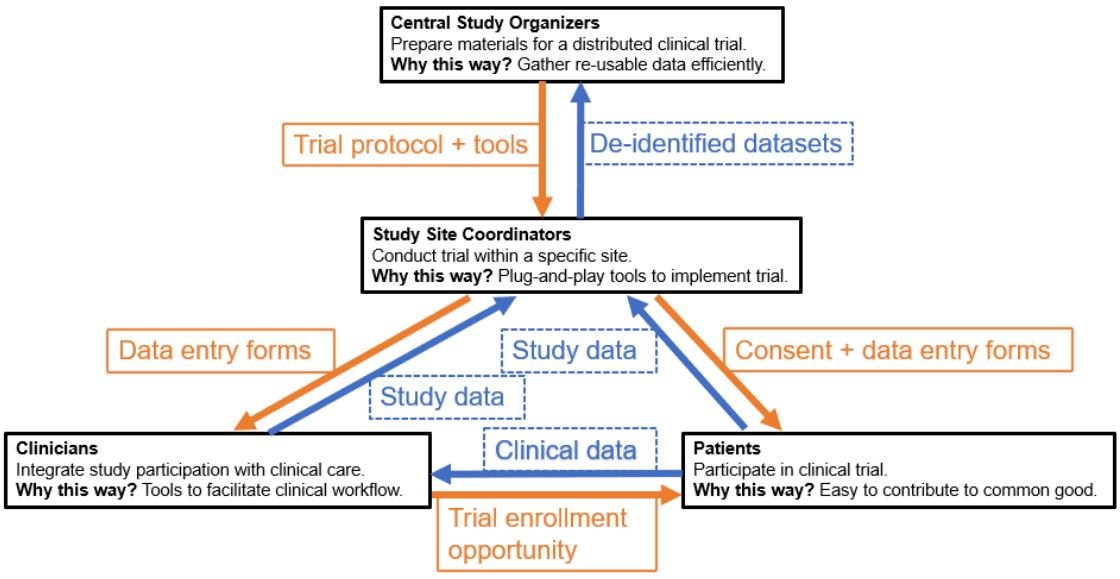
OSTP RFI on Data Collection for Emergency Clinical Trials and Interoperability Pilot

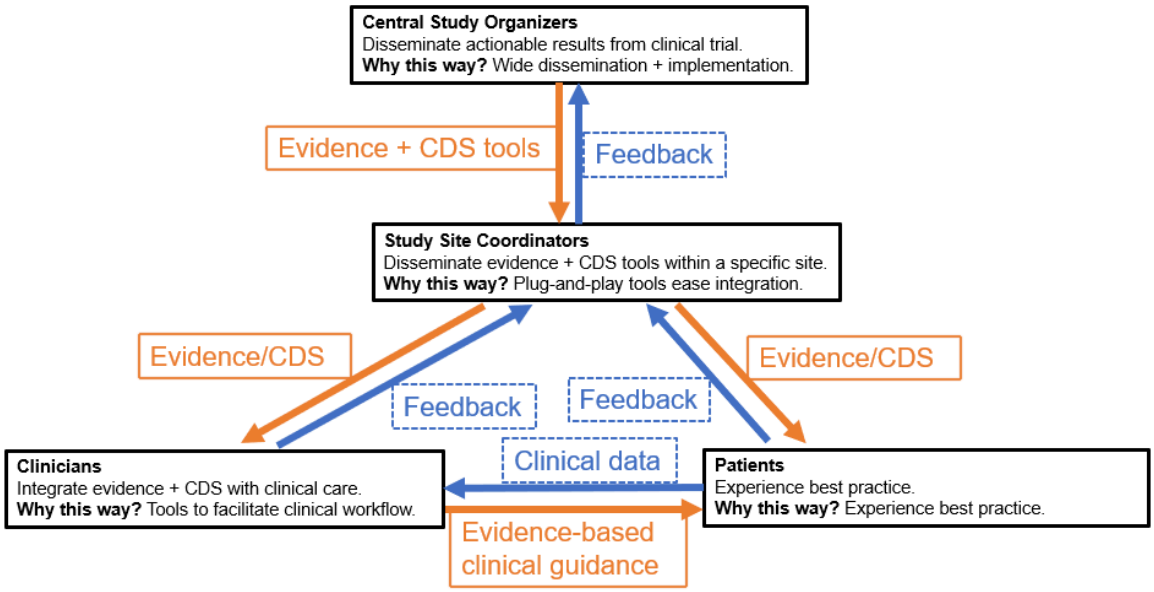
Response from Health Evidence Knowledge Accelerator, a virtual group associated with the Scientific Knowledge Accelerator Foundation. Correspondence to Brian S. Alper, MD, MSPH, President, Scientific Knowledge Accelerator Foundation, balper@computablepublishing.com

