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Interoperability in healthcare: a critical review of ontology approaches and tools for building prescription frameworks

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ABSTRACT

Efficient healthcare interoperability is pivotal for delivering high-quality patient care. This research article presents a critical review of ontology-based approaches and tools in the development of ontology-based electronic prescriptions (e-prescription), with a focus on enhancing healthcare interoperability. The investigation encompasses two major domains: ontology overview and healthcare interoperability using semantic e-prescription. In the ontology overview, we scrutinize various aspects of ontology development, including the methodologies, languages, tools, and evaluation metrics adopted from literature. Notable comparisons between ontologies and databases are explored. Additionally, we delve into the challenges associated with ontology development and provide a comprehensive summary of methodologies, languages, tools, and evaluation approaches. Healthcare interoperability using semantic e-prescription undertakes a detailed review of e-prescription systems, emphasizing their critical role in healthcare interoperability. A thorough examination of frameworks facilitating semantic e-prescription is presented, offering a nuanced perspective on their contributions and limitations. The section concludes with a concise summary of the key findings from the e-prescription framework review. The article further addresses challenges in healthcare interoperability, including data standardization and system integration issues. To direct continuing research efforts that integrate cutting-edge technologies and interdisciplinary collaborations, future directions and emerging trends are outlined.

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1. INTRODUCTION

The contemporary healthcare landscape is marked by an ever-growing volume of diverse health data generated across numerous entities such as hospitals, clinics, laboratories, and pharmacies. The seamless exchange and utilization of this information are paramount for delivering effective patient care, necessitating robust interoperability within healthcare systems [1], [2]. Interoperability, in this context, refers to the ability of disparate systems to exchange and interpret health data cohesively, ensuring a unified and meaningful approach to patient information [2]. Within healthcare interoperability, ontological approaches and tools have emerged as instrumental components, providing a structured and standardized framework for representing healthcare concepts and relationships [3], [4]. The utilization of ontologies facilitates a shared understanding of healthcare entities and their interconnections, transcending the constraints posed by varied data structures and formats [4]. This research article embarks on a critical review of the intersection between healthcare interoperability and ontology-based methodologies, with a specific focus on the development of prescription frameworks. As healthcare systems strive for cohesion in the exchange and use of prescription-related information, the incorporation of ontological approaches becomes integral to overcoming inherent challenges and fostering harmonious collaboration among diverse healthcare entities. Furthermore, the article delves into the methodologies, languages, tools, and evaluation methodologies employed in ontology development, paving the way for a comprehensive understanding of the landscape. The subsequent sections of this research article will scrutinize e-prescription systems and frameworks, providing a thorough examination of their gaps in healthcare interoperability. The challenges faced in healthcare interoperability, coupled with a visionary perspective on future directions, aim to contribute to the ongoing discourse and guide the trajectory of research in this vital domain. Below are the contributions of this review article:

a) To the best of our knowledge, this study has made its attempt to compare and construct existing ontology development approaches for healthcare interoperability in terms of ontology development methodologies, languages, tools, and evaluation approaches and deduced trends and insights.
b) The study investigated various healthcare interoperability e-prescription frameworks and performed a critical analysis of the existing gaps.
c) The study discussed the challenges and limitations of the current approaches and highlighted future research directions.

This article is organized as follows. Section 2 presents the research method adopted comprising of the review methodology and comparison between ontologies and databases, an in-depth review of various ontology development methodologies, languages, tools, and evaluation approaches. Section 3 presents the results and discussions of the review. Section 4 presents the challenges and future directions, and section 5 concludes the research study.

2. RESEARCH METHOD

The major objective is to critically review ontology-based approaches and tools in developing semantic e-prescriptions, emphasizing their role in enhancing healthcare interoperability and guiding future research with emerging trends. The review paper will focus on recent research published in peer-reviewed journals, conference proceedings, and other reputable sources. The time frame for selecting literature will be from 2013 to 2023. The review will follow a systematic approach to literature review [5], involving the following key steps: (i) literature searching using online academic databases including Web of Science, PubMed, ScienceDirect, SpringerLink, IEEE Xplore, ACM Digital Library, and Google Scholar to identify relevant articles using keywords such as “semantic healthcare interoperability”, “semantic prescriptions”, “ontology methodologies”, “ontology evaluation” and “semantic web and interoperability”. (2) Inclusion criteria of articles that specifically addresses ontology-based methods and tools and those for developing semantic e-prescriptions, emphasizing their pivotal role in advancing healthcare interoperability between 2013 and 2023. (3) Exclusion criteria of articles that are not focused on leveraging ontology-based methods and tools to develop semantic e-prescriptions. (4) Data extraction of key information from selected articles, including title, authors and years, approaches, research objectives, evaluation metrics, limitations, tools, and languages used. (5) Synthesis: organizing the extracted information into a summarized table and then extracting trends and patterns.

2.1. Ontologies

Ontologies describe a set of concepts and their relationship in a specific domain [4]. They are necessary for knowledge representation and knowledge exchange, in digital libraries, semantics web, and personal information management. More simply, an ontology is a way of showing the properties of a subject area and how they are related, by defining a set of concepts and categories that represent the subject [6]. This structured representation not only enhances information clarity but also facilitates the development of intelligent systems capable of understanding, reasoning, and making informed decisions based on the intricacies encapsulated within the ontology [7]. As technology evolves, ontologies become integral in shaping the future of information systems, influencing innovations in fields such as data analytics, machine learning, and knowledge-driven decision-making [8].

2.2. Comparison between ontologies and databases

Table 1 provides a comprehensive comparison between ontology and database [9], [10]. An ontology, focusing on preserving meaning for interoperability, uses an open world assumption, emphasizes is-a hierarchy, eg., “John is-a teacher” and employs logic-based syntax like web ontology language (OWL)

[9], [10]. In contrast, databases, with a local semantics focus, adopt a closed-world assumption, have less emphasis on the is-a hierarchy, and use entity-relationship diagrams with normal forms for optimization.

