Author’s response to reviews

Title: A Fast Healthcare Interoperability Resources (FHIR) Layer Implemented Over i2b2

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Author’s response to reviews:

Responses to reviewer 1: all the modifications bring to the text according to these comments are highlighted in yellow.

Reviewer reports:

Diego Bosca (Reviewer 1): This paper presents an implementation on providing a FHIR layer over an existing clinical data warehouse (CDW). Although FHIR is a popular topic, novelty of the paper should be better highlighted.

Comment 1:
Methodology should be revised, as comparison with other Clinical Information Models (CIM) specifications should be made more clear. In particular, authors state that FHIR resources are similar to archetypes, which differs from the opinion of Thomas Beale (see https://wolandscat.net/2017/01/29/fhir-compared-to-openehr/). Taking this into account can be very useful to your paper introduction.

Response:
We agree, we added a paragraph in the introduction section, in page 4, to compare fhir and openEHR according to this post.

We deleted the previous paragraphs according to comment 6 of reviewer 2.

Comment 2:
Also, it is not really clear which version of FHIR is this work based on, apart from looking at the now outdated bibliography link (your link does not point to FHIR 1.0.2 right now but to STU3). You should also state how your FHIR 1.0.2 solution compares to current STU3 FHIR version (and if you have any plans to update/move forward your system in the future).

Response:

We agree, our implementation is based on the hapi fhir api dstu2 version 1.2 corresponding to the fhir specification version dstu2 1.0.0. This version was the released version when we started our project.

According to the reviewer comment, we added a paragraph to describe which version we have used for our implementation in page 9.

Also, we described in the discussion section, in page 20 the main difference between the version used in this work and the current version and how we plan to upgrade our system to the most recent FHIR Specification.

Comment 3:

In addition to that, other available papers tackling the topic of applying FHIR to i2b2 CDW should be reviewed in the introduction/methodology in order to better assess this paper novelty (just to name a few: C3-PRO: Connecting ResearchKit to the Health System Using i2b2 and FHIR, Read only SMART-FHIR façade for i2b2, Evaluation of SMART-on-FHIR I2b2 cell using PCORNET data model, SMART on FHIR Genomics: Facilitating standardized clinico-genomic apps, etc.).

Response:

We read each of these articles, for “C3-PRO: Connecting ResearchKit to the Health System Using i2b2 and FHIR”, Pfifflner et al. developed an extension of the Apple’s ResearchKit framework. This extension allows integrating data from an app to an i2b2 database using fhir but it does not allow to expose i2b2 data using fhir.

For “SMART on FHIR Genomics: Facilitating standardized clinico-genomic apps”, Alterovitz et al. extended the SAMRT-on-FHIR framework to handle clinic-genomics data. This extension of the SMART-on-FHIR framework and also the framework itself (described here (1)) enables to develop medical applications compatible with the fhir standard.

In our knowledge, the only work in relation with the issue of exposing i2b2 data in fhir format is the work by Wagholikar et al. described her (2) and assessed here (3).
Our approach is an alternative to that described by Wagholikar et al. (2) It is based on a locally developed FHIR profile and a purely Java API for FHIR called HAPI FHIR and will not be limited to serve data on a per patient basis.

We added a paragraph at the end of the introduction section in page 5 to discuss this according also with comment 17 of reviewer 2.

Comment 4:

Another thing not really clear in the paper is if the authors should use FHIR profiles or just use the FHIR resources as is. This is an important issue as if only resources are used means that: A) You left part of your data out of the mapping (and you should discuss why you left it out) or B) your data is exactly as the FHIR resource states (which is unlikely, but in any case you should justify it). If you define profiles then you should better discuss what additional fields were/need to be added and how do you plan to make these profiles available.

Response:

We agree.

Defining a fhir profile is not only restricted to adding new elements to the resources which is not our case. Profiling as described by fhir authors (4) is also addressing changes operated on the resources when:

- resource elements are or are not used
- API features are used, and how
- terminologies are used in particular elements

and also by describing of how the resource elements and API features map to local requirements and/or implementations

In our case, we have not added new elements to the fhir resources targeted but we have constrained the resources in the terminologies used, also by defining which elements are used and which ones are not used and by describing the mapping between the fhir data resources elements and the local data elements.

