Making Science Computable: Introducing Evidence-Based Medicine on Fast Healthcare Interoperability Resources (EBMonFHIR)

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Abstract

Background: Evidence-Based Medicine (EBM) has the potential to improve health outcomes, but EBM has not been widely integrated into the systems used for research or clinical decision making. There has not been a scalable and reusable computer-readable standard for distributing research results and synthesized evidence among creators, implementers, and the ultimate users of that evidence. Evidence that is more rapidly updated, synthesized, disseminated, and implemented would improve both the delivery of EBM and evidence-based health care policy

Objective: To introduce the Evidence-Based Medicine (EBM) on Fast Healthcare Interoperability Resources (FHIR®) project (EBMonFHIR), which is extending the methods and infrastructure of Health Level Seven (HL7®) FHIR to provide an interoperability standard for electronic exchange of health-related scientific knowledge.

Methods: As an ongoing process, the project creates and refines FHIR Resources to represent evidence from clinical studies and syntheses of those studies and develops tools to assist with the creation and visualization of FHIR Resources.

Results: The EBMonFHIR project created FHIR Resources (i.e., ArtifactAssessment, Citation, Evidence, EvidenceReport, EvidenceVariable) for representing evidence. The COVID-19 Knowledge Accelerator (COKA) project, now Health Evidence Knowledge Accelerator (HEvKA), furthered this work and created FHIR Resources that express EvidenceReport, Citation, and ArtifactAssessment concepts. The group are (1) continually refining FHIR Resources to support the representation of EBM, (2) developing controlled terminology related to EBM (i.e., study design, statistic type, statistical model, and risk of bias), and (3) developing tools to facilitate the visualization and data entry of EBM information into FHIR Resources, including human-readable interfaces and JavaScript Object Notation (JSON) viewers.

Conclusions: EBMonFHIR Resources in conjunction with other FHIR Resources can support relaying EBM components in a manner that is interoperable and consumable by downstream tools and health information technology systems to support users of evidence.

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Keywords: Evidence-Based Medicine; FHIR; Computable Evidence; EBMonFHIR

Introduction

Background and Significance

Timely and relevant biomedical evidence is essential to provide high-quality health care. Decision-makers rely on “synthesized evidence” from systematic reviews (SRs) and clinical practice guidelines (CPGs) to inform clinical care decisions and policies at multiple levels.[1–7] Therefore, actionable evidence is key for optimizing health care delivery and outcomes. Yet, with an estimated 75 clinical trials and 11 SRs published every day,[8] efforts to synthesize, disseminate, and implement biomedical evidence throughout the evidence ecosystem to inform decision-making are unsustainable.[9]

Evidence-based medicine (EBM) is increasingly recognized as critical in the decision-making process related to patient care and policy development. EBM is “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.”[10] The practice of EBM depends on comprehensive and up-to-date synthesized research evidence,

which requires continuous updating and reconciliation of new scientific results with prior results. For example, early trial results on prenatal steroids for preterm births were initially inconclusive but evidence syntheses justified steroidal therapy as a best practice.[11–14] However, EBM practice is laborious, methodologically complex, and often error-prone.

Multiple barriers hinder the effective and efficient use of evidence syntheses. First, the time and effort required to synthesize evidence often leads to SRs and CPGs being out of date by the time of their publication.[15,16] Even when synthesized evidence is available in digital form, it is typically in narrative form and accessed via a bibliographical database that requires proactive searching (e.g., PubMed or a publisher), an email newsletter (e.g., JAMA Internal Medicine Newsletter), or social media notification (e.g., Twitter or Doximity). These "pull" methods of synthesized evidence are helpful means of dissemination, but they do not facilitate more efficient "push" methods that promote use, implementation, and action at scale. Second, the common mode of evidence dissemination, which is human readable text, is not standardized in ways that support technical solutions to scalable dissemination and implementation.[15–19] Despite notable past efforts for structuring and disseminating guidance, such as the GuideLine Interchange Format (GLIF)[20,21] and Standards-Based Sharable Active Guideline Environment (SAGE)[22] standards, there are no existing scalable and reusable computer-readable standards for distributing research results and synthesized evidence among creators, implementers, and the ultimate users of that evidence.

The current state is an ecosystem of researchers, informaticians, statisticians, policymakers, epidemiologists, librarians, and other stakeholders in the biomedical research community who synthesize evidence by manually searching for relevant studies, assessing the studies for quality and risk of bias, and compiling the results in labor-intensive ways. Evidence implementers, including CPG and clinical decision support (CDS) creators, whether they are creating or implementing local or third-party tools, must similarly review and verify the evidence prior to use. The challenges with finding and delivering evidence are amplified by needs due to the COVID-19 pandemic,[23–28] where "scientists [have] published well over 100,000 articles about the coronavirus pandemic in 2020"[29] and for which there are currently over 600,000 publications.[30] Today, these mostly manual, redundant, and disjointed processes seem to be the acknowledged status quo, even though new evidence continues to be generated at a rapid pace. The evidence synthesis ecosystem is therefore rife with duplication and uncoordinated efforts[31,32] for identifying, appraising, synthesizing and disseminating evidence, requiring considerable resources, expertise, and time.[33,34] Evidence that is more rapidly updated, synthesized, disseminated, and implementable would improve both the delivery of EBM and evidence-based health care policy.[4,35]