Table 1. A comparison between ontology and database [9], [10]

Aspect	Ontologies	Databases
Focus	-Preserves meaning for interoperability, emphasizing global semantics.	-Database schema stores and queries large data sets, emphasizing local semantics.
Design approach	-Developed by reusing existing ontologies, fostering flexibility.	-Created from scratch for specific purposes, limiting general reusability.
Manner of knowledge representation	-Utilizes open-world assumption (OWA) for dynamic adaptation.	-Relies on closed-world assumption (CWA) assuming complete model information.
Syntax	-Logic-based syntax with mandatory Semantic features.	-Entity-relationship diagrams define syntax, with less emphasis on semantics.
ISA hierarchy	-Emphasizes is-a hierarchical structure as a foundational backbone.	-Little emphasis on is-a hierarchy, focusing more on structured data.
Optimization	-Methodologies involve patterns for intricate knowledge structuring.	-Utilizes normal forms for optimizing structured data storage.
Flexibility and reusability	-Encourages flexibility through ontology reuse, facilitating interdisciplinary applications.	-Limited flexibility and reusability, designed for specific applications.
Representation of relationships	-Explicitly represents relationships between concepts for clarity.	-Relationships are implicit, with a rigid structure of the database schema.
Inference capability	-Supports automated inference and deduction, enhancing adaptive decision-making.	-Limited inference capabilities, primarily reliant on predefined queries.
Scope of application	-Widely applicable across diverse domains, fostering interdisciplinary collaboration.	-Primarily designed for specific applications, lacking adaptability across diverse fields.
Evolution and adaptability	-Adapts well to changes and evolving knowledge structures, ensuring longevity.	-Changes may require significant modifications to the database schema,
Complexity	-Suited for managing complex relationships and dynamic knowledge structures.	-Designed for structured data, potentially struggling with intricate relationships.

2.3. Ontology development methodologies

Table 2 shows the ontology development methodologies comparison. Table 2 compares the ten reviewed ontology development methodologies in terms of several features [11], [12]. A feature, in the context of the ontology development methodologies comparison, is a distinctive quality or characteristic that forms an integral aspect of an acceptable methodology [11], [12]. Each feature represents a specific dimension of the ontology development process and is employed as a criterion for comparative analysis. The presence or absence of a particular feature acts as a diagnostic indicator, highlighting the methodology's attributes and potential gaps in its approach. Each feature is explained as follows; sufficient details gauge the methodology's depth by evaluating the comprehensiveness of the information provided. Life-cycle recommendation involves proposing a suitable life-cycle model tailored for ontology development. pre-development process outlines activities before initiation, while the required process and designed process delve into mandatory steps and the conceptual modeling phase, respectively. Implementation assesses guidance for constructing the ontology, and post development covers ongoing processes post-implementation. Documentation scrutinizes guidelines for creating clear and comprehensive documentation. Configuration management involves handling changes and updates. Knowledge acquisition explores recommended strategies for gathering domain knowledge. Evaluation details define criteria and methods for assessing ontology quality. Distributed working addresses collaboration in dispersed teams, and project management covers planning and resource allocation. Supporting tools identifies recommended tools for ontology development. Together, these features offer a holistic view for comparing methodologies based on their depth, recommendations, and practical guidance throughout the ontology development life cycle. In conclusion, the meticulous examination of these fourteen features offers valuable insights into the strengths and potential gaps within each ontology development methodology. This comparative analysis serves as a robust foundation for decision-making in selecting the most suitable approach for semantic prescription interoperability development. The ongoing pursuit of enhancing ontology development methodologies is crucial for ensuring the effectiveness and adaptability of semantic technologies in diverse applications and domains.

2.4. Ontology languages

Eleven ontology languages will be reviewed to suggest the most suitable one for semantic interoperability development based on their feature strength and weaknesses. Table 3 shows a comparison of ontology development languages pinpointing the strengths and limitations in the form of the presence or a lack of an ontology language feature.

Table 2. Ontology development methodologies comparison

Feature/gaps	Ushcold [13]	Gruninger [14]	Methontology [15]	Otkm [16]	Senus [17]	Kactus [18]	Diligent [19]	Hcome [20]	McGuinness [21]	Upon [22]	% of Methodologies with the gap
Sufficient details	x	x	✓	x	x	x	✓	✓	x	✓	60%
Life-cycle recommendation	x	x	✓	✓	x	x	✓	✓	x	✓	50%
Pre-development process	x	x	x	✓	x	x	✓	x	x	x	80%
Required process	x	✓	✓	✓	x	x	✓	x	x	✓	50%
Designed process	x	✓	✓	✓	x	✓	✓	x	x	✓	40%
Implementation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0%
post Development	x	x	✓	✓	x	x	✓	✓	x	x	60%
Documentation	x	x	✓	✓	x	x	✓	✓	x	x	60%
Configuration management	x	x	✓	x	x	x	x	x	x	x	90%
Knowledge acquisition	x	x	✓	x	x	x	x	✓	x	✓	70%
Evaluation	x	x	✓	✓	x	x	x	x	x	✓	70%
Distributed working	x	x	x	x	x	x	✓	✓	x	x	80%
Project management	x	x	✓	✓	x	x	x	x	x	x	80%
Supporting tools	x	x	✓	✓	✓	x	✓	✓	✓	✓	30%
% of gaps per methodology	93%	79%	14%	29%	86%	86%	29%	43%	86%	43%	

Table 3. Comparison of ontology development languages

Ontology features	LOOM [23]	OCML [24]	FLOGIC [25]	SHOE [26]	OML [27]	XOL [28]	RDF [29]	OIL [30]	DAML&OIL [31]	OWL [32]	OWL2 [33]	% of languages with the gap
Concept partitions	✓	x	x	x	✓	x	x	✓	✓	x	✓	55%
Documentation	✓	✓	x	✓	✓	✓	✓	✓	✓	✓	✓	9%
Instance attributes	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0%
Class attributes	✓	✓	✓	x	✓	✓	x	✓	✓	✓	✓	18%
Local-global scope	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0%
Global scope facts	✓	x	x	x	✓	✓	✓	✓	✓	✓	✓	27%
Default slot value	✓	✓	✓	x	x	✓	✓	✓	✓	✓	✓	18%
Type constraints	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0%
Cardinality constraints	✓	✓	x	x	x	x	x	✓	✓	✓	✓	45%
Slot documentation	✓	✓	x	✓	✓	✓	✓	✓	✓	✓	✓	9%
Subclass of	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	0%
Disjoint decomposition	✓	✓	x	x	x	x	x	✓	✓	x	✓	55%
N-array relations	✓	✓	x	✓	✓	x	x	x	x	x	✓	55%
Operational definition	✓	✓	✓	x	x	x	x	x	x	✓	✓	55%
1st order logic	✓	✓	✓	x	✓	x	x	x	x	✓	✓	45%
2nd order logic	x	x	x	x	x	x	x	x	x	✓	✓	82%
Named axioms	x	✓	x	x	x	x	x	x	x	x	✓	100%
Embedded axioms	✓	✓	x	x	✓	x	x	x	x	✓	✓	55%
Concept instances	✓	✓	✓	✓	✓	x	✓	✓	✓	✓	✓	0%
Facts	x	x	x	x	✓	x	x	x	x	✓	✓	73%

In Table 3, ontology language key features define the qualities critical for their evaluation [23]. Concept partitions reveal how concepts are organized, reflecting the ontology's structure and clarity. Documentation assesses the availability and clarity of supporting materials. Instance attributes and class attributes pertain to the properties of individual instances and classes, respectively. Local-global scope distinguishes concepts with local versus global significance, shaping the ontology's context. Global scope facts and default slot value address global information and default assignments. Type constraints and cardinality constraints set boundaries on concept types and associations. Slot documentation evaluates the clarity of property descriptions. Subclass establishes hierarchy, and disjoint decomposition manages overlapping instances. N-array relations handle complex relationships, operational definition ensures precision in concept definition. 1st-order logic and 2nd-order logic gauge expressive power. Named axioms and embedded axioms contribute to clarity and traceability. Concept instances involve instantiation, facts represent verified knowledge, and rules enable automated reasoning.

