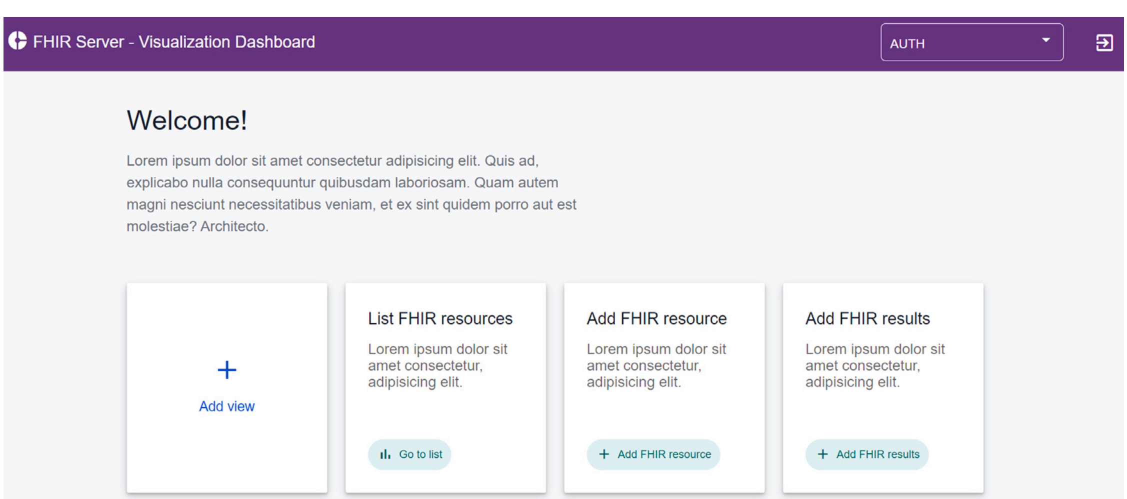

Fig. 4. HosmartAI FHIR server visualization tool — main dashboard.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

R1.1: Metadata and data are released with a clear and accessible data usage license.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

R1.2: Metadata and data are associated with detailed provenance.

- HosmartAI deployment: To cover this principle, collaboration with pilots is needed as it is related to how the server is used.

R1.3: Metadata and data meet domain-relevant community standards.

- HosmartAI deployment: Covered by default through the mapping of all variables to existing FHIR resources.

4.3. FHIR resource validation tool

To ensure that the resources used within the HosmartAI platform follow the FHIR standard, a web service that can validate whether a JSON resource is compatible with one of the pre-defined FHIR resources has been developed.[12] This service has to be accessed through Postman.[13] There, the user can POST a resource in JSON format and the service returns whether this is compatible with FHIR or not. This service uses a Node.JS library for serializing/deserializing FHIR resources between JS and XML and validating FHIR resources.[14] This library is one of the HL7 recommended libraries.[15] Although the HosmartAI FHIR server has an inbuilt resource validation, we argue that this service is still useful since users may want to validate resources without creating them in the central FHIR server. An example use of this service can be seen in Fig. 5.

5. Mapping clinical variables and KPIs

In this section, we provide two examples of how the FHIR server can be used within the HosmartAI platform. In this way we showcase and verify its efficiency and usefulness.

5.1. Mapping clinical variables

As it was mentioned earlier, one of the actions that was taken in order to achieve the semantic interoperability of the applications that are available through the HosmartAI platform, was to enforce the applications that utilize data to map each type of data into respective FHIR resources. In this way all different types of data that at first would be non-interoperable would translate to the open standard of HL7 FHIR.

One of the AI-based applications is related to the prediction of the presence of obstructive coronary artery disease (CAD). This application uses ML-based predictive models to accurately estimate the pretest likelihood of obstructive CAD higher than 50% on coronary computed tomography angiography (CCTA) in patients with suspected CAD. To accomplish this, it employs patients' measurable outcomes and extracted variables from the screening process, coupled with demographic information, medical history, social context, and additional medical particulars. To make this prediction, a plethora of numerical variables are used. Their complete list as well as the ML-model's preliminary results can be found in Kyparissidis Kokkinidis et al. (2022). All variables that are being used for the CCTA application, have been mapped into FHIR resources. For example, patient age is mapped to the DomainResource[16] resource, the Family history of premature CAD is mapped to the CodeableConcept[17] resource and the patient gender is mapped to the CodeSystem[18] resource. The whole procedure from data collection to predicting stenosis greater than 50% is depicted in Fig. 6. Specifically, the initial step consists of the identification of the variables that were needed to predict stenosis. Once these variables were selected, they were mapped into FHIR resources for interoperability purposes. Then the collection of a large number of patient data took place. To this end resources that correspond to the whole list of variables used for a single patient are available for reference.[19] Once the data collection was finalized the ML models were trained and tested for their ability to efficiently predict stenosis.