Computable Evidence

Solutions to improve the evidence-to-practice lifecycle[36] should begin with the transformation of study results into "computable evidence", or "knowledge artifacts", that could be consumed by software-based information systems. Key to computable evidence is knowledge representation in machine-interpretable formats that enable Findable, Accessible, Interoperable, and Reusable (FAIR)[37] information across the evidence ecosystem. Figure 1 depicts this vision where research results at many stages throughout analysis, publication, and synthesis (the EBMonFHIR area) can be extracted and transformed from numerous disparate sources (such as registry reports, gray literature, preprints, and peer-reviewed literature databases) and stored as machine-readable evidence in an interoperable standard format that could then be used by a wide variety of evidence users and developers from biomedical knowledge bases (i.e., evidence repositories) to SRs, CPGs, and CDS systems. Figure 1 also shows where related interoperability solutions[38] applied to CPG and CDS representation (the CPGonFHIR area), such as CDS Connect (a platform with a repository and authoring tool for CDS artifacts)[39] and CDS Hooks (an HL7 specification that provides a way to

embed CDS services within the clinician workflow of an electronic health record)[40], can complete the evidence-to-practice implementation within the evidence ecosystem.

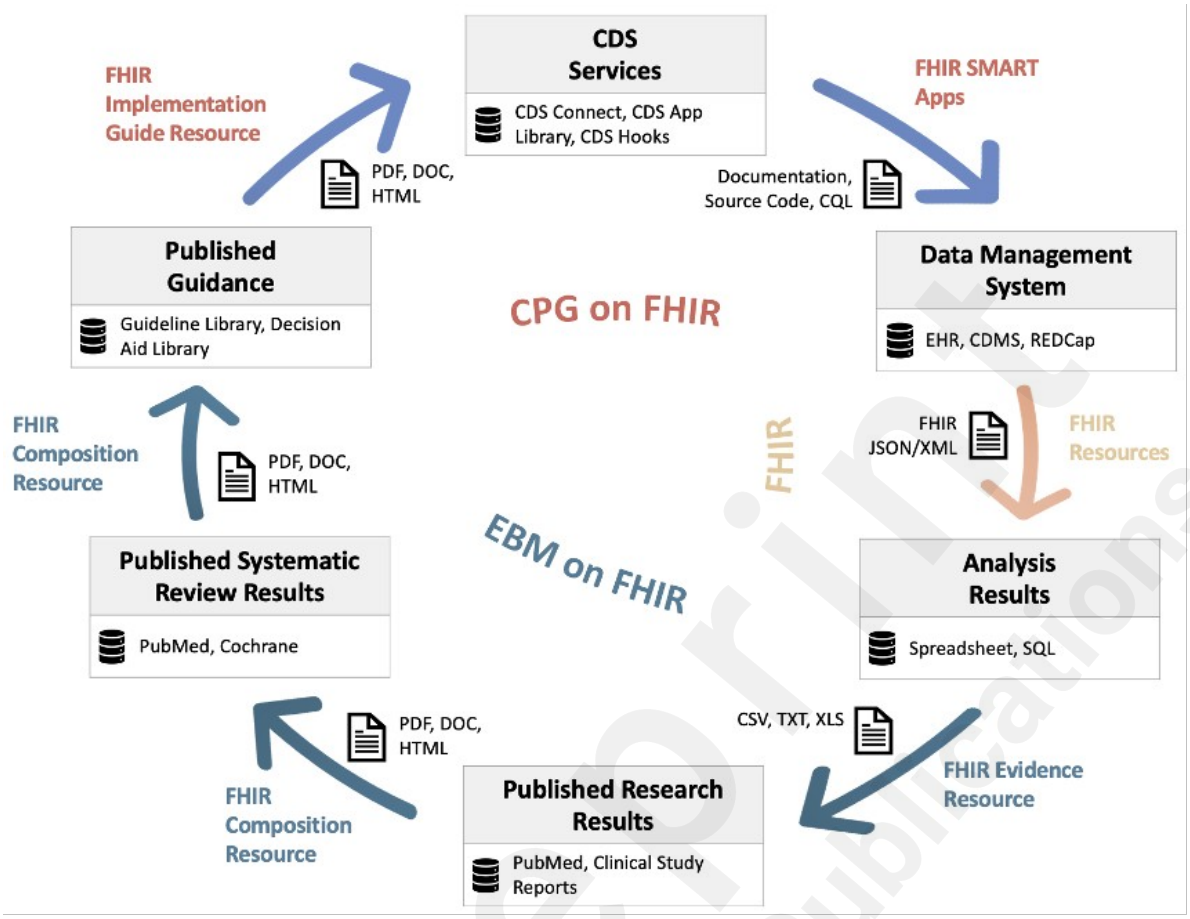

Figure 1: Application of Fast Healthcare Interoperability Resource (FHIR) Resources to the evidence ecosystem. Figure adapted from the "Digital and Trustworthy Evidence Ecosystem".[39] Evidence-Based Medicine (EBM) on Fast Healthcare Interoperability Resources (FHIR®) (EBMonFHIR) denotes application to results of scientific analysis, synthesis and publication. CPGonFHIR denotes application to guidance and decision support. CSV, TXT, XLS, PDF, DOC, HTML, JSON, and XML denote file formats. Other abbreviations include Apps for applications, CDMS for clinical data management system, CQL for Clinical Quality Language, EHR for electronic health record, REDCap for Research Electronic Data Capture, SQL for Structured Query Language.