2.5. Ontology development tools

Table 4 shows a comparison of eighteen reviewed and commonly used ontology development tools with their features where a feature refers to a distinctive attribute that serves as a crucial criterion for evaluating the suitability of a given tool [34]-[36]. Several ontology development tools were reviewed to choose the most suitable one for semantic interoperability development. The features are explained as follows [34]-[36]; the free attribute gauges whether the tool is available at no cost, addressing affordability. The open-source characteristic indicates the tool's transparency for community-driven enhancements. Java-based examines whether the tool is constructed using the Java programming language, important for compatibility and integration. Extensibility assesses the tool’s capacity for customization to meet specific project requirements. The collaboration feature evaluates support for concurrent development. Community support measures the presence and engagement of a user community. Web ontology language 2 (OWL2) support checks if the tool aligns with the latest OWL standards. The reasoner feature examines logical inference capabilities.

Table 4. A comparison of ontology development tools

Ontology development tools	Free	Open source	Java-based	Extensibility	Collaboration	Community support	OWL2 support	Reasoner	% of tools with the gap
Protégé [7], [37]	✓	✓	✓	✓	X	✓	✓	✓	13%
OntoEdit [38]	✓	X	✓	✓	X	X	X	X	63%
DOE [39]	✓	X	✓	X	X	X	X	X	75%
IsaViz [40]	✓	✓	✓	✓	X	X	X	✓	38%
Ontolingua [41]	✓	X	X	X	✓	X	X	✓	63%
Altova semantic [42]	X	X	X	X	X	X	X	✓	88%
OilED [43]	✓	✓	✓	X	X	X	X	✓	50%
WebODE [44]	✓	X	✓	✓	✓	X	X	✓	38%
Powl [45]	✓	✓	X	✓	✓	X	X	✓	38%
SWOOP [46]	✓	✓	✓	✓	✓	X	X	✓	25%
TopBraid [47]	X	X	✓	✓	✓	X	X	✓	50%
Neon toolkit [48]	✓	✓	✓	✓	✓	X	X	✓	25%
Mortar [49]	✓	✓	X	✓	X	X	X	✓	50%
OBO-edit [50]	✓	✓	✓	✓	X	X	X	✓	38%
Hozo [51]	✓	✓	✓	X	✓	X	X	✓	38%
OntoBuilder [52]	✓	✓	✓	✓	X	X	X	✓	38%
WSMO studio [53]	✓	✓	✓	✓	X	X	X	✓	38%
TODE [54]	✓	X	X	X	X	X	X	✓	75%
% of tools per gap	11%	37%	26%	32%	58	95%	89%	11%	

2.6. Ontology evaluation tools

Table 5 shows a comparison of commonly used tools in research for evaluating ontologies and their usability characteristics in the form of features. These tools can be categorized as web-based tools that operate online through web browsers, eliminating the need for installation, plug-in tools that seamlessly integrate into existing software tools, acting as extensions enhancing specific platforms or editors, and desktop application programming interface (API) tools that cater to local machine usage by providing functionalities through a desktop API. Key features of ontology evaluation tools include a graphical user interface (GUI) for visually intuitive interaction, API for seamless integration into various applications, and no formal installation process for enhanced user accessibility. Editor independence ensures compatibility with various ontology editing tools, promoting flexibility. Custom evaluation empowers users to define specific assessments tailored to unique requirements. The offline use feature allows users to perform evaluations without an internet connection, providing adaptability for scenarios with limited online access.

Table 5. Ontology evaluation tools

Features/gaps	Web based OOPS [55]	Web based Moki [56]	Web based OQuaRE [57]	Plug-in based XD [58]	Plug-in based OntoCheck [59]	Desktop API eyeball [60]	% of evaluation tools with the gap
GUI	✓	✓	✓	✓	✓	×	16%
API	✓	×	✓	×	×	✓	50%
No installation process	✓	×	✓	×	×	×	60%
Editor independence	✓	×	✓	×	×	✓	50%
Custom evaluation	✓	×	×	×	×	✓	60%
Offline use	×	✓	×	✓	✓	✓	30%
% of gaps per evaluation tool	16%	60%	30%	60%	60%	30%	

2.7. A review of semantic e-prescriptions healthcare interoperability frameworks

Table 6 shows a comprehensive comparison of healthcare interoperability prescription ontology frameworks. Eleven ontology frameworks are compared from ontology one (O1) to ontology eleven (O11). Table 6 will be analyzed and summarized in the results section. The comparison is facilitated through a detailed examination of various features within distinct categories. Each category encompasses a set of features, each with its unique role and purpose. Prototype aspects encompass features such as having a GUI, being open source, requiring no installation, being platform independent, and ensuring security. These attributes collectively contribute to the user-friendliness, accessibility, and robustness of the prototype framework. In the realm of medical error detection within the framework, critical aspects of patient safety are addressed, including drug-drug interaction (DDI), monitoring interactions with food, detecting disease interactions, and identifying wrong drug prescriptions. These features play a crucial role in the prevention of medication-related errors. Health monitoring within the ontology framework includes temperature monitoring, BMI monitoring, pulse rate monitoring, and blood pressure monitoring. These aspects collectively contribute to comprehensive healthcare monitoring, covering vital health indicators for effective patient care. Semantic aspects involve the use of ontologies, SPARQL endpoint API utilization, free ontology download, SWRL implementation, adherence to formal conceptualization, automated axiom import, and formal ontology development. These features ensure a semantic foundation, supporting advanced knowledge representation and reasoning capabilities. In the category of ontology evaluation, aspects include domain knowledge ontology evaluation, competency questions, interoperability evaluation, usability evaluation, and ontology pitfall evaluation. These features contribute to the continuous improvement and refinement of the ontology framework, ensuring its effectiveness, user-friendliness, and alignment with interoperability standards. Interoperability aspects address features such as drug information view, patient history, pharmacist access history, prescriber access history, pharmacy drug recommendations, and prescription analysis, facilitating seamless information exchange and collaboration among different stakeholders within the healthcare ecosystem. An e-prescription system is an electronic health record (HER) healthcare system that facilitates the interaction between physicians and pharmacies by enabling physicians to create and pass on prescriptions electronically to pharmacies [61]. E-prescriptions are being implemented in clinical settings to reduce medication-related risks and enhance patient safety [62].