Table 1
Summary of FAIR principles and analysis of HosmartAI's FHIR server coverage.

Category	Principle	Is it covered?
Findability	F1: (Meta)data are assigned a globally unique and persistent identifier	Yes
	F2: Data are described with rich metadata	It depends on how pilots will use the FHIR server
	F3: Metadata clearly and explicitly include the identifier of the data they describe	Yes
	F4: (Meta)data are registered or indexed in a searchable resource	Yes
Accessibility	A1: Metadata and data are retrievable by each of their identifiers using a standardized communication protocol	Yes
	A1.1: The protocol is open, free and universally implementable	Yes
	A1.2: The protocol allows for an authentication and authorization, where necessary	Yes
	A2: Metadata should be accessible even when the data is no longer available	Yes
Interoperability	I1: Metadata and data use a formal, accessible, shared, and broadly applicable language for knowledge representation	Yes
	I2: Metadata and data use vocabularies that follow the FAIR principles	Yes
	I3: Metadata and data include qualified references to other metadata and data	It depends on how pilots will use the FHIR server
Reusability	R1: Metadata and data are richly described with a plurality of accurate and relevant attributes	It depends on how pilots will use the FHIR server
	R1.1: Metadata and data are released with a clear and accessible data usage license	It depends on how pilots will use the FHIR server
	R1.2: Metadata and data are associated with detailed provenance	It depends on how pilots will use the FHIR server
	R1.3: Metadata and data meet domain-relevant community standards	Yes

12 https://hosmartai-registry.med.auth.gr/fhir-validator/validate.
13 https://www.postman.com/downloads/.
14 https://www.npmjs.com/package/fhir.
15 https://confluence.hl7.org/pages/viewpage.action?pageId=35718838#OpenSourceImplementations-Javascript.
16 https://build.fhir.org/domainresource.html.
17 https://build.fhir.org/datatypes.html#CodeableConcept.
18 https://build.fhir.org/codesystem.html.
19 https://t.ly/QMIfb.