The EBMonFHIR Project

Built upon the success of FHIR[41–43] to promote interoperability and standards for data exchange, we initiated Evidence-Based Medicine (EBM) on Fast Healthcare Interoperability Resources (FHIR®) project (henceforth, EBMonFHIR) in May 16, 2018. The aim was to extend the methods and infrastructure of HL7 FHIR to provide an interoperability standard for electronic exchange of biomedical knowledge from and about clinical research and recommendations.[44] We sought to stand on the shoulders of those who have before made strides in structuring evidence and standardizing the means to share that evidence (e.g., GLIF) by leveraging FHIR's growing popularity and acceptance. The project solicits participation of known experts and gathers input from broad communities in the evidence ecosystem to determine the data exchange needs for interoperable knowledge assets[44] and defines the FHIR Resources related to the domain of clinical research evidence. We have begun showing that FHIR can deliver not just clinical data but also synthesized evidence and knowledge to end users.

Historical Context

The project started with implementers from EBSCO Health, Duodecim Medical Publications Ltd, HarmoniQ and MAGIC Evidence Ecosystem Foundation and expanded to a multi-sector project with participation from academia, industry, government, and nonprofit organizations[45].

The COVID-19 pandemic introduced a new impetus in the quest to make biomedical evidence computable and interoperable. In light of the pandemic, where scientists and clinicians urgently needed timely results and evidence, the EBMonFHIR project leaders organized a larger group named the "COVID-19 Knowledge Accelerator (COKA) Initiative" and shifted their focus to the biomedical evidence regarding SARS-CoV-2.[46] COKA is a non-profit virtual organization with global collaboration to develop and advance interoperability standards for COVID-19 knowledge and to enhance the evidence exchange standards. As of January 2023, the COKA initiative was renamed to Health Evidence Knowledge Accelerator (HEvKA) to better represent the group's now broader scope that is inclusive of clinical, public health, and environmental health domains.

Objectives

In this paper, we introduce the EBMonFHIR project that aims to produce a Health Level Seven International (HL7®) FHIR schema to express biomedical evidence as computable evidence—as well as FHIR Resource instances, terminologies, and tools— and to promote an effective and efficient evidence ecosystem. We describe the participants involved in this effort, the process to develop the EBMonFHIR standards, and the progress made to represent evidence findings as FHIR Resources. We also provide information on initial impacts, limitations, and next steps for stakeholders involved in standards and controlled terminology development, EBM implementation, and evidence use for both clinical studies and syntheses of those studies. We lastly describe how others can get involved in the EBMonFHIR effort by way of the Health Evidence Knowledge Accelerator (HEvKA) initiative.

Methods

HEvKA is advancing EBMonFHIR according to the five aspects of the HL7 standards development process[47]: (1) foster consensus, (2) ensure content is fit for purpose, (3) ensure content is implementable, (4) establish an appropriate implementer community, and (5) ensure ongoing maintenance of the standard. Through up to 15 virtual meetings each week and up to three HL7 FHIR Connectathons[48] each year, HEvKA creates and refines FHIR Resources to represent evidence from clinical studies and syntheses of those studies and develops tools to assist with the creation and visualization of FHIR Resources. "Updates and improvements for any FHIR specification can be developed, proposed, reviewed, improved, voted on and released within a documented environment in accordance with the American National Standards Institute (ANSI)-sectioned HL7 ballot process, and ultimately published as part of the official HL7 FHIR specification."[49] The FHIR Resources that HEvKA develops are continuously revised and adapted to reflect the best representation of the knowledge from the community. The HL7 CDS Work Group[50] is responsible for evaluating and approving the additions and changes to these FHIR Resources.

With the goal of supporting a culture of transparency and openness about the process to develop the FHIR Resources and supporting tools, HEvKA makes use of numerous digital approaches to document and keep track of its activities and disseminate its progress, including the HL7 Confluence Web Page (content management),[44] Google Drive (content repository),[51] and Microsoft Teams (video conference).[52] The content produced is open-source and freely available to the community, with examples published on the Fast Evidence Interoperability Resources (FEvIR) Platform.[53] HEvKA also coordinates input and dissemination across many communities in the

evidence ecosystem.

HEvKA has 14 active working groups that meet weekly to address different aspects of the project (i.e., Communications, Computable EBM Tools Development, CQL Development, EBM Implementation Guide, Eligibility Criteria, Funding the Ecosystem Infrastructure, GRADE Ontology, Measuring the Rate of Scientific Knowledge Transfer, Ontology Management, Project Management, Risk of Bias Terminology, Setting the Scientific Record on FHIR, Statistic Terminology, StatisticsOnFHIR). Visit our Confluence Page for information about HEvKA.[54]

Results

EBM representation with FHIR Resources

HEvKA first created FHIR Resources for representing research results (Evidence) and variable definitions (EvidenceVariable); and after March 2020, HEvKA further created FHIR Resources that express compositions (EvidenceReport), citations (Citation), and judgments about knowledge (ArtifactAssessment). To ease the readability of this article, we will broadly refer to these FHIR Resources as the "EBMonFHIR Resources." Table 1 shows the list of EBMonFHIR Resources the project developed. From here on, we list any FHIR Resource in **bold** and any FHIR elements and data types [55] in *italic*.

