Dear madam, sir,

We thank you for providing detailed feedback on our manuscript. We are happy to see that overall the reviewers have responded positively and gladly take the opportunity to submit a revised version.

We found the comments from the five reviewers useful and have made the following major changes, roughly in order as they appear in the new manuscript:

1. Moved discussion on the spanning layer and open source towards beginning of the document thereby providing a clear outline of the main arguments of the paper, following the comment 1 from reviewer F and comment 7 from reviewer O;
2. Revised the text on the comparison of GitHub search results, following comment 1 from reviewer I and comment 1 from reviewer J;
3. Added sections to the text explaining technical terms and added a list of abbreviations, following comment 1.1 from reviewer G and comment 5 from reviewer O;
4. Added a statement that the EHDS does not mandate the use of FHIR, in response to comment 2 from reviewer J;
5. Added a reflection on the implications for openEHR and OMOP following comment 1 and 2 from reviewer G;
6. Rephrased our conclusion, following comment 4 from reviewer G;
7. Added a reflection on why FHIR has emerged as a single standard in LMIC, following comment 5 from reviewer I;
8. Added a section on future research following comment 6 from reviewer O.

While a large part of the comments from the five reviewers were consistent (or at least not contradictory), we observed that reviewer F argues for shortening the paper while reviewer O argues for a longer paper that includes an explanation of technical terms. We have chosen for the latter, given our intention to reach a wide audience and introduce the most relevant issues for federated learning and LMICs in an accessible manner.

Besides these changes, we hereby provide specific responses to each comment made by the reviewers, often clarifying our intention or responding to a specific question. We found that reviewer I was the most critical reviewer, whose comments sometimes were also in stark contrast to that of the other reviewers. We have aimed to strike a fair and objective balance in our responses and changes to the manuscript.

We hope this revised manuscript will result in a publication of our paper in JMIR and look forward to the re-review. In the case you decide the paper is not suitable for publication in JMIR, we kindly ask you to consider it for publication in JMIR Medical Informatics.

Your sincerely, on behalf of all the authors,

Dr. Daniel Kapitan

Reviewer F

General comments

Review of Viewpoint on JMIR Editorial on Health Informatics Standards
This viewpoint raises important considerations in response to a recent JMIR editorial, which advocated for convergence on FHIR, openEHR, and OMOP as key standards within the health informatics community. The authors argue that openEHR may not be sufficiently widely adopted to be a universal standard, especially in lower- and middle-income countries (LMICs), where FHIR might be the only feasible common standard among the three. Additionally, the viewpoint highlights several other significant standards that the editorial overlooks. The viewpoint effectively challenges the editorial's recommendations and presents a valid critique of openEHR as a universal standard. Emphasizing these well-supported arguments and reducing extraneous details will strengthen the viewpoint's position.

Major comments

1. *The writing could be more effective with a clearer structure. For example, the viewpoint opens with strong arguments regarding gaps in the editorial's reasoning but the concept of a "spanning layer" isn't introduced until the end. It would be more impactful if moved to the beginning alongside the main arguments. Also, at one point the authors remind the reader that their main point is about open source, but this isn't clearly stated earlier in the manuscript.*

   We agree with the two points made here and have updated the manuscript accordingly. The concept of the spanning layer and the main point of open source are now mentioned earlier.

2. *The middle sections delve into technical discussions of Federated Learning architectures, the PLUGIN framework in the Netherlands, and LMICs' specific informatics needs While these examples illustrate the complexity of standard selection, the level of detail given to PLUGIN and LMICs seems tangential in a rebuttal viewpoint. Reducing these sections` length would improve focus and cohesion.*

   We recognize that the arguments for both use cases are lengthy. However, we do feel that it supports the main arguments of our paper. Our intention with this Viewpoint is to address a wide audience and introduce the most relevant issues for federated learning and LMICs in an accessible manner, hence a more lengthy description. Furthermore, given that reviewer O commented that the section on PLUGIN could be longer, we have tried to strike a balance between all the feedback that we have received.

Reviewer G

General comments

This is a very detailed review of a highly technical subject. The review relates to a previous publication /review of the subject and presents a reasoned set of arguments to support the authors' proposed position on the adoption of open health data standards.

Major comments

1. *The review supports the adoption of the three standards but also concludes that FHIR alone might be adequate (with specific caveats for required adjuncts / complementary systems). It is not clear to the less technically proficient reader which outcome should be preferred. The authors correctly conclude that mandated update of FHIR based systems has contributed materially to uptake and use but discussion of the implications of this for the other two systems could be extended.*

   One of the key arguments is that indeed the uptake of FHIR has been spurred by the fact that it has been mandated as the primary exchange standard. One of the implications of this, is that FHIR is used beyond its original scope (exchange) but also as the standard for longitudinal storage (as exemplified by the PLUGIN use case) and as the standard for the system-of-record (LMIC use case).
   We do not argue for or against any preferred outcome, and feel that the choice of standards will remain context dependent to a large extent. Whether the increasing adoption of FHIR will lead to less adoption of the other two standards remains to be seen and is not something that we aim to make an explicit claim for.