3. RESULTS AND DISCUSSION

3.1. Summary of ontology development methodologies

Based on the observations of Table 2, this research suggests Methontology as the best option for semantic prescription ontology development because it covers 86% of features compared to other methodologies, lacking only 14% of the useful features required in ontology development tools. Methontology is easy to follow and has been widely adopted in the research field. Figures 1 and 2 analyze Table 2 further to validate the justification for suggesting the adoption of Methontology.

Figure 1 shows that the Ushcold methodology has a maximum of 93% of gaps while the Methontology has a minimum of 14% of gaps. On average, Table 2 suggests that 50.8% of gaps exist in the literature to be addressed. Figure 2 shows the percentage of specific gaps in current literature with 90% lacking configuration management but all having implementation activities.

Table 6. A comparison of eprescription frameworks

	Framework features/gaps		[63] O1	[64] O2	[65] 03	[66] O4	[67] O5	[68] O6	[69] O7	[70] O8	[71] 09	[72] O10	[73] O11	% of gaps in literature
1	Prototype aspects	Has GUI	x	x	x	x	x	x	x	x	x	✓	✓	82%
2		Open source	x	x	x	x	x	x	x	x	x	x	x	100%
3		No installation Required	x	x	x	x	x	x	x	x	x	x	x	100%
4		platform Independent	x	x	x	x	x	x	x	x	x	x	x	100%
5		Secure	x	x	x	x	x	x	x	✓	✓	✓	✓	64%
6	Medical errors	DDI	x	x	x	x	x	x	✓	✓	✓	x	x	73%
7		Food interactions	x	x	x	x	x	x	x	✓	x	✓	x	82%
8		Disease Interaction	x	x	x	x	x	x	x	x	x	x	x	100%
9		Wrong drug Detection	x	x	x	x	x	x	x	x	x	x	x	100%
10	Health monitoring	Temperature monitoring	x	x	x	x	x	x	x	x	x	x	x	100%
11		BMI monitoring	x	x	x	x	x	x	x	x	x	x	x	100%
12			x	x	x	x	x	x	x	x	x	x	x	
		Pulse rate monitoring	x	x	x	x	x	x	x	x	x	x	x	100%
13		Blood pressure monitoring	x	x	x	x	x	x	x	x	x	x	x	100%
14	Semantic aspects	Uses ontologies	✓	✓	✓	✓	✓	✓	✓	x	✓	x	✓	82%
15		SPARQL Endpoint API	x	x	x	x	x	x	x	x	x	x	x	100%
16		Free ontology download	x	x	x	x	x	x	x	x	x	x	x	100%
17		SWRL Implementation	x	x	x	x	x	x	x	x	x	x	x	100%
18		adhere to formal conceptualization	x	x	x	x	x	x	x	x	x	x	x	100%
19		Automated axiom import	x	x	x	x	x	x	x	x	x	x	x	100%
20		Formal ontology development	x	x	x	x	x	x	x	x	x	x	x	100%
21	Ontology evaluation	Domain knowledge ontology evaluation	x	x	x	x	x	x	x	x	x	x	x	100%
22		Competency questions	x	x	x	x	x	x	x	x	x	x	x	100%
23		Interoperability evaluation	x	x	x	x	x	x	x	x	x	x	x	100%
24		Usability evaluation	x	x	x	x	x	x	x	x	x	x	x	100%
25		Ontology pitfall evaluation	x	x	x	x	x	x	x	x	x	x	x	100%
26	Interoperability aspects	Drug information view	x	x	x	x	✓	✓	✓	x	x	✓	✓	55%
27		Patient history	x	x	x	x	x	x	x	✓	✓	✓	✓	64%
28		Pharmacist access history	x	x	x	x	x	x	x	x	x	x	x	100%
29		Prescriber access history	x	x	x	x	x	✓	✓	x	x	x	x	82%
30		Pharmacy drug recommend	x	x	x	x	x	x	x	x	x	x	x	100%
31		Prescription analysis	x	x	x	x	x	x	x	x	x	x	x	100%
Percentage of gaps per framework	97%	97%	97%	97%	94%	90%	87%	87%	84%	84%	84%			