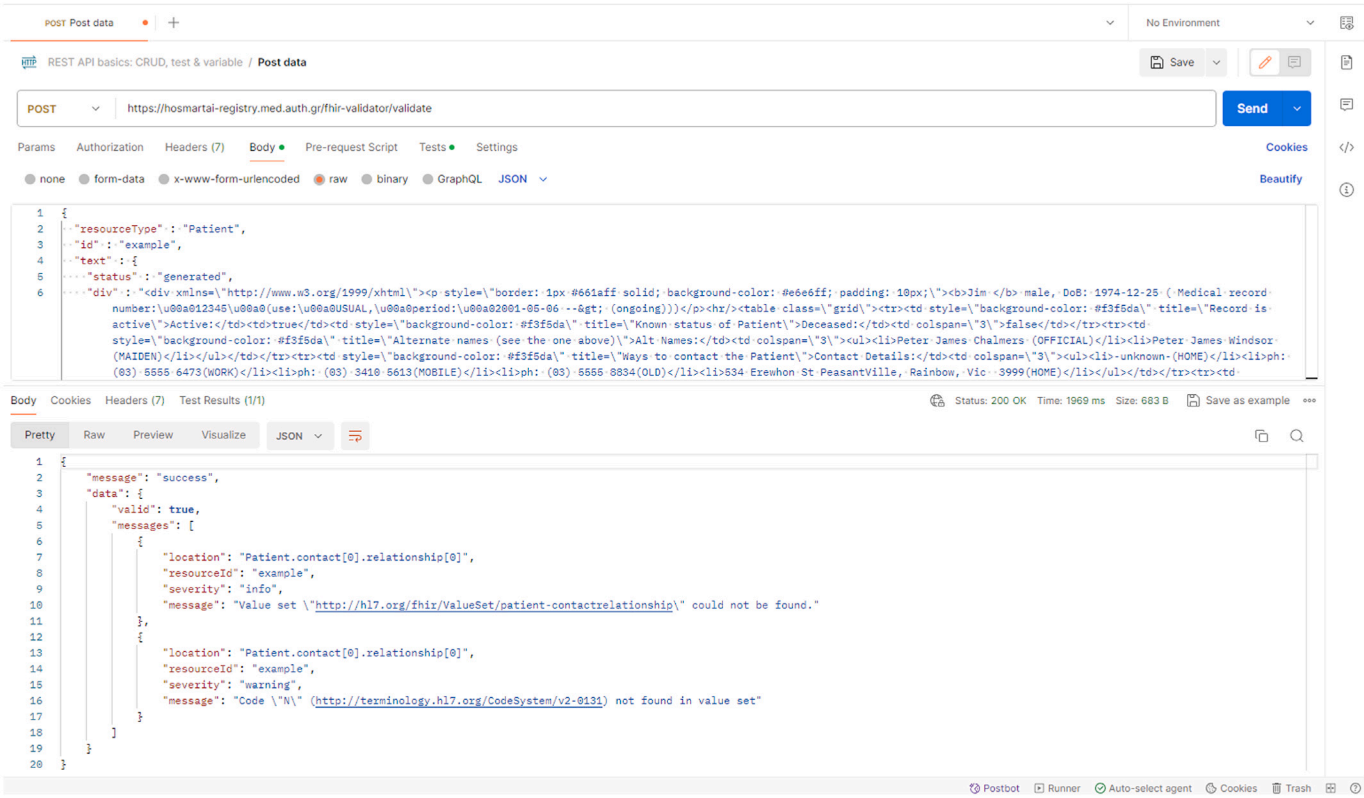

Fig. 5. Example use of FHIR resource validation tool.

Fig. 6. Stenosis prediction application — Data collection and ML development.

Table 2
Summary of the mapping of KPIs' categories to FHIR.

KPI category	Mapping
Clinical	http://hl7.org/fhir/diagnostics-module.html#uses and http://hl7.org/fhir/medications-module.html#uses
Patient/User experiences measures (PREMs, UREMs)	http://hl7.org/fhir/clinicalreasoning-module.html#index-profiles
Patient reported outcome measures (PROMs)	http://hl7.org/fhir/clinicalreasoning-module.html#index-profiles
Productivity	http://hl7.org/fhir/clinicalreasoning-module.html#index-profiles
Economic	http://hl7.org/fhir/financial-module.html#13.0.2.3

Up to this point, the HL7 FHIR standard is utilized for the mapping of the variables, but the HosmartAI FHIR server is not. The FHIR server comes into play in the next phase, where the application is used to predict stenosis in a patient by patient manner. This procedure is depicted in Fig. 7. Specifically, a lab report containing the values of the necessary variables for a single patient is collected and these values are used to create the equivalent FHIR resources. Once this step is finalized, they are provided to the ML algorithms which calculates the prediction related to whether this patient is classified as having stenosis or not. The decision is explained to enhance transparency. Values related to KPIs such as number of correct decisions of the algorithm are accumulated and periodically send to the FHIR server.

5.2. Mapping KPIs

The KPIs for all applications have been separated in five main categories namely (1) Clinical, (2) Patient/User Reported Experiences Measures (PREMs/UREMs), (3) Patient Reported Outcome Measures (PROMs), (4) Productivity and (5) Economic data. These KPI categories have been mapped to a set of FHIR resources (summarized in Table 2) that have been found to best conceptually describe each category.

Specifically, the Clinical KPIs are mapped to the diagnostics[20] and medication[21] modules. The Diagnostics Module focuses on the arrangement and communication of clinical diagnostic procedures, encompassing activities like laboratory tests, imaging, and genomics analysis. The Medications module pertains to resources and functions within three primary domains: (1) Managing the prescription, distribution, application of medications, and documenting statements regarding medication usage. (2) Documenting the administration or non-administration of immunizations, assessing administered immunizations, and providing

[20] http://hl7.org/fhir/diagnostics-module.html#uses.
[21] http://hl7.org/fhir/medications-module.html#uses.