Table 1: List of Fast Healthcare Interoperability Resources (FHIR) Resources developed by the Evidence-based Medicine on FHIR (EBMonFHIR) and Health Evidence Knowledge Accelerator (HEvKA) projects. (FHIR version 6.0.0 Current Build, as of November 2, 2023)

FHIR Resource	Description	Reference to URL
ArtifactAssessment	The ArtifactAssessment Resource provides one or more comments, classifiers or ratings about a Resource and supports attribution and rights management metadata for the added content	[56]
Citation	The Citation Resource enables reference to any knowledge artifact for purposes of identification and attribution. The Citation Resource supports existing reference structures and developing publication practices such as versioning, expressing complex contributorship roles, and referencing computable resources.	[57]
Evidence	The Evidence Resource provides a machine-interpretable expression of an evidence concept including the evidence variables (e.g., population, exposures/interventions, comparators, outcomes, measured variables, confounding variables), the statistics, and the certainty of this evidence.	[58]
EvidenceReport	The EvidenceReport Resource is a specialized container for a collection of resources and codeable concepts, adapted to support compositions of Evidence, EvidenceVariable, and Citation resources and related concepts.	[59]

EvidenceVariable	The EvidenceVariable Resource describes an element that knowledge (Evidence) is about.	[60]

An **Evidence** Resource[58] provides an expression of the most granular components of evidence. Evidence is often represented by values and parameters of statistical measures (e.g., mean, confidence interval, relative risk, hazard ratio, etc.) and expressions of certainty or classifications of these statistical findings. These statistics are about a particular combination of variables from a particular study, so the **Evidence** Resource can reference **EvidenceVariable** Resources for definitions of the observed and/or intended variables. However, to support interoperability across systems, the **Group** Resource[61] may be used instead of an **EvidenceVariable** Resource[60], especially when referring to a group of people such as a population, sample, or subgroup.

The **Evidence** Resource refers to statistical measures and their values with a machine-interpretable expression of a statistic, including the quantity; unit of measure; classification of statistic type; sample size; attribute estimates such as confidence intervals, p-values, and heterogeneity estimates; and statistical model characteristics (Figure 2). The *statisticType* element has, as of November 2, 2023, a suggested set of 22 possible codes[62], assembled by the HEvKA team, that represent types of statistics (e.g., median, relative risk, incidence rate ratio, etc.). HEvKA has drafted 139 terms for statistic types in total (these will eventually replace the Statistic Type Value Set).

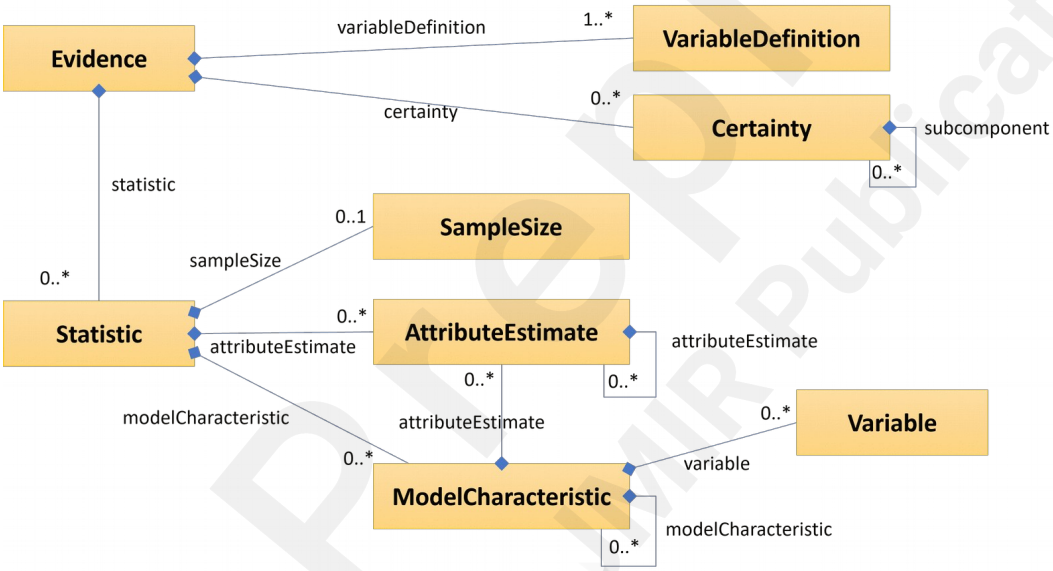

Figure 2: **Evidence** Resource backbone elements represented with an abbreviated unified modeling language (UML) diagram.

Biomedical evidence is comprised of facts and interpretations derived from an analysis of observations of a selective sample. Certainty about any evidence may change due to methodological factors, statistical factors, contextual factors, and the relatedness between the sample the evidence was derived from and the population to which the evidence is applied. The *certainty* element provides a machine-interpretable expression of confidence in, or certainty or quality of, the evidence. The *type* sub-element can express the aspect of the certainty being rated, using codeable concepts from a suggested value set (e.g. including the overall certainty, risk of bias, inconsistency, indirectness, imprecision, publication bias, dose response gradient, plausible confounding, and large effect size[63]).

An **EvidenceVariable** Resource[60] provides an expression of a single evidence variable (e.g., a single exposure or a single outcome/measured variable).

The **Citation** Resource “enables reference to any knowledge artifact for purposes of

identification and attribution,"[57] including "location, authorship, and contributorship to a journal article, report, document, resource, or other knowledge artifact."[57] For instance, the **Citation** Resource[64] is a reference to the **Evidence** Resource[65] representing the primary outcome from an article reporting results of a randomized clinical trial[66].