Figure 4 details all this. We also added a new section, profiling, to detail our method in page 8. Our method is partly based on the method described by Lee et al. (5).

We also added a new paragraph in the discussion section, in page 19, to explain that we plan to share our profile in Simplifier.net.
Comment 5:

Discussion section also needs to be improved, as I believe that you have misinterpreted the "six-step" (there are seven...) CIM design and implementation process. It is strange that you argue that you did not do an analysis of the information of your domain (i.e. your CDW) when you discuss on the paper that FHIR resources covered all the concepts needed. I recommend you that you review again the steps of this methodology and try to classify the things you already did (scope definition, analysis, design or selection of CIMS...). Also, it is possible that you have not performed the steps 6 & 7 of the process, but probably it is useful for your project that you think about how you would deal with publishing, maintaining, and governing problems that can arise (and tell the reader your plans so we can all learn).

Response:

We agree. We added several paragraphs to the implementation section (in page 8 and 9) to better describe our method and we have also modified the discussion section in consequences in order to discuss each of these steps (in Page 17, 18 and 19).

Comment 6:

Some final considerations

The paper is full of links to external sites, please try to put them as proper bibliography or either footnotes if the journal allows it.

Response:

Done !

Comment 7:

Please review the "FHIR query" from table 2, as even if the text has been masked, the URI still points to "10.149.219...".

Response:

Done !

Comment 8:
This in fact brings the topic of security to the table: Have the authors implemented any of the security mechanisms provided by the FHIR standard?

Response

The security layer is under development according to the recommendation of the fhir authors described here (6). The server will soon include two level of security recommended by the FHIR authors:

- Authentication: where verifying that the user is who they say they are. This layer will implement an HTTP basic Auth coupled with the local Lightweight Directory Access Protocol (LDAP) server.

- Authorization: where verifying that the user is allowed to perform the given action. This layer will implement the AuthorizationInterceptor class of the Hapi FHIR API to examine the client request in order to determine whether a “write” or a “read” operation is legal.

We added a paragraph in the discussion section, page 20 to describe that.

Comment 9:

Finally, please review the use of English. Even if English quality is fine for most of the paper, a few pages should be revised in order to make them more understandable (e.g. second half of page 15)

Response

An English native speaker has reviewed the paper

References


Responses to reviewer 2: all the modifications bring to the text according to these comments are highlighted in yellow.

Philipp Bruland, Ph.D. (Reviewer 2): The manuscript entitled: "A Fast Healthcare Interoperability Resources (FHIR) Layer Implemented over i2b2" deals with the connection of their hospital-network wide clinical data warehouse (CDW) with a FHIR server. The described proof-of-concept is a promising approach for extracting data from a CDW via FHIR resources, which helps to access data on a standardized way from the popular i2b2 CDW. Nevertheless, the manuscript suffers from several inconsistencies and questions which should be answered before re-submission:

Comment 1:
- Please try to reduce the use of abbreviations (mainly FHIR) in the abstract.

Response:
We have deleted 8 instances (5 fhir) of abbreviations in the abstract section.

Comment 2:
- At the end of the "Introduction" you firstly mention the topic of CDW (& i2b2). This should be introduced more early and motivate why it would be so interesting to use FHIR over i2b2 to underline the need for your new concept. You have introduced FHIR in a very detailed way later, but i2b2 is only dignified with very less words.

Response:
In the introduction section, page 2, since the first paragraph we discuss the advantages of data warehousing EHR data for research purposes and the inconvenient of using operational database (ehr) for this purpose. The paragraph starts with “Deriving benefits from the reuse of EHR data through data warehousing seems to be the best strategy…”

Nevertheless we added a new paragraph (In page 2) to detail the case of the i2b2 clinical data warehouse and how it was used in the ehr4cr project where the interoperability between the i2b2 sites was an important challenge for the researcher.

Comment 3:
- I would also add a statement, about why you connect it to your CDW and not to DXcare/ORBIS? This would strengthen also table 1.