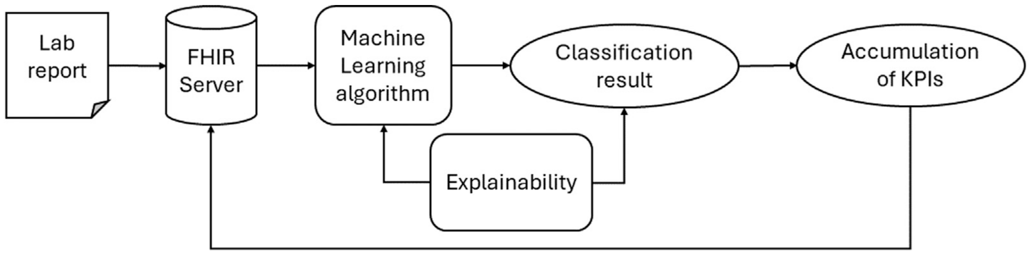

Fig. 7. Stenosis prediction procedure.

recommendations specific to an individual patient's situation. (3) Generating or querying information about medications as a component of drug-related information or pharmaceutical knowledge.

The PREM and the PROM KPIs are mapped to the clinical reasoning module.[22] The Clinical Reasoning module furnishes tools and functions to facilitate the depiction, dissemination, and assessment of clinical knowledge elements, encompassing items like clinical decision support rules, quality metrics, public health benchmarks, order sets, and clinical protocols. This module also elucidates the utilization of expression languages across the specification to impart dynamic functionalities. Clinical Reasoning entails the aptitude to encapsulate and encode a comprehensive range of clinical knowledge, making it adaptable for integration into clinical systems. The Productivity KPIs are mapped to the Workflow module.[23] The Workflow module focuses on the coordination of activities within and across systems. Finally, the Economic KPIs are mapped to the financial module.[24] The Financial module encompasses FHIR resources and functionalities aimed at facilitating cost calculation, financial transactions, and billing processes within a healthcare provider's realm. It also addresses aspects like eligibility, enrollment, authorizations, claims, and payments that transpire between healthcare providers and insurers. Moreover, the module handles reporting and notifications exchanged between insurers, subscribers, and patients.

6. Implications to practitioners

The adoption of common semantic data models, such as the HL7 FHIR standard, presents significant implications for healthcare practitioners (i.e., either clinicians, or engineers and computer scientists working in the healthcare domain). Firstly, the standardization afforded by HL7 FHIR can lead to more streamlined and efficient healthcare processes. Clinicians would be able to access and share patient data more readily, leading to faster, more accurate diagnoses and treatment plans. This interoperability reduces information silos, ensuring that patient information is complete, up-to-date, and readily available across different healthcare settings. Moreover, the integration of AI and machine learning into healthcare applications facilitated by these standardized data models, could significantly augment clinical decision-making. Practitioners could leverage predictive analytics for conditions such as coronary artery stenosis, enhancing early detection and enabling more personalized and effective treatment strategies. Additionally, the use of common data standards can improve the management of KPIs, allowing healthcare providers to monitor and optimize their services more effectively. The artifacts (i.e., FHIR resources) that have become available together with this work can assist practitioners in familiarizing themselves with how clinical variables can be transformed into machine readable formats with common semantics, that can then be effectively used by AI-based applications.

However, while these advancements promise to improve healthcare delivery and outcomes, they also require practitioners to adapt to new technologies and workflows. There will be a need for ongoing education and training to ensure that healthcare professionals can effectively utilize these digital tools. Furthermore, the shift towards more data-driven approaches necessitates stringent data privacy and security measures to protect sensitive patient information. Overall, the implications for practitioners involve not only the potential for improved patient care but also the need for adaptation to a rapidly evolving digital healthcare landscape.

7. Conclusions and future work

In this study, we highlighted the adoption of HL7 FHIR to support the interoperability within an AI-based medical applications platform designed for smart hospitals. Interoperability stands as a crucial element in such domains, ensuring seamless communication and data exchange among diverse healthcare systems. By integrating HL7 FHIR, we significantly enhanced the platform's ability to communicate effectively across different systems and devices, thereby facilitating a more cohesive and efficient healthcare environment. We addressed the critical need for enhanced security within the platform and described the adaptations implemented to strengthen data protection, safeguarding patient information. Additionally, we evaluated how well the platform aligns with the FAIR principles, which are essential for the ethical and effective management of digital assets in the healthcare sector.

The development of a FHIR resource validation tool represented an advancement, enabling the consistent and accurate implementation of FHIR standards across the platform. Furthermore, we showcased the application of HL7 FHIR within a specific medical application and in the management of the platform's KPIs, underscoring the versatility and utility of FHIR in enhancing operational efficiency and clinical outcomes.

