



association for **clinical data management**

EHR Integration

ACDM eDigital Data Management Expert Group

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Electronic Health Records, are we there yet?

This reflection paper is a collation of our considerations on the practicalities of integrating Electronic Health Records (EHR) into the trial data for secondary or exploratory endpoints.

We discussed several things such as, what systems are used, how to integrate with these systems and the challenges still faced. Our intent is to share the information we have discussed to date, most of which was pre-COVID, with a view of building on this in the future so we can deliver a position paper to help advise on the practicality of integrating this data into clinical datasets.

This reflection paper is based on the conversations we had as a group and the questions we put forward to Francis Kendall who offered to share his knowledge of how EHR is being utilised in our Clinical Trial space.

Which EHR systems are used in different countries?

Some members of the group with experience of working in Sweden, informed us that each province can choose their own supplier and as there are 17 different provinces, only some are sharing the same EHR provider. Despite being neighbouring provinces two health systems may not talk to each other, which can cause an issue for both researchers but also for patients.

On 5th August 2019, NHS England and NHSX published a list of 8 accredited suppliers (Allscripts, Cerner, DXC, IMS Maxims, Nervecentre, Meditech, TPP, System C)¹ to help organisations and integrated care facilities get the best value for their solutions for electronic health records. A key part of the selection was for integration with other IT systems.

Question to Francis Kendall

The variabilities between EHRs across different countries can be a challenge. In your experience how much variation can we expect to see?

We have limited experience of working across different European countries which have a lot more variability, but even in the US there is a lot of variability. Different centres can be using different systems and collecting different types of information about the subject. In addition to these variations, there can also be subtle differences in the way data is collected and treatment recorded depending on the physician or how the department operates. One of the challenges is understanding where these differences are and it is not something that is necessarily written down. It could easily be a "gotcha" in certain therapeutic areas and that is why you need to work closely with your clinical experts to understand what their treatment protocol is to avoid any potential pitfalls. The original key driver for EHR systems in the USA was for Payment/insurance purposes and thus these systems will need to be modified to have a more clinical outcome focus.

Have you seen any integration with EHR to date?

IQVIA and EMIS have worked together on real world evidence trials to great success and through the years there have been several clinical trials that have each paired with a single EHR with similar success. Indeed, the ability to integrate is not the issue.

In global clinical trials there can easily be 150 sites across a wide number of countries, therefore it is the number of EHR systems you may encounter that could be the limiting factor. In addition to this, the site may have had their EHR system configured differently, creating different versions of the core architect. There could be 30-35 different versions of any one system, which is then repeated across different sites, meaning you could be dealing with 400-500 versions all of which contain different puzzle pieces of the total available information on the subject. This poses a question of how do you integrate so many versions and systems in real life? It is possible the only way this may be feasible is to have a standard interface everyone supports.

The guidance in Britain is for each system and version to share a common backbone, but the reality is that they do not talk to each other all that well, yet.

Questions to Francis Kendall

What is your experience of utilising EHR integration?

When considering EHR data, there are lots of opportunities and the application is fraught with challenges. Remember EHR data is not traditional clinical trial data, and it will never be traditional clinical trial data, therefore EHR data should be used to support evidence where it is complimentary to clinical trial data, at least in the short term. It is not going to replace Randomised Control Trials (RCTs) but will be complimentary to RCTs to support submissions.

To highlight where some of the EHR data opportunities are, firstly, when you are dealing with rare populations you can use the detail within the EHR data to help create synthetic control arms or reference groups. Another opportunity is that it gives more of a longitudinal view of the patient, you are not just looking at one snapshot during the clinical trial, you can follow the patient before and after and potentially explore progression of disease states before a trial starts which may impact outcome. In addition to this there is also the potential to access a wider variety of patient data, such as their imaging and lab data as well as patients from a more diverse background.

Whereas some of the challenges surround the quality of the data, missing data, the multitude of data sources. Any new variables of interest such as biomarkers or labs of interest, likely will not be in the EHR data. It becomes very challenging if you are looking to utilise EHR data on novel new therapeutic areas.

In Roche & Genentech, I worked with Flatiron who are generally seen as gold standard Oncology data source in the industry. They started their business by creating great links within community oncology hospitals, many of which did not have a good robust EHR system. In exchange for providing this good robust EHR system and some good overview reporting, they were able to retain ownership of the data. They invested in an army of medical professionals to help clean the data which they could then sell on. I can bring my experience of working with Flatiron to this conversation and since moving to Cytel I've worked with a number of clients to identify what other data assets are out there, especially when it comes to rare populations. One of those companies that we work with is a partner company of Cytel called Ciox. They process medical records, primarily for health insurance companies and we are started to work with them to transition EHR data into a clinical trial data asset. This provided an eye-opening experience as to the differences in terminology and processes in clinical trial vs how EHR is processed for insurance purposes, such as handling laboratory data and dates.

What is the main issue when we are considering the challenge of collecting new data into EHR?

In this case, we may be asking the different centres to get data from a specific lab for example, but this requires the centre to complete an extra step outside of business as usual as opposed to just requesting to just pulling their EHR data. This also potentially requires them to set up agreements with a third party in order to pull additional data in or to send bloods elsewhere, which can be a difficult ask.

In relation to extraction of the data followed by integration, do you use a particular standard?

I've worked in the past with a company called Precision Data Health to bring the data into a bespoke data model as the first step and then transition it in a SDTM format if that is what is required by the client.

Electronic Health Records, are we there yet?

Do you use EHR data live or for multiple transfers or is it a single retrospective data request? In particular this is in consideration to safety reporting.