Response:

We have connected the fhir server to the i2b2 cdw because the most efficient way to take benefit from reusing ehr data for research seems to be to data warehouse these data as stated by Weng et al. (1) and De Moor et al. (2). Querying operational databases for the purpose to reuse ehr data for research could be computationally intensive and requires local specific expertise, also, because operational databases relying upon EHRs are difficult to query knowing the multiplicity of relational tables, which are optimized to facilitate patient management but are not suitable for research purposes …

This is detailed in the first paragraph of the introduction section with multiple references.

However, for other purposes than research, connecting the fhir server to our ehr is a good perspective to enhance his interoperability.

Comment 4:

Reference 24 is enough in the text; can be removed from the table legend.

Response:

Deleted

Comment 5:
- In 2.2 I would suggest to formalize the "functional requirements" of your software; this is currently very narrative.

Response:
We agree, we added two new figures to formalize the end user requirements using UML diagrams: Figure 1 and 2 and a paragraph to describe them in page 8.

Comment 6:
The manuscript contains several passages that don't provide added value to the reader and can be looked up elsewhere. This concerns almost the whole "Implementation" section. What FHIR resources, profiles, terminologies and the API are, can all be cited. At this stage the reader would expect how you have implemented it.

Response:
We agree, we deleted all the paragraphs describing the different FHIR components. We rewrote the implementation section in order to better describe our method.

Comment 7: Section 4.2 also contains description about ICD and ATC codes which could be assumed as known.

Response:
We deleted these paragraphs

Comment 8:
In addition, please take a careful look into the "Submission Guidelines" for "software paper". Some text passages do not belong to its current section. The architecture (Figure 1) should be placed in the "Implementation" section. E.g. the HL7 HAPI should be mentioned here and not introduced in the "Results".

Response:
We agree, we put the paragraph describing the architecture of the server under the implementation section. We made the same thing for the other sub titles related to the architecture of the server. According to the submission guideline, the results section contains only the paragraphs in relation with the assessment of the server.
Comment 9:
- Section 4.3: The Oracle URL could be cited and put in the "References".

Response:
Done !

Comment 10:
- At the end of 4.4 I’m not sure what you mean with this suffix.

Response:
We deleted this sentence and replaced it with: “…identified its system with an uri like:…” in page 12.

Comment 11:
- What is exactly shown by figure 4? Is it the query or the results of a query?

Response:
Figure 4 and 5 are now Figure 7 and 8. They represent the set of data displayed by the fhir server in response to fhir queries described in Table 2. We changed the title of each figure to better describe these two figures.

Comment 12:
- Last sentence of 4.5 is about validation. Here I would expect to see any validation results as we are in the "Results" section. I also could not find any information about how you did the validation. Ad-hoc SQL queries are only mentioned here and in the introduction. You should explain it in detail.

Response:
We agree, we added a paragraph at the end of the results section, Page 15, where we better explain how we have validated the results.
“We validated the results displayed by the FHIR server in response to these two queries by asking the HEGP i2b2 database administrator to query the i2b2 database server to respond to the “client” requirements described in Figure 1 and 2. The database administrator wrote two ad-hoc SQL queries for these two objectives and the results were extracted in csv files. All results (80 FHIR DiagnosticReport for 36 patients) displayed for query type #1 were manually verified and compared. For query type #2, we randomly chose 30 patients from the results displayed by the FHIR API and manually compared them to the corresponding results of the SQL query. The comparison showed exactly the same results.”

Comment 13:
- In the first part of the "Discussion" section, you are introducing three new concepts (virtual federated view, VMR, VHR). Why are they only here relevant and not mentioned earlier? Same with "data client system" and "data source system".

Response:
We preferred to raise the research trait of this work from two points of view. The first one described in the introduction section describes a more recent point of view related to concepts like “dual model approach”, the overall of references cited are more recent and exclusively related to the healthcare domain.

In the discussion section, the research problem is presented from a less recent point of view as we start with this sentence: “Data integration is neither a recent research question nor exclusively related to the healthcare domain”.

The point of view described in the discussion section is also in relation with concepts that are not only related to the healthcare domain like “virtual federated view”, etc.

Comment 14:
- On the second page of the "Discussion" you are stating "…Several articles reported works…” which are these articles? Please give references.

- You also state that "…most used CIM is openEHR...." From where did you know? References?