The adoption of HL7 FHIR is not without its challenges. Potential limitations include the complexity of FHIR standards which can pose integration challenges, particularly in legacy systems that were not designed with FHIR compatibility in mind. Additionally, while FHIR aims to support a wide range of healthcare data types and use cases, there may be scenarios where its current specifications do not fully meet specific needs, necessitating further customization or extension.

In terms of future work, we aim to examine this interoperability component in large-scale scenarios to identify and address any scalability issues. Moreover, we plan to develop and integrate an online FHIR resource editor into the platform. This addition will empower users to create, modify, and manage FHIR resources more efficiently, thereby enhancing the platform's adaptability and user-friendliness. Also, DOME recommendations forms (Walsh et al., 2021) for the applications that utilize supervised machine learning will be considered.

CRediT authorship contribution statement

Emmanouil S. Rigas: Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Paris Lagakis:** Software, Methodology. **Makis Karadimas:** Software, Methodology. **Evangelos Logaras:** Formal analysis. **Dimitra Latsou:** Methodology. **Magda Hatzikou:** Methodology. **Athanasios Poulakidas:** Supervision,

22 http://hl7.org/fhir/clinicalreasoning-module.html#index-profiles.
23 http://hl7.org/fhir/clinicalreasoning-module.html#index-profiles.
24 http://hl7.org/fhir/financial-module.html#13.0.2.3.

Project administration, Funding acquisition. **Antonis Billis:** Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Panagiotis D. Bamidis:** Supervision, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgments

This work has been supported by the HosmartAI project – "Hospital Smart development based on AI", which has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101016834

References

Baskar, S., Shakeel, P.M., Kumar, R., Burhanuddin, M., Sampath, R., 2020. A dynamic and interoperable communication framework for controlling the operations of wearable sensors in smart healthcare applications. Comput. Commun. 149, 17–26.

Cardoso, L., Marins, F., Quintas, C., Portela, F., Santos, M., Abelha, A., Machado, J., 2018. Interoperability in healthcare. In: Health Care Delivery and Clinical Science: Concepts, Methodologies, Tools, and Applications. IGI Global, pp. 689–714.

Collaboration, O.S., 2015. Estimating the reproducibility of psychological science. Science 349 (6251), aac4716.

Duda, S.N., Kennedy, N., Conway, D., Cheng, A.C., Nguyen, V., Zayas-Cabán, T., Harris, P.A., 2022. HL7 FHIR-based tools and initiatives to support clinical research: a scoping review. J. Am. Med. Inform. Assoc. 29 (9), 1642–1653. http://dx.doi.org/10.1093/jamia/ocac105.

Hodapp, D., Hanelt, A., 2022. Interoperability in the era of digital innovation: An information systems research agenda. J. Inf. Technol. 37 (4), 407–427.

Iroju, O., Soriyan, A., Gambo, I., Olaleke, J., et al., 2013. Interoperability in healthcare: benefits, challenges and resolutions. Int. J. Innov. Appl. Stud. 3 (1), 262–270.

Kiourtis, A., Nifakos, S., Mavrogiorgou, A., Kyriazis, D., 2019. Aggregating the syntactic and semantic similarity of healthcare data towards their transformation to HL7 FHIR through ontology matching. Int. J. Med. Inform. 132, 104002.

Kush, R., Warzel, D., Kush, M., Sherman, A., Navarro, E., Fitzmartin, R., Petavy, F., Galvez, J., Becnel, L., Zhou, F., Harmon, N., Jauregui, B., Jackson, T., Hudson, L., 2020. FAIR data sharing: The roles of common data elements and harmonization. J. Biomed. Inform. 107, 103421.

Kyparissidis Kokkinidis, I., Rigas, E.S., Logaras, E., Samaras, A., Rampidis, G.P., Giannakoulas, G., Kouskouras, K., Billis, A., Bamidis, P.D., 2022. Towards an explainable AI-based tool to predict the presence of obstructive coronary artery disease. In: Proceedings of the 26th Pan-Hellenic Conference on Informatics. pp. 335–340.

Lehne, M., Sass, J., Essenwanger, A., Schepers, J., Thun, S., 2019. Why digital medicine depends on interoperability. NPJ Digit. Med. 2 (1), 79.

Mirowski, P., 2018. The future (s) of open science. Soc. Stud. Sci. 48 (2), 171–203.