2. *The discussion of federating learning is very detailed but the conclusion that OMOP is desirable for this function seems slightly at odds with the arguments presented. I would take issue with the distinction between routine health data and clinical research data and the consequent argument that different data standards might be appropriate. In an evolving real time clinical outcomes monitoring environment, all health data should be research grade and applicable to analysis for quality monitoring and improvement.*

   In our presentation of the PLUGIN use case, our main points are i) that OMOP and FHIR can interchangeably serve as a standard; and ii) that FHIR is more amenable to be integrated with the principle of late binding. We agree with reviewer G that in an ideal world all health data should be research grade. However, in practice we observe that in a clinical research setting, much more

time and effort is spent to collect and curate data by hand using electronic data capture systems that feed into OMOP. In comparison, in a routine healthcare setting, resources are very limited to curate records one by one before it is made available for secondary re-use. One of the motivations of using FHIR in conjunction with late binding for PLUGIN is to use machine learning techniques to improve the data quality in the data pipeline.

3. *The argument for standards in LMICs is again ambiguous. There is support for FHIR based systems but a conclusion in favour of Open EHR that does not seem entirely consistent with the narrative.*

   Our intention was not to argue in favour of OpenEHR, on the contrary: we argue that the convergence towards FHIR for all types of data usage (clinical administration, exchange and longitudinal storage) is a good thing that will help in health data standardization in LMICs going forward. Upon reviewing our manuscript, we don't see how we could formulate that more clearly. For example, we state "... openEHR is rarely used as the standard for clinical administration in LMICs" and "... OMOP and openEHR are less modular in their design and are thereby less suitable as a standard to implement the subsystems defined, for example, in the OpenHIE specification."

4. *The conclusions that the authors agree with the proposal of Tsafnat et al may be conciliatory but is not totally consistent with the arguments advanced. A clearer statement of the author's position would be desirable.*

   We agree that our concluding paragraph can be clearer, and have changed the wording accordingly.

Reviewer I:

General comments

The paper is a response to the recently published Tsafnat et al paper. While the subject and discussion is interesting, it is overall quite superficial with regards to its methodology and also its contributions. The discussion of the standards is descriptive and does not engage deeply with technical or operational challenges. Incorporating more specific metrics or lessons learned from real-world implementations would enhance credibility.

We regret to read that reviewer I finds the paper superficial. Based on the feedback from the other reviewers, however, we feel that it has sufficient depth to warrant publication. With respect to the structure and format of the paper: given the subject at hand, we have chosen to take a narrative approach which fits the scope and purpose of a Viewpoint article. Our aim is not to provide original data or lessons learned, but to offer arguments for a different perspective on health data standards.

In addition, we feel that the reviewers comment to more "... deeply engage with technical or operational challenges" is beyond the scope of this Viewpoint article and more suitable in, say, an original article describing a case study. Our intention with this Viewpoint is purposely to sketch more overarching trends which exemplify the various technical and operational challenges, without going too much into the details.

Major comments

1. *To illustrate this, a search on GitHub on "FHIR" yields 8.2 thousand results, "OMOP or OHDSI" one thousand results, and "openEHR" returns 400 results. Isn't this also a result of the difference in scope between the two standards? While OMOP is arguably limited to analytics it provides a ton of functionality out-of-the-box with the ecosystem provided by OHDSI around it (ATLAS, etc.). While FHIR is inherently broader in scope providing more opportunity for writing software around it.*

   because it has been mandated in certain jurisdictions.

   Given the above observation, is the jurisdication truly the reason behind it? With larger commercial players like Microsoft, Google and AWS also providing FHIR-based services and e.g. Apple integrating it in consumer products, what drives adoption.

   Regarding the first comment, we agree that the comparison of the GitHub search is only indicative; it is not intended as 'hard evidence' given the inherently different scope of OMOP compared to FHIR. At the same time, one of our arguments pertains to complementarity and composability of any given standard. The referred difference in scope only adds to our argument, as the extended

scope of FHIR broadens its applicability across the ecosystem. The fact that FHIR is more modular, and allows implementation of sub-systems (see discussion on LMICs) is one of the benefits of this standard, which we see as an additional driver for adoption.

Regarding the second comment, we argue that adoption by larger commercial players is driven (at least in part) because the FHIR standard has been mandated in certain jurisdictions.

2. *The description on the lakehouse architecture on FHIR is interesting, but seems fairly anecdotal. What is the relevance of the technologies described to the rest of the paper or the initial message?*

   We regret to hear that reviewer I finds our argument for a lakehouse architecture on FHIR anecdotal. Within the scope of a Viewpoint paper, we feel that we have presented a clear narrative of the importance of this concept, with references to extant literature on lakehouses. This concept supports one of our arguments, namely that complementarity and composability are important drivers for adoption of standards, too. Given that other reviewers see merit in our argument, we feel that it is an appropriate contribution to the discussion at hand.