Response:
All these sentences are in relation with the same reference: the systematic review of Moreno-Conde et al. reference number 13.
We have added this reference for each of these sentences in page 17.

Comment 15:
- On page x line 30, below the reference of Table 3, the sentence "Fortunately…" is quite narrative.

Response:
This sentence have been deleted according to comment 16.

Comment 16:
- Why did you place Table 3 and Figure 5 in the "Discussion"? Is it not worth for "Results"? If it does not add anything to your message I would suggest removing them.

Response:
According to your comment number 8, we followed the submission guideline and Figure 8 are now a part of the results section and we have deleted Table 3 and the corresponding paragraph as we agree that it does not add anything to the message.

Comment 17:
- A major point is that you state in the beginning of the "Conclusion" (much too late) that this (your) work is an alternative to "SMART-on-FHIR implemented over i2b2". Since this work seems to be very similar to what you have done in your work, you must provide a statement on how your work is different to "SMART-on-FHIR …over i2b2" and this should happen in the "Introduction" or at least in the "Discussion".

Response
We have not yet been able to install and test the i2b2 fhir cell and to compare it to our server.

However, according to the descriptions made in the articles (1) (2) and the technical supplements attached, the mains differences are:
- Our approach doesn’t use the SMART-on-FHIR specifications but it is based on a locally developed FHIR profile,
- Our approach is based on a pure Java API for FHIR called HAPI FHIR
- Our approach is not limited to serve data on a per patient basis

We added a paragraph in the introduction section to address this point in Page 5.

Comment 18:

- Further questions concerning the overall idea of your manuscript are:

-- Did you use the standard FHIR resources or did you create some new or did some extensions? If so, are they provided as such?

Response:

Defining a fhir profile is not only restricted to adding new elements to the resources which is not our case. Profiling as described by fhir authors (3) is also addressing changes operated on the resources when:

- resource elements are or are not used

- API features are used, and how

- terminologies are used in particular elements

and also by describing of how the resource elements and API features map to local requirements and/or implementations

In our case, we have not added new elements to the fhir resources targeted but we have constrained the resources in the terminologies used, also by defining which elements are used and which ones are not used and by describing the mapping between the fhir data resources elements and the local data elements.

Figure 4 details all that. We also added a new section, profiling, to detail our method in page 8-9. Our method is partly based on the method described by Lee et al. (4).

Comment 19:

-- You mentioned a clinical decision system. In this regards it would be good to know whether in France is any kind of legislation concerning the medical device directive for which CDSS need to be certified for daily clinical usage.

Response:
In France the certification by the Haute Autorité de Santé (HAS) which is the equivalent of the Joint Commission in the USA is in relation with the CPOE system in his whole, there is no certification in relation especially with CDSS systems.

Here is a link about the cpoe certification (in French): https://www.has-sante.fr/portail/jcms/r_1499086/fr/certification-par-essai-de-type-des-logiciels-d-aide-a-la-prescription-en-medecine-ambulatoire

Comment 20:

-- For users and developers it could be helpful to know how they could enhance this server towards additional FHIR resources.

Response

We added two paragraphs in the implementation section (Pages 12, 13) to better indicate to the developers which classes should be modified in the case of serving new resources and which classes should not be modified at all only if the i2b2 data model is modified.

Comment 21:

Overall, please read your manuscript carefully concerning typos and wording, and provide page numbers which make it easier to reference positions.

- E.g. second page line 46: "Tow type" should be "Two types…"

- Same page, line 52: "We are able…."

- Section 2.1, second chapter: "…inpatient and outpatient reports, etc." No dots. And start a new sentence.

- Section 2.2: "The present […] project whose aim it is to design…"

- Please use consistent spelling of words, such as Java.

- Discussion: "Data integration is neither a …(29) nor exclusively…."

- Please check if you already have introduced abbreviations. Such as "CIM", "CPOE" and capitalize them in its list at the end.
- "in order to" could be shortened to "to".

Response:

Done!

Comment 22:

Finally, please take a look into your source code which shows a lot of hard coded URLs and SQL parameters. I'm not sure whether it is helpful for the re-use of your application to claim going through all the source code to identify variables to be adapted.

Response

We agree, the code is currently under refactoring and a new version should be soon shared on GitHub.