The respondent organization is a nonprofit organization with a multidisciplinary constituency including health IT companies, app developers, clinical trial designers, and users of health IT products. The corresponding individual respondent is president of the organization, CEO of a small business that is an IT company providing platform and tooling to support electronic data exchange for scientific knowledge, and project lead for an HL7 project (EBMonFHIR) which is extending FHIR to support data exchange of scientific knowledge including development of FHIR Resources for Citation, Evidence, EvidenceVariable, and ArtifactAssessment.

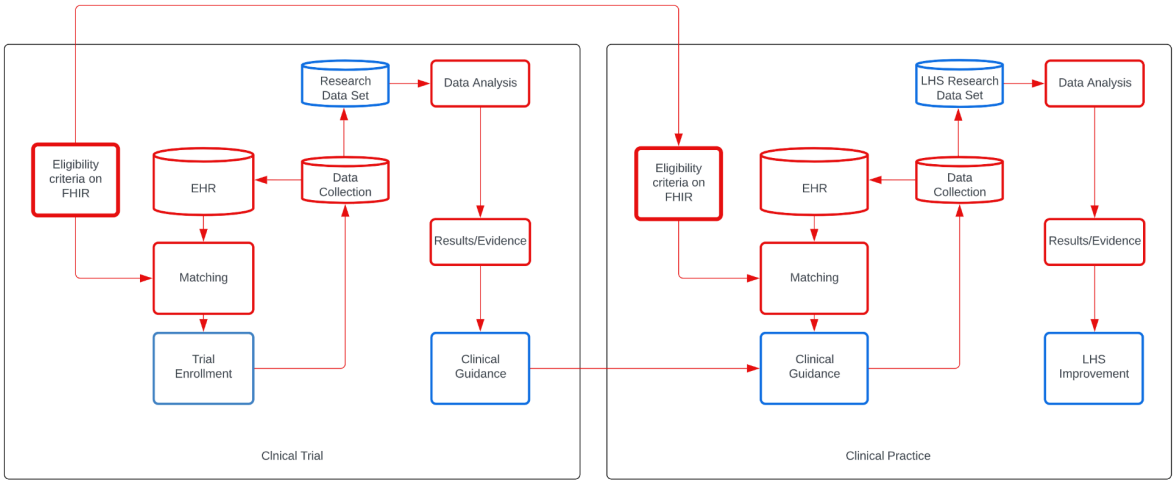
The RFI requests input to support an information sharing model that can be represented as the sharing of knowledge resources between four groups (Central Study Organizers, Study Site Coordinators, Clinicians, and Patients):



The same information sharing model can also be used to facilitate dissemination and implementation of evidence resulting from the clinical trial:



A technical entity diagram showing the similar model for integrating clinical trial conduct with the EHR and integrating clinical decision support with the EHR is:



The model similarities show that the efforts to achieve interoperability for the execution of the clinical trial will also facilitate dissemination and implementation of trial results in subsequent clinical practice.

This RFI response is specific to step 2 of the desired use case:

> "Study sites would enroll participants in the trial (potentially using software mechanisms that can alert sites to potential subjects for a specific protocol in a manner that increases the diversity of trial populations). Sites would obtain appropriate e-consents and authorizations from participants."

Specifically, this RFI response describes how trial eligibility criteria structured in FHIR EvidenceVariable Resources could facilitate this step for a rapid interoperability pilot.

Lacking a simple, re-usable form for the expression of eligibility criteria is a common interoperability challenge for:

- study site selection (based on determination of an adequate number of patients eligible to participate),
- clinical trial recruitment (based on matching eligible patients), and
- the use of trial results for decision support (based on matching eligible patients).

Such eligibility criteria may also be called cohort definitions or clinical phenotypes.

Existing efforts to model structured eligibility criteria include formal expression languages, such as Clinical Quality Language (CQL), and non-FHIR specialized data structures, such as Phenotype KnowledgeBase (PheKB).

The ease of implementation for these efforts has not advanced sufficiently to support an interoperability pilot in 6-12 months. It would take longer to develop and scale tooling and training materials to involve these technologies on such a rapid timeline.

HL7 members, seeking to define eligibility criteria for clinical trials in a FHIR Resource, collaborated with the EBMonFHIR project and we adapted the EvidenceVariable Resource for this use case.