Morley, J., Machado, C.C., Burr, C., Cowls, J., Joshi, I., Taddeo, M., Floridi, L., 2020. The ethics of AI in health care: a mapping review. Soc. Sci. Med. 260, 113172.

Ngiam, K.Y., Khor, W., 2019. Big data and machine learning algorithms for health-care delivery. Lancet Oncol. 20 (5), e262–e273.

Nosek, B.A., Alter, G., Banks, G.C., Borsboom, D., Bowman, S.D., Breckler, S.J., Buck, S., Chambers, C.D., Chin, G., Christensen, G., et al., 2015. Promoting an open research culture. Science 348 (6242), 1422–1425.

Olaronke, I., Oluwaseun, O., 2016. Big data in healthcare: Prospects, challenges and resolutions. In: 2016 Future Technologies Conference. FTC, IEEE, pp. 1152–1157.

Panch, T., Mattie, H., Celi, L.A., 2019. The "inconvenient truth" about AI in healthcare. NPJ Digit. Med. 2 (1), 77.

Qayyum, A., Qadir, J., Bilal, M., Al-Fuqaha, A., 2020. Secure and robust machine learning for healthcare: A survey. IEEE Rev. Biomed. Eng. 14, 156–180.

Reda, R., Piccinini, F., Carbonaro, A., 2019. Semantic modelling of smart healthcare data. In: Arai, K., Kapoor, S., Bhatia, R. (Eds.), Intelligent Systems and Applications. Springer International Publishing, Cham, pp. 399–411.

Rubí, J.N.S., Gondim, P.R.d.L., 2020. Interoperable internet of medical things platform for e-health applications. Int. J. Distrib. Sens. Netw. 16 (1), 1550147719889591.

Saripalle, R., Runyan, C., Russell, M., 2019. Using HL7 FHIR to achieve interoperability in patient health record. J. Biomed. Inform. 94, 103188. http://dx.doi.org/10.1016/j.jbi.2019.103188.

Secinaro, S., Calandra, D., Secinaro, A., Muthurangu, V., Biancone, P., 2021. The role of artificial intelligence in healthcare: a structured literature review. BMC Med. Inform. Decis. Mak. 21, 1–23.

Vicente-Saez, R., Martinez-Fuentes, C., 2018. Open science now: A systematic literature review for an integrated definition. J. Bus. Res. 88, 428–436.

Vorisek, C.N., Lehne, M., Klopfenstein, S.A.I., Mayer, P.J., Bartschke, A., Haese, T., Thun, S., 2022. Fast healthcare interoperability resources (FHIR) for interoperability in health research: Systematic review. JMIR Med. Inform. 10 (7), e35724. http://dx.doi.org/10.2196/35724.

Walsh, I., Fishman, D., Garcia-Gasulla, D., Titma, T., Pollastri, G., Harrow, J., Psomopoulos, F.E., Tosatto, S.C., 2021. DOME: recommendations for supervised machine learning validation in biology. Nat. Methods 18 (10), 1122–1127.

Dr. Emmanouil S. Rigas holds a B.Sc. degree from the Department of Informatics of the Aristotle University of Thessaloniki (AUTh), Greece (2011), an M.Sc. with distinction in Web Technology from the University of Southampton, UK (2012) and a Ph.D. from the Department of Informatics at AUTh (2018). During his Ph.D. studies he specialized in the area of Artificial Intelligence (AI) and specifically in optimization techniques, heuristic and meta-heuristic algorithms, multi-agent systems and the semantic web and he applied his research in the area of Electric Vehicles. He subsequently collaborated with the University of Cyprus (2019 - 2021), initially as a Research Associate at the KIOS Research and Innovation Center of Excellence where he studied the use of AI in drones, and later as a Special Teaching Scientist at the Department of Computer Science where he taught undergraduate and postgraduate courses. Currently, he is a PostDoc researcher at the Medical Physics and Digital Innovation Lab, AUTh working as a scientific project manager and interoperability expert. He has (co-) authored several papers published in prestigious journals and conferences and has participated in several national and European research projects.

Mr. Paris Lagakis is a Software Engineer with an EQF level 7 degree in Electrical and Computer Engineering from the Polytechnic School of the Aristotle University of Thessaloniki. His specialization was in Computers & Microelectronics, and his thesis focused on NLP and sentiment analysis, applied to the Greek language. He is currently working mainly as a Software Engineer, with over 8 years of professional experience. His research interests revolve around the fields of IT in education as well as medical informatics and include natural language processing, conversational agents, automated essay scoring, and automated essay feedback. He is currently working towards his PhD degree focusing on utilizing LLMs in designing conversational agent software, intended for usage in MOOCs and other e-learning environments.