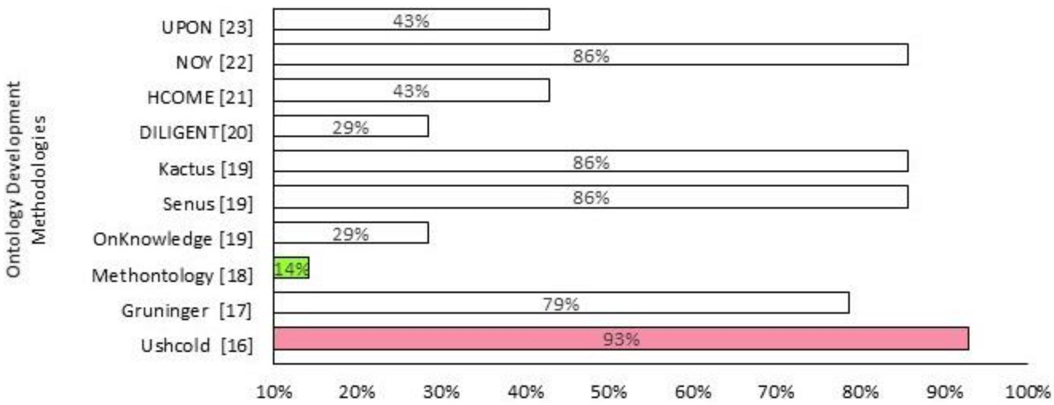

Figure 1. Percentage of gaps per ontology development methodology

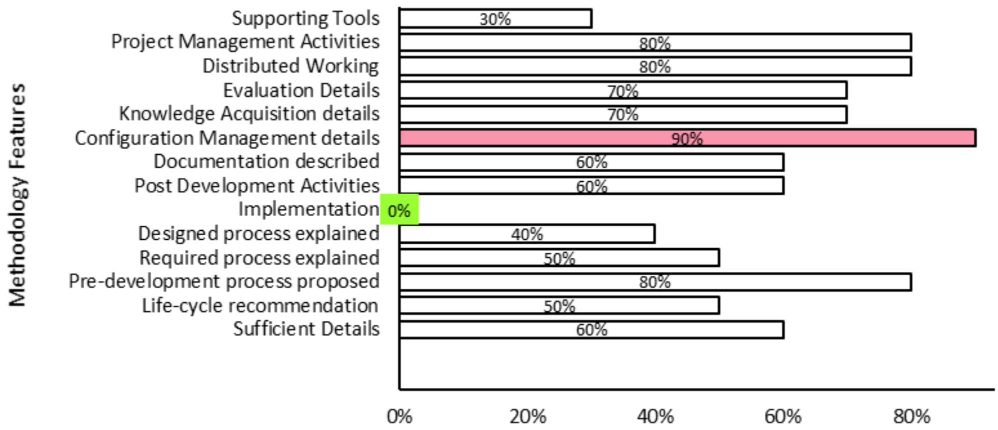

Figure 2. Percentage of specific gaps in current literature

3.2. Summary of ontology languages

Based on Table 3, this research suggests the adoption of the OWL2 language for healthcare interoperability ontology development with the justification that OWL2 has 0% of ontology issues compared to others. Figures 3 and 4 further analyze Table 3 to validate the justification for adopting OWL2. OWL2 supports several features compared to others like concept instances, facts, rules, based on instances, 1st order logic, 2nd-order logic embedded axioms, operational definition, subclass of, disjoint decomposition, concept partition and it allows an ontology to augment the meaning of the pre-defined (RDF or OWL) vocabulary and complete reasoning. The comparison of ontology languages based on various features reveals distinct patterns in their support for specific aspects. In terms of concept partitions, LOOM, OML, RDF(s), DAML + OIL, and OWL2 exhibit strong support, each scoring 55%. Documentation is a widely supported feature, with an average of 9% of the languages lacking this aspect. Instance attributes receive unanimous support across all languages, indicating comprehensive coverage. Class attributes see a mix of support, with LOOM, OCML, Flogic, OML, RDF(s), OIL, DAML + OIL, and QWL endorsing the feature, while SHOE lacks support. From Table 3, the global scope facts feature sees variable support, with LOOM, OML, RDF(s), OIL, DAML + OIL, and QWL supporting the feature, while OCML, Flogic, and SHOE do not. Default slot values receive substantial backing from most languages, excluding SHOE. Type constraints and subclasss are universally supported features. Cardinality constraints see varying degrees of endorsement, with LOOM, OCML, RDF(s), OIL, DAML + OIL, and QWL supporting the feature, while Flogic and SHOE lack this support. Slot documentation is well-supported, but SHOE lacks this feature.

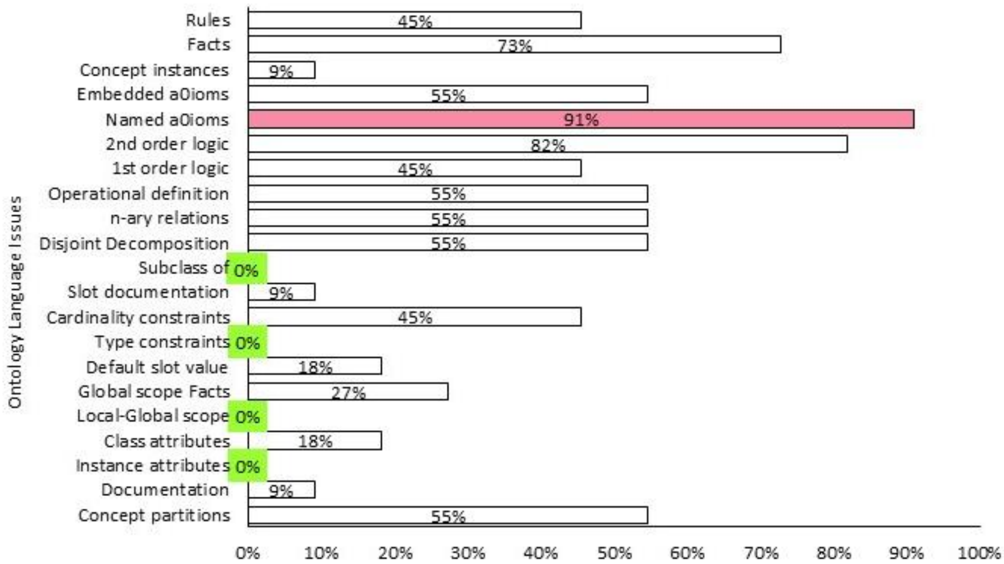

Figure 3. Percentage of affected ontology languages per issue

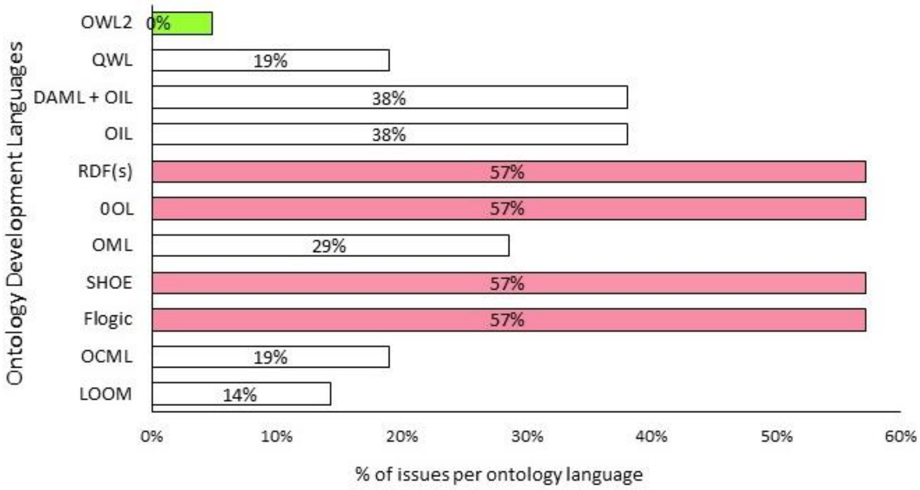

Figure 4. Percentage of issues per ontology language

Disjoint decomposition, N-array relations, and operational definition are features supported by LOOM, OML, RDF(s), OIL, DAML + OIL, and QWL, with OCML, Flogic, and SHOE lacking these aspects. First-order logic garners support from LOOM, OCML, RDF(s), OIL, DAML + OIL, and QWL, with Flogic and SHOE lacking this feature. Notably, second-order logic is a substantial gap, with only OWL2 providing support. Named axioms are a rare feature, supported only by DAML + OIL. Embedded axioms see support from LOOM, OCML, RDF(s), OIL, DAML + OIL, and QWL, while Flogic and SHOE lack this feature.