References


Responses to reviewer 3: all the modifications bring to the text according to these comments are highlighted in yellow.

Kavishwar Wagholikar (Reviewer 3):
This work investigates the feasibility of applying the HL7 FHIR standard to modeling and exposing EHR data of the Georges Pompidou European Hospital (HEGP) i2b2 clinical data warehouse (CDW). The authors have implemented a FHIR server over the i2b2 CDW in order to expose EHR data for 5 FHIR resources. Results have been validated by requesting the i2b2 database using an ad-hoc SQL query.

Overall the paper presents a good perspective on FHIR specification and would be useful for research community. However the paper lacks critical details about the presented work.

Following are suggestions for improving the paper:

Comment 1

1) How was the evaluation carried out? Was it a manual comparison of results provided by the FHIR API compared with the SQL queries on the i2b2 database. How many patient records were used for validation?

Response

Yes, for query number 1, all the results (36 patients) have been checked and compared manually between the fhir api and the corresponding ad-hoc query. For query number two, thirty (30) patients have been randomly chosen from the results displayed by the fhir api and we manually compared them to the corresponding results of the ad-hoc sql query.

We added a paragraph in page 15 to explain that.

Comment 2

2) How is the presented work different with the approach provided by the i2b2 FHIR cell. These differences need to be highlighted, to demonstrate novelty of the paper.

Response

We have not yet been able to install and test the i2b2 fhir cell and to compare it to our server.

However, according to the descriptions made in the articles (1) (2) and the technical supplements attached, the mains differences are:

- Our approach doesn’t use the SMART-on-FHIR specifications but it is based on a locally developed FHIR profile,

- Our approach is based on a pure Java API for FHIR called HAPI FHIR
Our approach is not limited to serve data on a per patient basis.

We added a paragraph at the end of the introduction section according to a comment from reviewer 2 to detail this point in page 5.

Comment 3

3) What is the mechanism for securing the FHIR API?

Response

The security layer is currently under development. The server will include two level of security recommended by the FHIR authors (3):

- Authentication: where verifying that the user is who they say they are. This layer will implement an HTTP basic Auth coupled with the local Lightweight Directory Access Protocol (LDAP) server.

- Authorization: where verifying that the user is allowed to perform the given action. This layer will implement the AuthorizationInterceptor class of the Hapi FHIR API to examine the client request in order to determine whether a “write” or a “read” operation is legal.

Other aspects of security should be taken into consideration by developers when installing the server, for example: all clocks should be synchronized using NTP/SNTP, all exchange of production data should be done using TLS/SSL,…

We added a paragraph in page 20 to detail this.

Comment 4

4) Is the resultant FHIR resource complaint with the SMART profile?

Response

Definitely no!

The smart-on-fhir profile is now defined under the Argonauut project as stated here (http://docs.smarthealthit.org/profiles/). We compared the different resources of the Argonaut profile described here (http://build.fhir.org/ig/Healthdata1/Argo-DSTU2/) with those defined in our project:
- May be we are wrong, but we have not seen a definition of an Encounter resource in the Argonaut profile!

- In the other resources i.e. Patient, Medication, medicationOrder and DiagnosticReport, several attributes are mandatory in the Argonaut profile, but not in our resultant fhir classes

Comment 5

5) How are the local codes converted to the standard coding system?

Response

A terminology enrichment layer is currently under development. The implementation of this layer within the French context depends mainly on mapping efforts performed between the French and international coding systems. For medication, the French medication identification coding system is already mapped to ATC at the HEGP and has been used to enrich the FHIR server query results as depicted in Figure 8. This mapping should be externalized for use in the implementation of the terminology enrichment layer.

For the other coding systems, the HEGP hospital was a data provider in a large European project called EHR4CR (4), as a part of this project, Two terminological mappings have been performed for a sub set of codes

- an HEGP local coding system for health measurements and LOINC

- a French local coding systems for clinical and surgical procedures (called CCAM) and SNOMED.

We plan to use these mappings to enhance the terminology enrichment layer of the fhir server.

We added a paragraph to discuss this in page 19.

Comment 6

6) There are several grammatical corrections needed.

Response

An English native speaker read the new version of this article.
References