The **EvidenceReport** Resource represents a "container for a collection of resources and codeable concepts, adapted to support compositions of **Evidence**, **EvidenceVariable**, and **Citation** Resources and related concepts."[59] This Resource may bundle knowledge from one or multiple studies.[59] The report can be represented in sections of different forms including text, references to codeable concepts, or other FHIR Resources and sections. The **EvidenceReport** Resource is "suited for communicating reports about research and data analysis not specific to individual persons,"[59] distinct from the FHIR **Composition** Resource commonly used for reports specific to individual persons. However, the **EvidenceReport** Resource will be deprecated as the **Composition** Resource has been modified to include an EvidenceReport profile to support EBMonFHIR use.

The **ArtifactAssessment** Resource[56] "represents one or more assessments of another record or resource." This Resource covers assessments about clinical records, healthcare provision, and records related to community knowledge (e.g., evidence), and may include comments, corrections, classifications, ratings, questions, and responses.

Terminologies

The use of controlled terminologies supports the interoperable representation of multiple concepts. In FHIR, controlled terminologies[67] are represented in code systems and value sets. Reporting a specific term in FHIR uses a *Coding* data type. The *Coding* data type includes a *system* element to identify the terminology system, a *code* element for the precise code for machine use, and a *display* element for human-readable expression. A *CodeableConcept* data type is "a value that is usually supplied by providing a reference to one or more terminologies or ontologies but may also be defined by the provision of text."[55] A *CodeableConcept* is composed of a *coding* element (with none, one or more instances) and a *text* element (with none or one instance).

The *coding* element of a *CodeableConcept* can use a variety of terminologies, such as Systematized Nomenclature of Medicine - Clinical Terms (SNOMED CT), Logical Observation Identifiers Names and Codes (LOINC), RxNORM and Identification of Medicinal Products (IDMP). FHIR has a non-comprehensive registry of external code systems[67]. New items can be proposed by the community, and implementers can choose to use other code systems not listed in the registry. Figure 3 shows a sample *CodeableConcept* for the "Disease caused by severe acute respiratory syndrome coronavirus 2."

```
"valueCodeableConcept": {
  "coding": [
  {
     "system": "http://snomed.info/sct",
     "code": "840539006",
     "display": "Disease caused by severe acute respiratory
        syndrome coronavirus 2 (disorder)",
     "userSelected": true
  },
  {
     "system": "http://hl7.org/fhir/sid/icd-10",
     "code": "U07.1",
     "display": "COVID-19, virus identified",
     "userSelected": true
  }
  ],
  "text": "COVID-19"
}
```

Figure 3: Sample *valueCodeableConcept* element showing multiple *coding* elements. In this example, the *coding* element represents the COVID-19 disease with both SNOMED CT and ICD-10 terminologies.

HEvKA has used, developed or extended over 40 terminologies for use with **Evidence**, **EvidenceVariable**, **EvidenceReport**, **Citation** and **ArtifactAssessment** Resources. Consolidation of several of these terminologies has resulted in HEvKA leading the effort to create a Scientific Evidence Code System (SEVCO) with nearly 600 terms for study design, risk of bias, and statistics[49]. See Multimedia Appendix 1 for a list of FHIR Data Elements with reference to controlled terminologies.

Walkthrough: Sample study result represented with EBMonFHIR Resources

HEvKA tested the EBMonFHIR standard by conducting a successful proof-of-concept exercise that used the FHIR **Evidence** Resource to represent a critically appraised summary of the primary outcome of a multi-platform RCT of anticoagulation for hospitalized non-critically ill patients with COVID-19.[68] The primary outcome was “organ support–free days, evaluated on an ordinal scale that combined in-hospital death and the number of days free of cardiovascular or respiratory organ support up to day 21 among patients who survived to hospital discharge.”[68] The primary result for the overall group was reported as a median adjusted odds ratio 1.27 (95% credible interval 1.03 to 1.58), with 939 out of 1171 (80.2%) in Therapeutic-Dose Anticoagulation group and 801 out of 1048 (76.4%) in Usual-Care Thromboprophylaxis group. An overview of FHIR Resources used to represent the appraisal of this outcome is shown in Table 2. See the EBMonFHIR walkthrough[69] of this study with details about how the resources are used to represent the study including samples of JSON code to illustrate the EBM representation with FHIR Resources.

Table 2. List of EBMonFHIR Resources that represent the result for primary outcome of the sample study.

Title	Reference to URL	FHIR Resource Type	Description
Anticoagulation for COVID-19 Combined RCTs in NEJM	[70]	Citation	Citation for the article in the NEJM
Citation for FEvIR Evidence 7637: Critically appraised summary of primary outcome of multi-platform RCT of anticoagulation for non-critically ill COVID-19	[64]	Citation	Citation for Evidence Resource with FEvIR Object Identifier (FOI) 7637
Critically appraised summary of primary outcome of multi-platform RCT of anticoagulation for non-critically ill patients with COVID-19	[65]	Evidence	Summary of one unit of evidence (statistical findings for one set of variables) from the study
Therapeutic-dose anticoagulation with heparin	[71]	Evidence Variable	Exposure in Intervention arm of the study
Usual-care pharmacologic thromboprophylaxis	[72]	Evidence Variable	Exposure in Comparator arm of the study

Organ support-free days	[73]	Evidence Variable	Measured variable for Primary Outcome of the study
Patients who are hospitalized for COVID-19 and who are not critically ill	[74]	Group	Group description for the Intended Population for evidence interpretation
Participants in Anticoagulation for COVID-19 Combined (ATTACC, ACTIV-4a, and REMAP-CAP) RCT (hospitalized, not critically ill)	[75]	Group	Group description for the Observed Population in the study

Discussion

HEvKA is spearheading transformations and advances of EBMonFHIR on several fronts to support the process of exchanging biomedical evidence in a machine-readable format. As a continuously evolving effort, HEvKA has coordinated efforts and collaborated with industry, academia, government and nonprofit organizations to develop EBMonFHIR Resources and related tools, and has presented progress reports and results of the project to both EBM and informatics communities at several national and international events such as American Medical Informatics Association (AMIA) Annual Symposium, AMIA Informatics Summit, Guidelines International Network (GIN) Conference, Mobilizing Computable Biomedical Knowledge (MCBK), and Cochrane Colloquium.