Concept instances receive broad support, excluding OML and SHOE. Facts see support from RDF(s), OWL2, and QWL, while LOOM, Flogic, and SHOE lack this feature. Rules are endorsed by LOOM, OCML, RDF(s), OIL, DAML + OIL, and QWL, while Flogic and SHOE lack support for this feature. In summary, this analysis highlights the nuanced strengths and weaknesses of ontology languages, providing valuable insights for researchers and practitioners seeking languages aligned with specific requirements.

3.3. Summary of ontology development tools

Figures 5 and 6 analyze Table 4 further to validate the justification for adopting Protégé. Protégé is mainly open source and is used by many researchers with a lot of community support. Figure 5 shows the percentage of affected ontology development tools per issue or gap. The major common issue is the lack of community support at 95%. In terms of reasoner capabilities and open source or free, 11% of the tools lack these two. On average, 45% of tools lack critical ontology development features. Figure 6 shows the percentage of gaps in each ontology development tool. Protégé and OWLGrED have the least gaps at 11% while the Altova Semantic tool has the most gaps at 88%. On average, 43% of gaps exist in current ontology development tools. The research suggests the Protégé tool for ontology development with the justification that Protégé has 13% of issues compared to others and it has a lot of community support compared to OWLGrED.

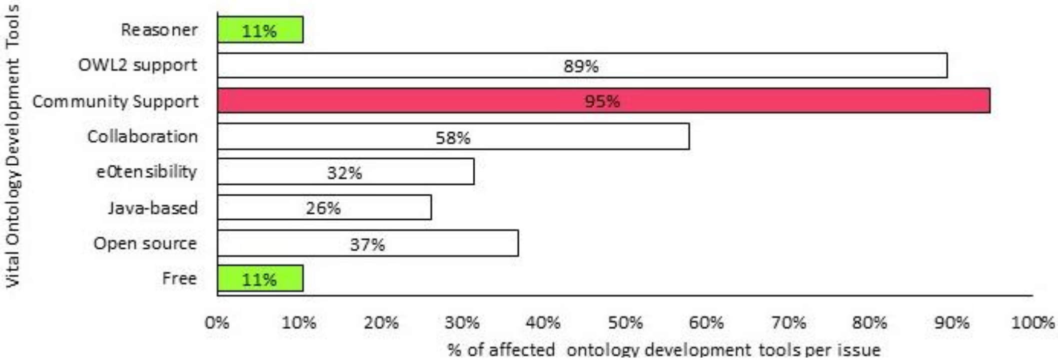

Figure 5. Percentage of affected ontology development tools per issue (gaps)

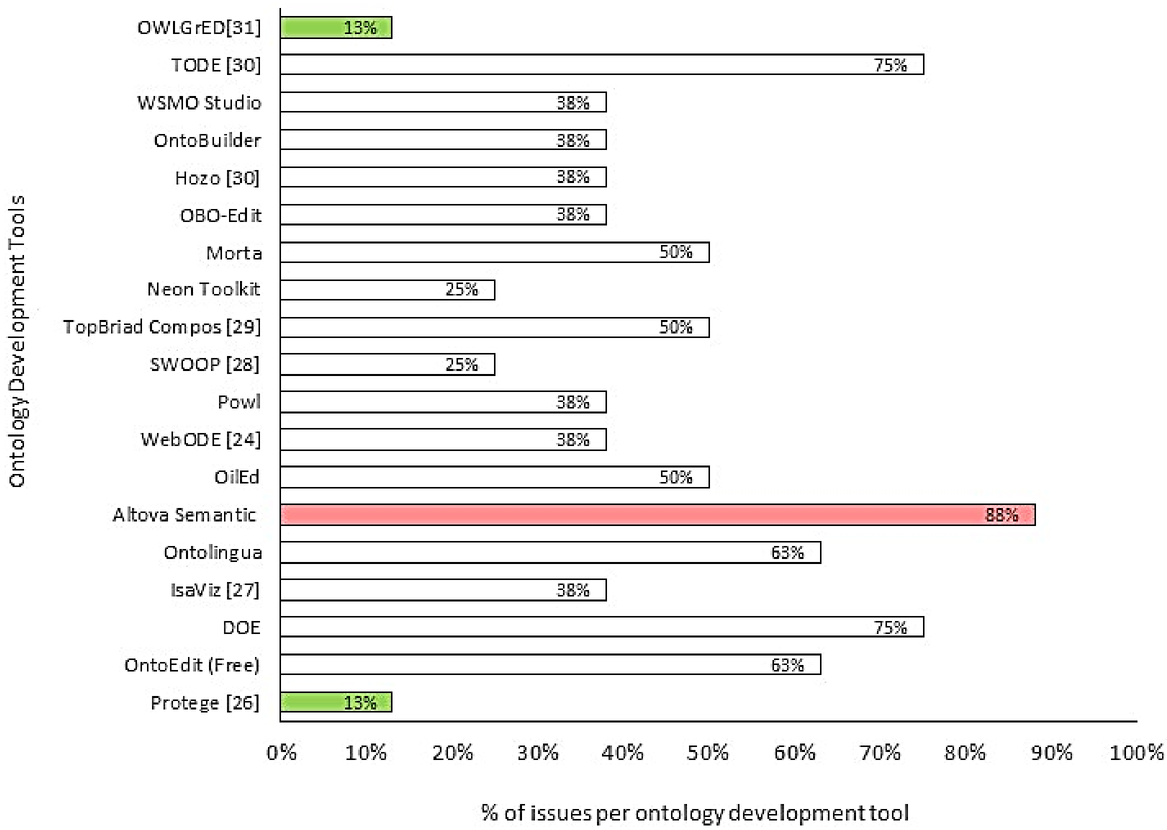

Figure 6. Percentage of gaps in each ontology development tool

3.4. Ontology evaluation tools

The research suggests the adoption of the OOPS tool for ontology evaluation with the justification that OOPS has 16% of issues compared to others. Figures 7 and 8 analyze Table 5 further to validate the justification for adopting the OOPS tool. The justification for the choice of the OOPS tool is that it meets many usability characteristics compared to others as it is open source, requires no installation, has a user-friendly web-based GUI that is customizable, and is used in detecting ontology pitfall errors and also gives solution on how the pitfall errors will be corrected. Figure 5 shows the percentage of literature gaps per ontology evaluation tool. The OOPS tools have fewer issues at 16% while the Onto-Chek, XD Analyzer, and Moki tools have 60% of gaps. On average, 43% of gaps exist in the current ontology evaluation tools.