Mr. Makis Karadimas is a computer scientist. He worked formerly at Netcompany-Intrasoft, mainly in software and data engineering tasks in research and innovation projects.

Mr. Evangelos Logaras is a computer scientist and does his research on medical informatics field and more specific at the cancer data management area. Through new techniques, he tries to develop safe patient-centered networks for the benefit of both the patient himself and the treating physician.

Dr. Dimitra Latsou is a graduate of Political Science and Public Administration from the University of Athens, Greece. She completed the postgraduate program in Management and Economic Evaluation of Professional and Environmental Health, at the Medical School of the University of Athens. She holds a PhD from the University of Peloponnese in the scientific field: Economic Analysis of Social Policies. Dimitra has more than 12 years of experience in the field of social policy, patient reported outcomes, patient reported experience studies and economic analysis in health issues.

Dr. Magda Chatzikou holds a PhD by University of Thessaly in health economics with an 18 year experience in the pharmaceutical industry. She is currently adjunct faculty at Open University of Greece at post graduate course of Health Care Management. She has served many roles in market access departments of the multinational industry emphasizing on pricing, reimbursement and health economics. Magda can be considered as the "linking chain" between clinical research and commercial value. She has worked in various therapeutic areas such as cancer, haematological disorders, diabetes, hypertension, COPD, autoimmune diseases and biosimilars. After 18 years in the industry, she decided to continue with her profession from a different perspective always linked with the pharmaceutical industry.

Dr. Athanasios Poulakidas is the coordinator of the HosmartAI large-scale-pilot project and a Senior R&I Manager at Netcompany-Intrasoft. Since 2005 he has been working continuously in the enterprise side. Till 2014 he was with Hellenic Aerospace Industry S.A. where he headed the Satellite and Space Applications Dept., served as the local project and technical manager for several EU research projects, as well as the manager of a number of large development projects. Between 2014 and 2016 he was with

Akazoo S.A. where he led the infrastructure and research teams. Since 2017 he is with INTRASOFT International. In academic positions till 2005, he has been a Lecturer at the Univ. of California, a Visiting Assistant Professor at the Univ. of Ioannina and the Univ. of Patras and a Researcher at the Computer Technology Institute, Patras. He graduated from the Dept. of Computer Engineering and Informatics, Univ. of Patras and received his MSc and PhD from the Dept. of Computer Science, Univ. of California, Santa Barbara. Dr Poulakidas has participated from various responsible positions in over 30 large and small sized collaborative research projects in USA, EU and Greece. He has also served in international bodies, as a member of the governing board or industry representative.

Dr. Antonis Billis is an Electrical and Computer Engineer specializing in the research of digital biomarkers for remote patient monitoring. He is a postdoctoral researcher at the Laboratory of Medical Physics and Digital Innovation at the Medical School of Aristotle University of Thessaloniki (AUTH). His research interests focus on eHealth/mHealth, digital biomarkers, clinical decision support, smart patient monitoring systems, and assistive technologies for vulnerable populations. He has published numerous scientific articles and presentations at international conferences and has over 10 years of research experience, including participation in numerous national and European projects, including the recent coordination of the LifeChamps project, which focuses on machine learning and Big Data to support the quality of life of elderly cancer survivors.

Prof. Panagiotis Bamidis is a distinguished academic at the Medical School of Aristotle University of Thessaloniki (AUTH), where he serves as a professor of Medical Physics, Informatics, and Medical Education, and as the Director of the Laboratory of Medical Physics and Digital Innovation. He leads numerous international and national conferences and committees, is the president of the Hellenic Society of Biomedical Technology and HL7 Hellas, and holds leading roles in many scientific and social organizations. In 2013, he founded the Thessaloniki Action for Health & Wellbeing Living Lab (ThessAHALL), which became a member of the European Network of Living Labs (ENoLL) in 2018. He has received recognition for his research and academic performance, including awards from AUTH and other academic authorities. Since 2020, he has been the head of the Special Unit of Biomedical Research and Education (EMBIEE) at AUTH and a visiting professor at the University of Leeds in the United Kingdom. Additionally, he is the director of OpenLearn4Health.gr, a MOOC that examines contemporary medical topics.