The EvidenceVariable Resource can be used to provide each eligibility criterion in structured form, and the form can be applied with any of the following datatypes:

1) A string, used when structured form is unnecessary or inappropriate
2) A reference to another FHIR Resource where the criterion is defined
3) A canonical URL for a direct link to where the criterion is defined
4) A codeable concept in which the criterion is defined in a structured terminology
5) An expression in which CQL or another expression language can be used
6) A type-and-value combination in which the type of criterion can be expressed with a codeable concept and its value (the values within which the criterion would be met) can be defined with a variety of datatypes (codeable concept, boolean, quantity, range, or reference to another FHIR Resource).
7) A combination of criteria, in which a code can be used to define the method of combination (such as all-of, any-of, at-least, or at-most)

In addition, timing elements can be added to define when any criterion is met.

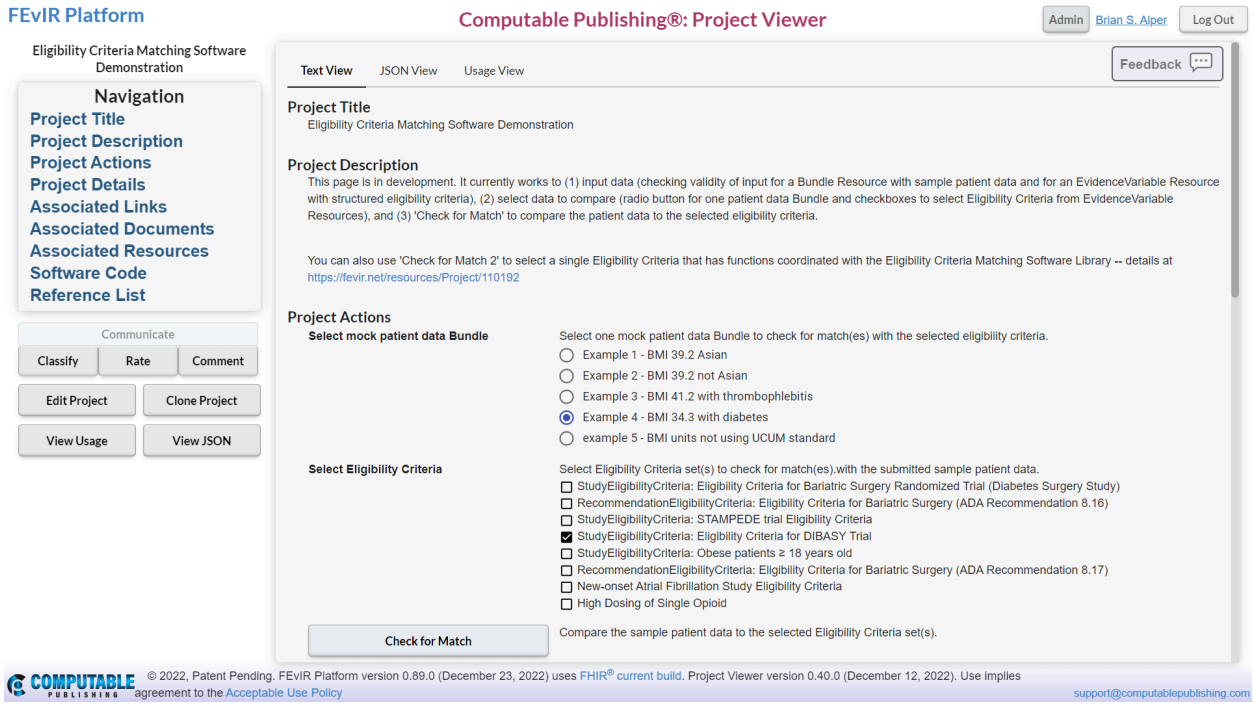
Regardless of the specific datatype used to express eligibility criteria as structured data in a FHIR EvidenceVariable Resource, the ability to use a FHIR-based Resource enables:

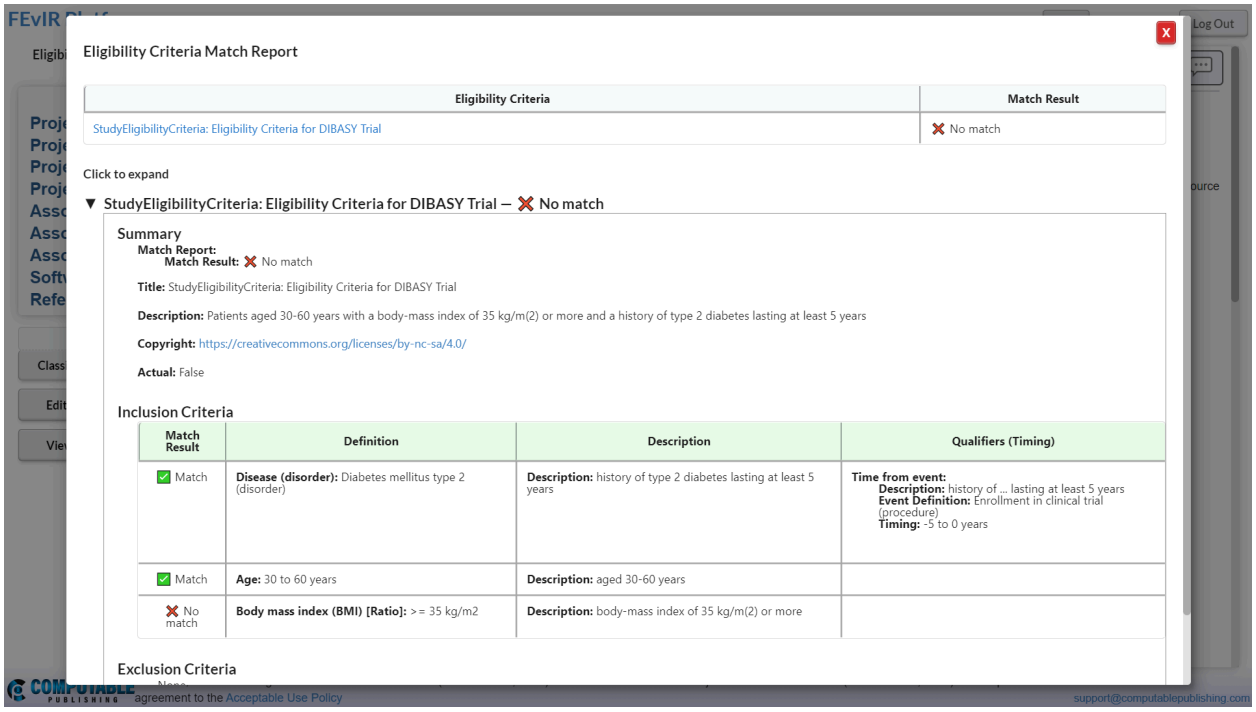
1) Developers already using FHIR can use the same systems for data exchange for eligibility criteria.
2) The tools in development to support human-friendly data entry to express eligibility criteria and automatically convert the data to FHIR EvidenceVariable Resource structure can be completed in time for scaled pilot use in 6 months.
3) Tools to convert FHIR EvidenceVariable expressions of eligibility criteria to CQL expressions can be developed more efficiently than either developing tools to convert natural language data to CQL or training new people to use CQL authoring tools directly.

Three project pages on the Fast Evidence Interoperability Resources (FEvIR) Platform can be viewed to demonstrate these concepts as they are developing.

First, the 'Eligibility Criteria specification with EvidenceVariable' project at https://fevir.net/32444 can be used to view multiple examples of structured eligibility criteria in FHIR EvidenceVariable Resources. When ready we will add links to an Implementation Guide developed by an HL7 project (FHIR Representation of Eligibility Criteria for Clinical Trials at https://jira.hl7.org/browse/PSS-2127) that has been approved and will develop an Implementation Guide in 2023. This effort could be coordinated with an Interoperability Pilot.

Second, the 'Eligibility Criteria Matching Software Demonstration' project at https://fevir.net/51402 can support demonstration of a simple matching algorithm. On this page you can enter a mock patient data bundle (a FHIR Bundle Resource with 1 Patient Resource and any number of Observation and Condition Resources) or select an example mock patient data bundle. You can then enter eligibility criteria as an EvidenceVariable Resource or select an example. Screenshots on the next page will show the result of selecting "Example 4 - BMI 34.3 with diabetes" and "StudyEligibilityCriteria: Eligibility Criteria for DIBASY Trial" and then clicking the "Check for Match" button.