Status and maturity of evidence-related standards: The EBMonFHIR standard contains five FHIR Resources (i.e., **Evidence**, **EvidenceVariable**, **Citation**, **EvidenceReport**, and **ArtifactAssessment**) and HEvKA is continually revising and refining the Resources with support from members of the EBM community. Currently, the **ArtifactAssessment**, **Citation**, **Evidence** and **EvidenceVariable** Resources are at FHIR Maturity Level 1, "the artifact produces no warnings during the build process and the responsible WG has indicated that they consider the artifact substantially complete and ready for implementation."[76], while **EvidenceReport** is Maturity Level 0 (i.e., Draft) and will be deprecated. Dedicated HEvKA working groups are developing functional examples to confirm and demonstrate the use of EBMonFHIR Resources and data elements in various use cases. The examples are published on the FEvIR Platform.[53] In addition, following efforts for developing an implementation guide for representing evidence-based clinical practice guideline recommendations[77], the EBMonFHIR project is producing an EBM on FHIR Implementation Guide[78,79] with 73 Profiles of 12 Resources to fully represent clinical research and evidence-based guideline.

The role of controlled terminologies: Communicating evidence in coded and structured forms requires controlled terminologies (or code systems) to uniquely and accurately express essential concepts. HEvKA created a Code System Development protocol to enable standardized terminologies for exchange of scientific evidence.[49] This protocol is being executed to develop four code sets related to EBM: study design, statistic type, statistical model, and risk of bias.

Relatedly, the SEVCO Expert Working Group (an offshoot of HEvKA) has 39 members from 18 countries as of November 3, 2023. SEVCO has identified 23 commonly used tools and methods for what the code system will support, such as the ROBINS-I tool for risk of bias assessment.[80] As of this writing, there are 602 prospective terms (253 for Risk of Bias, 76 for Study Design, 273 for Statistics) to support all recognized commonly used tools and systems. Coordination with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group, a collaboration to develop a common and transparent approach to grading quality (or certainty) of evidence and strength of recommendations, is underway to support a GRADE Ontology.

Tools for end-users: HEvKA participants have developed tools to facilitate the visualization and data entry of evidence into EBMonFHIR Resources, including human-readable interfaces and JavaScript Object Notation (JSON) viewers. The tools are integrated in the FEvIR Platform[54], and include intuitive forms, purposefully created to not require manual JSON coding or working knowledge of FHIR, for viewing and building **Citation**, **Evidence**, **EvidenceVariable** and **Group** Resources; for viewing and building multiple profiles of **Composition** Resource (Guideline, Recommendation, SummaryOfFindings); for viewing and building multiple profiles of **ArtifactAssessment** Resource (Classification, Rating, RiskOfBiasAssessment, RecommendationJustification); and automated converters to translate data from Medline, RIS, ClinicalTrials.gov, and MAGICapp into the FHIR specification. The viewing of Resources created with these tools is open without an account, but an account (at no cost) is required to create content.

This environment may reduce the time spent on systematic review evidence gathering. The laborious process of searching for articles and screening them by hand could be automated because the search query would be expressed in the "language" of EBMonFHIR and judgments made by previous searchers (such as population classification) can be recorded for re-use. Similarly, automated tools could be used to update evidence within systematic reviews rather than relying on manual updates.

With data available in the "language" of EBMonFHIR, it will become easier to develop tools to analyze and process scientific knowledge. Automated meta-analysis tools could be developed based on recognition of **Evidence** Resources with matching *variableDefinition* content and processing algorithms mapped to the structured *statistic* content. Tools to accelerate original research will also be developed, such as tools to match clinical trials with potentially eligible patients. [81]

The **ArtifactAssessment** Resource can also be used to represent the quality or certainty of the evidence itself. The Evidence Based Medicine on FHIR Implementation Guide includes a *CertaintyOfEvidence* Profile for this purpose. There is also a *DatasetCitation* Profile of the **Citation** Resource and an **ArtifactAssessment** Resource referencing a *DatasetCitation* can be used to represent the data quality.

Conclusions

Continuously identifying, synthesizing, and incorporating evidence into care are the key tasks of medical knowledge management, yet they are also prohibitively labor intensive. HEvKA has taken approaches to standardize and eventually automate these tasks through its efforts around EBMonFHIR, an HL7 standard for making biomedical evidence computable. EBMonFHIR will be used for enabling seamless data flow between published evidence reports, repositories, systematic review authoring tools, and guideline development tools; automating the searching and matching of evidence with any subgroups of patients; connecting individual patient data with medical knowledge for computerized clinical decision support; and providing individualized effect estimates for different outcomes to facilitate shared decision-making. EBMonFHIR Resources in conjunction with other FHIR Resources can support relaying EBM components in a manner that is interoperable and consumable by downstream tools and health information systems to support evidence users (e.g., creators of biomedical knowledge bases, CPGs, CDS artifacts and SRs). Anyone may join HEvKA to engage a community of FHIR users and committed volunteers for accelerating the development and implementation of standards for evidence exchange.