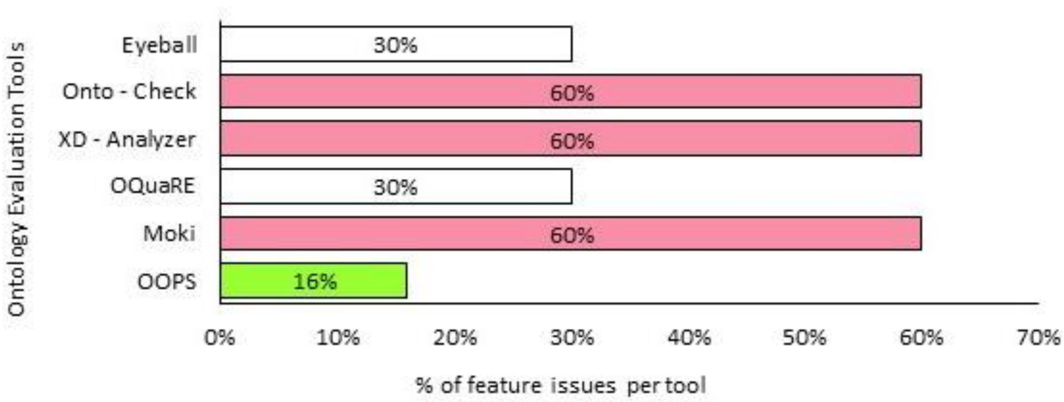

Figure 7. Percentage of gaps per ontology evaluation tool

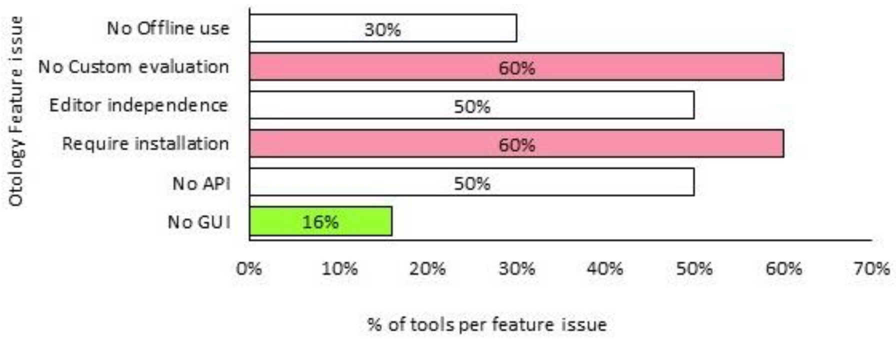

Figure 8. Percentage of ontology evaluation tools in literature per gap

3.5. Summary of e-prescription frameworks review

Figure 9 summarizes the percentage of gaps found in current semantic e-prescription interoperability frameworks. As shown in Figure 9, more than 80% of gaps exist in current frameworks showing the need for further research to improve the healthcare interoperability domain in terms of semantic prescription. Figure 10 shows the percentage of current e-prescription frameworks having issues that will need to be addressed. Figure 10 shows that on average, 91% of frameworks have issues that need to be addressed with 74% of the framework having almost all the critical evaluation features at 100%. The problem with the above semantic e-prescription frameworks is that most of them are still non-interoperable with other healthcare systems like the pharmacy, medical aid, insurance, patient, or even future virtual pharmacies involving autonomous robotic dispensing by machines and delivery by drones to patient’s houses. The e-prescription systems are only accessed by the prescribers at the clinic or hospital and paper versions of the e-prescription are printed and given to the patient to take to the pharmacy causing them to still be insecure as they can be lost or duplicated. To the best of our knowledge, the current frameworks do not allow the pharmacist to recommend alternative drugs to the patient when the specific drug is unavailable or too expensive by sending a real-time request to the prescriber system to validate the alternative drug and give a response with the updated prescription within seconds. This is very important in cases where the patient’s health is in an emergency and moving from pharmacy to pharmacy might be detrimental. The current frameworks do not address prescription medical errors like DDI, drug-to-food interactions, drug-disease interactions, wrong drug, and wrong dosage rote or strength.

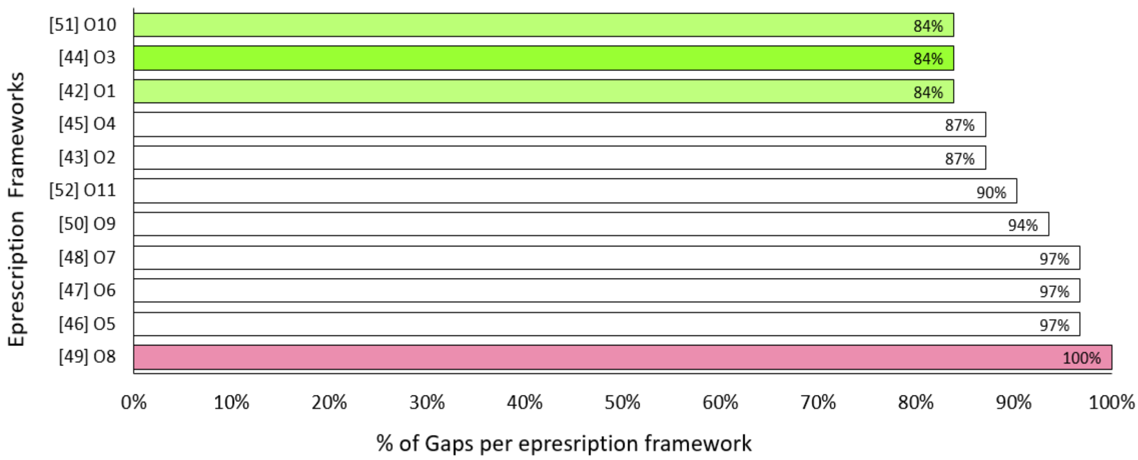

Figure 9. Percentage of gaps in each e-prescription framework

3.6. Challenges and future directions

Challenges in the existing semantic e-prescription frameworks identified from the literature include a notable gap in domain knowledge coverage, potentially compromising the frameworks' ability to comprehensively represent the intricacies of the e-prescription domain. The lack of a standardized mechanism for implementing and evaluating DDI detection features raises concerns about the completeness and reliability of these critical functionalities. Current frameworks also face difficulties in seamlessly integrating with expensive drug interaction checking APIs, leading to a reliance on manual checking and introducing the risk of errors in patient safety. The absence of ontology evaluation practices in these frameworks poses challenges in ensuring their trustworthiness and interoperability within healthcare systems. Moreover, the frameworks do not provide a real-time mechanism for pharmacists to recommend alternative drugs, hindering timely access to medications and potentially impacting patient outcomes. The high costs associated with drug interaction checking APIs present financial challenges, limiting the broader adoption of advanced checking capabilities in healthcare settings. Addressing these challenges is essential to enhance the robustness and reliability of semantic e-prescription frameworks. Future directions in the field involve advancing the current frameworks to overcome these challenges. This includes strategies to augment domain knowledge coverage, standardize the implementation and evaluation of DDI detection mechanisms, and improve integration with drug interaction checking APIs for seamless interoperability. Advocacy for the incorporation of ontology evaluation practices becomes imperative to ensure the quality, correctness, and effectiveness of semantic e-prescription ontologies. The development and implementation of real-time prescription update mechanisms within these frameworks are crucial to facilitate prompt access to medications and enable pharmacists to recommend alternative drugs efficiently. Exploring cost-effective solutions for drug interaction checking, such as open-source or more affordable APIs, becomes a key focus to broaden the accessibility of advanced checking capabilities across diverse healthcare settings. These future directions collectively aim to address the challenges identified in current semantic e-prescription frameworks and contribute to their continual improvement for enhanced patient safety and healthcare quality.