FEvIR Platform
Computable Publishing®: Project Viewer
Admin
Brian S. Alper
Log Out
Eligibility Criteria Matching Software Demonstration
Navigation
Project Title
Project Description
Project Actions
Project Details
Associated Links
Associated Documents
Associated Resources
Software Code
Reference List
Communicate
Classify
Rate
Comment
Edit Project
Clone Project
View Usage
View JSON
Text View
JSON View
Usage View
Feedback
Project Title
Eligibility Criteria Matching Software Demonstration
Project Description
This page is in development. It currently works to (1) input data (checking validity of input for a Bundle Resource with sample patient data and for an EvidenceVariable Resource with structured eligibility criteria), (2) select data to compare (radio button for one patient data Bundle and checkboxes to select Eligibility Criteria from EvidenceVariable Resources), and (3) 'Check for Match' to compare the patient data to the selected eligibility criteria.
You can also use 'Check for Match 2' to select a single Eligibility Criteria that has functions coordinated with the Eligibility Criteria Matching Software Library -- details at https://fevir.net/resources/Project/110192
Project Actions
Select mock patient data Bundle
Select one mock patient data Bundle to check for match(es) with the selected eligibility criteria.
Example 1 - BMI 39.2 Asian
Example 2 - BMI 39.2 not Asian
Example 3 - BMI 41.2 with thrombophlebitis
Example 4 - BMI 34.3 with diabetes
example 5 - BMI units not using UCUM standard
Select Eligibility Criteria
Select Eligibility Criteria set(s) to check for match(es).with the submitted sample patient data.
StudyEligibilityCriteria: Eligibility Criteria for Bariatric Surgery Randomized Trial (Diabetes Surgery Study)
RecommendationEligibilityCriteria: Eligibility Criteria for Bariatric Surgery (ADA Recommendation 8.16)
StudyEligibilityCriteria: STAMPEDE trial Eligibility Criteria
StudyEligibilityCriteria: Eligibility Criteria for DIBASY Trial
StudyEligibilityCriteria: Obese patients ≥ 18 years old
RecommendationEligibilityCriteria: Eligibility Criteria for Bariatric Surgery (ADA Recommendation 8.17)
New-onset Atrial Fibrillation Study Eligibility Criteria
High Dosing of Single Opioid
Check for Match
Compare the sample patient data to the selected Eligibility Criteria set(s).
© 2022, Patent Pending. FEvIR Platform version 0.89.0 (December 23, 2022) uses FHIR® current build. Project Viewer version 0.40.0 (December 12, 2022). Use implies agreement to the Acceptable Use Policy
support@computablepublishing.com


Eligibility Criteria Match Report
Eligibility Criteria
Match Result
StudyEligibilityCriteria: Eligibility Criteria for DIBASY Trial
No match
Click to expand
StudyEligibilityCriteria: Eligibility Criteria for DIBASY Trial — No match
Summary
Match Report:
Match Result: No match
Title: StudyEligibilityCriteria: Eligibility Criteria for DIBASY Trial
Description: Patients aged 30-60 years with a body-mass index of 35 kg/m(2) or more and a history of type 2 diabetes lasting at least 5 years
Copyright: https://creativecommons.org/licenses/by-nc-sa/4.0/
Actual: False
Inclusion Criteria
Match Result
Definition
Description
Qualifiers (Timing)
Match
Disease (disorder): Diabetes mellitus type 2 (disorder)
Description: history of type 2 diabetes lasting at least 5 years
Time from event:
Description: history of ... lasting at least 5 years
Event Definition: Enrollment in clinical trial (procedure)
Timing: -5 to 0 years
Match
Age: 30 to 60 years
Description: aged 30-60 years
No match
Body mass index (BMI) [Ratio]: >= 35 kg/m2
Description: body-mass index of 35 kg/m(2) or more
Exclusion Criteria
None

Third, the ‘Eligibility Criteria Matching Software Library’ project at https://fevir.net/110192 provides shareable code (JavaScript functions) to support re-usable criteria expression and criteria matching expressions. This project was initially created to demonstrate simple functions without integration with CQL or other scaled systems, but the project can be adapted to share code and expressions using languages other than JavaScript.

We have also used FHIR EvidenceVariable (for the eligibility criteria for a research study), ResearchStudy, ResearchSubject, and Consent Resources to facilitate online enrollment and consent for a non-clinical study. In this context, we provided a human-friendly display of the eligibility criteria for potential participants to confirm their eligibility, then provided the consent document as an attachment for viewing, and upon electronic confirmation of consent, created Consent and ResearchSubject Resources to use for documentation and subsequent research conduct. The original project was ‘Risk of Bias Assessment Tool (RoBAT) Usability Research (RoBATUR)’ at https://fevir.net/29571 but that project is closed so you cannot view the enrollment process directly. We later created a ‘Risk of Bias Assessment Tool (RoBAT) Usability Research (RoBATUR) 2’ project at https://fevir.net/52377 which is inactive but you can view it to experience the enrollment process.

These projects are advanced through the Health Evidence Knowledge Accelerator, a virtual group with 14 active weekly working group meetings. The meeting schedule can be found at https://fevir.net/29272 and these activities can be adapted to coordinate with an Interoperability Pilot.