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Conflicts of Interest

Alper owns Computable Publishing LLC and leads the Health Evidence Knowledge Accelerator (HEvKA) and EBMonFHIR projects. Dehnbostel and Shahin are employees of Computable Publishing LLC. Alper, Shahin, Dehnbostel, Afzal, Kommadi, Lehmann, Robinson, Subbian, and Kunnamo are board members of the Scientific Knowledge Accelerator Foundation (SKAF). Soares, Schilling, and Richardson have no disclosures to report.

Abbreviations

AMIA: American Medical Informatics Association
CDS: Clinical Decision Support
COKA: COVID-19 Knowledge Accelerator
CPGs: clinical practice guidelines
EBM: Evidence-Based Medicine
EBMonFHIR: Evidence-Based Medicine on Fast Healthcare Interoperability Resources
FAIR: Findable, Accessible, Interoperable, and Reusable
FEvIR: Fast Evidence Interoperability Resources
FHIR: Fast Healthcare Interoperability Resources
GRADE: Grading of Recommendations Assessment, Development and Evaluation
GIN: Guidelines International Network
GLIF: GuideLine Interchange Format
HEvKA: Health Evidence Knowledge Accelerator
HL7: Heath Level Seven
ICD-10: International Classification of Diseases, Tenth Revision
IDMP: Identification of Medicinal Products
JAMA: Journal of the American Medical Association
JSON: JavaScript Object Notation
MCBK: Mobilizing Computable Biomedical Knowledge
NEJM: New England Journal of Medicine
RCT: randomized controlled trial
RECap: Research Electronic Data Capture
SAGE: Standards-Based Sharable Active Guideline Environment
SEVCO: Scientific Evidence Code System
SNOMED CT: systematically organized computer-processable collection of medical terms
SQL: Structured Query Language
SRs: systematic reviews
UML: unified modeling language
WG: Working group