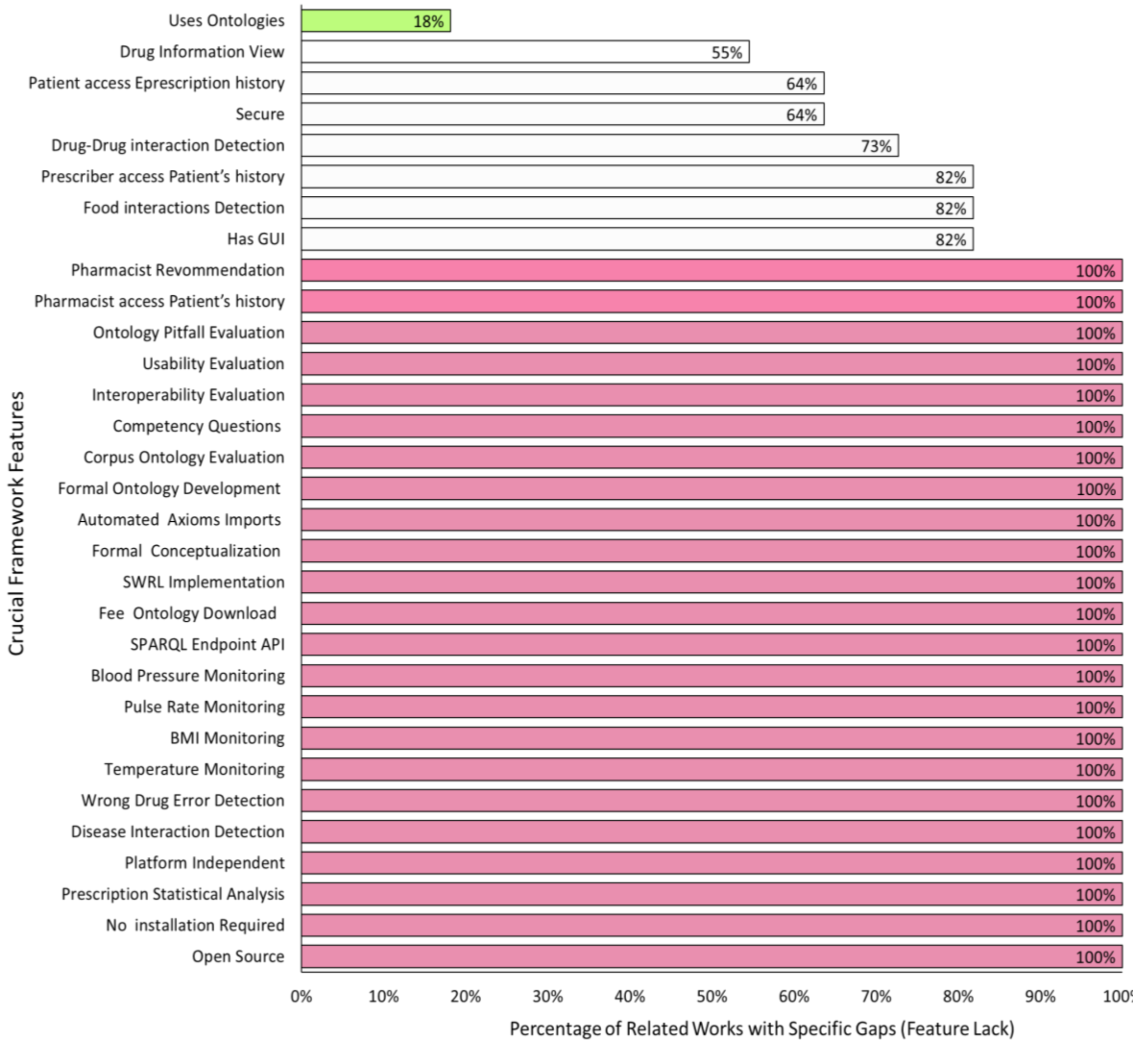

Figure 10. Percentage e-prescription frameworks with specific gaps

4. CONCLUSION

In conclusion, the review article provides a comprehensive examination of ontology-based approaches and tools in the development of semantic e-prescription systems with a focus on healthcare interoperability. The research critically evaluates various aspects, including ontology development methodologies, languages, tools, and evaluation approaches. The research suggests Methontology as the best option for semantic prescription ontology development because it covers 86% of features compared to other methodologies, lacking only 14% of the useful features required in ontology development tools. This research suggests the adoption of the OWL2 language for healthcare interoperability ontology development with the justification that OWL2 has 0% of ontology issues compared to others. The research suggests the adoption of the Protégé tool for ontology development with the justification that Protégé has 13% of issues compared to others and it has a lot of community support. The research also suggests the adoption of the OOPS tool for ontology evaluation with the justification that OOPS has 16% of issues compared to others. It was also deduced from the research that more than 80% of gaps exist in current semantic prescription interoperability frameworks showing the need for further research to improve the healthcare interoperability domain in terms of semantic prescription. The review highlighted challenges in current semantic e-prescription frameworks, such as limited concept coverage, reliance on expensive drug interaction checking APIs, and the absence of real-time prescription updates. The literature underscores the need for standardized mechanisms for DDI detection, implementation transparency, and ontology evaluation. Future directions involve advancing current frameworks to address these challenges, emphasizing standardized protocols, cost-effective solutions, and real-time functionalities. The research advocates for robust ontology evaluation practices to enhance the trustworthiness and interoperability of semantic e-prescription ontologies

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AUTHOR CONTRIBUTIONS STATEMENT

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Eunice Okon	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓			
Tshiamo Sigwele	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Galani Malatsi				✓	✓	✓				✓	✓	✓	✓	✓
Tshepiso Mokgetse				✓	✓	✓				✓	✓			
Hlomani Hlomani				✓	✓	✓				✓	✓	✓	✓	

C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

CONFLICT OF INTEREST STATEMENT

Authors state no conflict of interest.

DATA AVAILABILITY

Data availability is not applicable to this paper as no new data were created or analyzed in this study.

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