3. *While the OpenHIE specification is agnostic to which data standard should be used, in practice the digital health community in LMICs have de facto converged towards FHIR as the primary standard for health information exchange, in line with the proposal by Tsafnat et al.*

   Is there even a reasonable alternative to FHIR at this point which is as comprehensive in its coverage of health informatics concepts? Or what exactly drove this de-facto convergence?

   There are health data exchange standards. As an example, the OpenHIE specification for the Client Registry (link) mentions quite a few, most of which are managed by the IHE International. Most of these standards are quite old, for example HL7 v2. Although there are other, more recent, standards for health data exchange, such as Clinical Document Architecture (CDA), we agree with reviewer I that as of today FHIR seems to be the only reasonable choice. Also here, we argue that the drivers for this are that FHIR has been mandated and that FHIR can be easily combined with complementary technologies and allows for composition of sub-systems. Perhaps it may seem obvious to reviewer I that the FHIR standard is the most logical one to use, however, the whole debate on choosing standard just goes to show that many practitioners and scholars in the field of digital health do not share this view.

4. *SQL-on-FHIR is mentioned repeatedly, but what is the actual adoption of the proposal? As far as I know, e.g. the HAPI FHIR server has not implemented SQL-on-FHIR yet.*

   Reviewer I is right to point out that the SQL-on-FHIR standard is relatively new. The standard, however, has quickly gained traction within the global community: the source code repository mentions 9 implementations at the time of writing (link). While the HAPI FHIR server has not implemented it yet, one of the advantages of the standard is that it allows for various so-called Runners to be implemented as a complement to an existing FHIR server. This way, an existing HAPI FHIR user could start using the standard directly by adding Pathling or Flatquack as an in-memory implementation of SQL-on-FHIR, separate from the existing FHIR server, as explained in the documentation here.

5. *Is a complete convergence towards FHIR as a single standard really something specific to LMIC, or is the reason that western countries have more legacy systems to deal with first, whereas LMIC can start anew on a green field?*

   Whether a complete conference towards FHIR as a single standard is specific to LMICs or not, is something that is beyond the scope of our paper. We do see that LMICs, as of today, are the only place where such convergence takes place. This may well be the case because the context is more greenfield. Another driver could be that the resource-constrained context pushes developments towards just one standard.

Reviewer J:

General comments

This paper (viewpoint) gives a critical overview on the usage of open source health data standards for clinical care and administration, data exchange and analysis/research. In depth federated learning and data sharing are discussed.
The viewpoint is concise, to the point and addresses the relevant aspects, reflecting current developments.

Major comments

1. *Referring to "By comparison, OMOP and openEHR have not yet profited from external incentives to spur the adoption and thereby growing the ecosystem beyond a certain critical mass. To illustrate this, a search on GitHub on "FHIR" yields 8.2 thousand results, "OMOP or OHDSI" one thousand results, and "openEHR" returns 400 results." → These results have to be explained in a more thorough way; OMOP and FHIR cannot be directly compared, it is not a question of either or....Probably an exchange format will have more use cases than a model?*

   We agree that the comparison of the GitHub search is only indicative, see also our response to reviewer I, first comment.

2. *Check for recent updates of the European Health Data Space (EHDS) concerning the requirements (standards).*

   We have checked for recent updates on the EHDS legislation and added this to the manuscript.

3. *By chance one or two spelling errors → check the article.*

   We have done a final spell checking on the manuscript.

Reviewer O

General Comments:

This paper presents an innovative approach to applying FHIR profiles in data warehousing, which aligns with the principles of late binding. The authors' use of concentric circles to illustrate the different levels of constraint is a great visual aid.

Specific Comments

1. *I appreciate how the authors highlight the advantages of using FHIR profiles in data warehousing, particularly in terms of flexibility and scalability.*
2. *The inclusion of real-world examples from PLUGIN's experience with FHIR extensions adds depth and credibility to the manuscript.*
3. *The writing is generally clear and concise, making it easy for readers to follow the authors' train of thought.*

Major Comments

4. *While the concept of late binding in data warehousing is well-explained, I would have liked more concrete examples or case studies to illustrate its practical applications.*

   There are limited concrete examples currently implemented. However, we are in the process of implementing this in one of the projects referenced as an example. We expect to be able to publish this concrete example in the second half of 2025.

5. *Some of the technical jargon may be unfamiliar to non-experts; consider adding definitions or explanations for key terms.*

   We have added sections to the text explaining technical terms, as described in our general changes.

Minor Comments:

6. *Consider adding a section on future research directions or potential areas for improvement in applying FHIR profiles in data warehousing.*

   We agree with the reviewer and have updated the manuscript accordingly.

7. *A brief summary or abstract would help readers quickly grasp the main ideas and implications of the manuscript.*

   A similar comment was made by another review and we have updated the manuscript accordingly.