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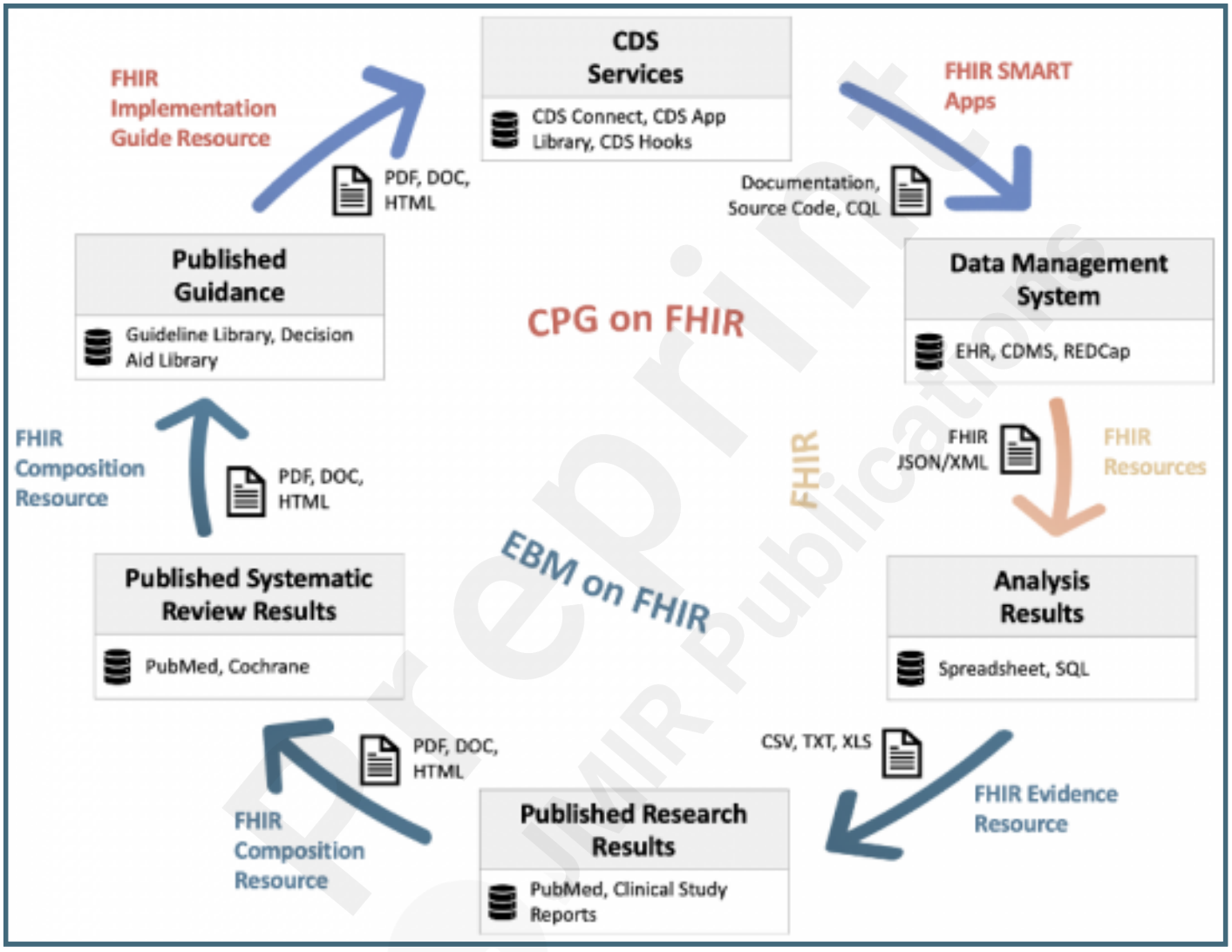
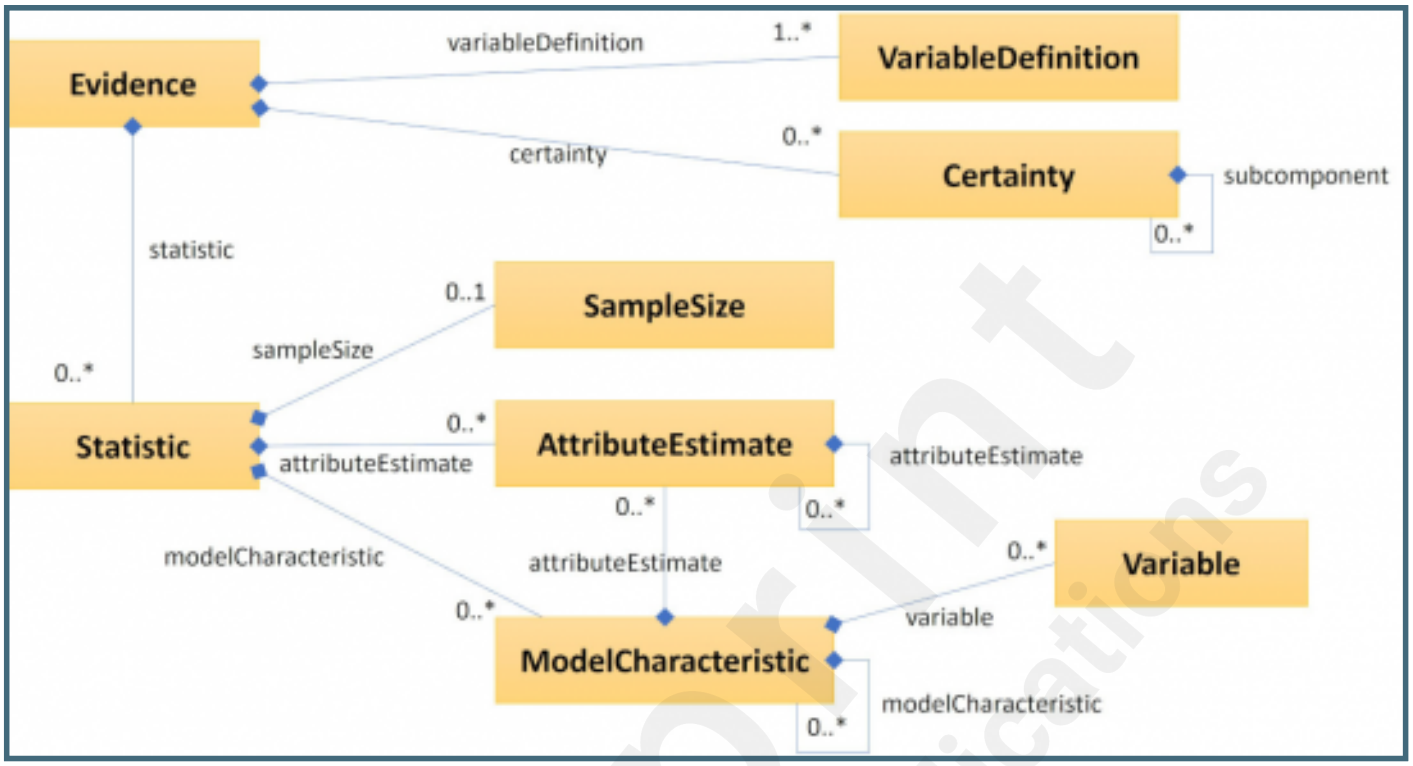
Supplementary Files

Figures

Application of Fast Healthcare Interoperability Resource (FHIR) Resources to the evidence ecosystem. Figure adapted from the "Digital and Trustworthy Evidence Ecosystem".[39] Evidence-Based Medicine (EBM) on Fast Healthcare Interoperability Resources (FHIR®) (EBMonFHIR) denotes application to results of scientific analysis, synthesis and publication. CPGonFHIR denotes application to guidance and decision support. CSV, TXT, XLS, PDF, DOC, HTML, JSON, and XML denote file formats. Other abbreviations include Apps for applications, CDMS for clinical data management system, CQL for Clinical Quality Language, EHR for electronic health record, REDCap for Research Electronic Data Capture, SQL for Structured Query Language.



Evidence Resource backbone elements represented with an abbreviated unified modeling language (UML) diagram.



Sample valueCodeableConcept element showing multiple coding elements. In this example, the coding element represents the COVID-19 disease with both SNOMED CT and ICD-10 terminologies.


```
"valueCodeableConcept": {
  "coding": [
  {
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     "code": "840539006",
     "display": "Disease caused by severe acute respiratory
        syndrome coronavirus 2 (disorder)",
     "userSelected": true
  },
  {
     "system": "http://hl7.org/fhir/sid/icd-10",
     "code": "U07.1",
     "display": "COVID-19, virus identified",
     "userSelected": true
  }
  ],
  "text": "COVID-19"
}
```

Multimedia Appendixes

List of FHIR Data Elements with reference to controlled terminologies introduced by the EBMonFHIR project.
URL: http://asset.jmir.pub/assets/bca6c2b70c32bfdb93f9ced93462b594.docx