It is usually regular extraction over a period of time, e.g., over one or two months, which may be aligned to a particular visit. In the case of safety reporting, it is important to note not all EHR data will include everything you want, which is where an EDC system may come in. Another consideration is that in order to get as much data as possible, companies like Flatiron and Ciox can go back to the patient notes to give the completeness to the EHR data that is in the system.

Some EHR systems have integrated clinical trial data modules so that you can run the clinical trial in the EHR system. Have you come across that?

Yes, but where we're seeing people using the EHR systems at the moment tends to be in rare populations, which is usually done in more than one centre so it makes it a bit redundant to use the EHR/EDC module. This could however be something to consider for the future.

Each extraction often has to be individually mapped because to use an example of taking a blood pressure reading, the nurse may have taken three readings, therefore someone with medical knowledge has to make a judgement of which reading to take as the relevant data point. Have you experienced this extra mapping requirement for the site investigator?

Yes, absolutely. What we are trying to do is place some rules around these decisions. For example, getting the closest variable to a particular date or taking the average of the blood pressure readings. Companies you may be working with might not be used to thinking this way, therefore as a clinical data manager, we have to think about how we want to collect this data, how we want to use it and be clear about what is required. Not all the data is in an electronic health record, some of it will be in the patient notes that will have to be extracted as well, which costs extra each time you request an extraction so you want to be prepared for this up front. Generally, this tends to be a manual process and not natural language processing. Most companies still rely on an army of medical professionals to help extract the data.

Is integrating with EHR a viable option now or in the future?

We hope that it will be an option in the future, providing we can get an international agreed standard. The healthcare sector is ten times larger than research, therefore it will likely need to be led by healthcare and for research to adopt the chosen method.

"PATIENTS KNOW BEST"® a company with an aim of putting patients in control of their own medical records and it may be a viable solution for patients to take ownership of their data and choose to actively share it with research.

Question to Francis Kendall

Where do you see the integration of EHR going in the future? Is it possible to automate this process?

In the short term, we still have to work out the true value proposition for the EHR data and where it can be improved. Then we need to decide how we approach this from a data model or standard point of view. It's probably taken us 20+ years to get to a CDISC standard and EHR data is a much bigger data paradigm so if we're going to go down that route it could take us 50+ years. I believe we need to step back and think about the context of the data and not try to make it clinical trial data.

We also need to look at the way healthcare is changing. More and more medical records are being recorded in an electronic way. With that big push on electronic data capture we have to understand how we can utilise this. There will be more connections with electronic devices and more use of data collected over the phone in a passive way as well as with other devices in the home. It is going to be the future. We have the next 5-10 years to view how we need to handle the data and where we can use this data to support the evidence generation for submissions

As well as your clinical experts, who else would you recommend bringing in to ensure the right level of data is collected?

The system controllers for each health centre need to understand how you want to connect, the scope and the frequency of data collection. They need to work closely with your IT group. In addition to this, you need to ensure all patient confidentiality documents are in place to allow access to the data. You must try to specify everything you need up front and remember there are different stakeholders within each hospital who may have different policies. For example, you may find you need genetic records or imaging, but in order to access these you need to ensure this has been included in the patient confidentiality documents which may also require specific permission from the relevant department.

Why is integrating EHR such a challenge?

As well as there being many different EHR systems, the unstructured way the data is collected and stored continues to make integration hugely challenging and until clinicians stop using paper in the first instance, we will not be able to truly integrate electronically.

During a recent presentation, an American EHR system company discussed their attempt to make a clinical research module for their system, similar to an EDC system but more primitive. Coming back to our earlier example of a blood pressure reading; if 3 measures were taken, which one do you integrate? The investigator found they had to make decisions in real time, which adds to the complexity. It's not just a 1 value to 1 value mapping, you need to add intelligence to the interface.

We also need to decide whether we are discussing a one-off transfer or continual data, in which case should we be using the EHR system to collect data instead of the electronic Case Report Form (eCRF)? Some analysis on CRFs through the years have discovered that depending on the trial and indication there was between 15% and 40% of the data for the clinical trial that could come from EHR. The majority of the data they would still need to collect separately. It may be possible for lab data to eventually go through the EHR instead of the CRF.

Question to Francis Kendall

What would be your advice regarding the challenge around quality of EHR data?

It is about setting your expectations accordingly because you are dealing with this data as it is, we do not have the option to follow up on many data points. Be clear on what you want to get out of the extraction and be realistic on what is achievable. Make sure you sit down with the IT and data management on your chosen sites to discuss this up front.

During our eDigital Team meeting we put together some additional questions that we felt could be of interest to the ACDM members and asked Francis to provide his practical considerations for approaching a project to integrate EHR data:

1. Is there a central person you use for coordinating this within a hospital?

The way we have approached this in the past is to work with the lead clinical investigator in the hospital together with the legal departments, you are then usually guided to the right stakeholders and contacts at the hospital.

2. Do you use any data standards for the integration and which ones would you recommend?

We use a model loosely based on OMOP to get the data in, which seems to mirror some of the dynamics of EHR data and then we can target other data models. It may take another couple of years to get a good EHR data model. It may be that this needs to be more of an approach or how to handle and manage the data as part of a framework as opposed to having a defined CDISC EHR concept.

3. Is there no API involved in the extraction?

Currently we are extracting directly into a data warehouse. We've found that is the easiest way to do it because the IT departments in hospitals can easily provide you the data in different formats in excel files. To start to create a live link would require a lot of negotiations in place.

4. How do you manage unstructured data?

They provide an unstructured data file, which then requires data managers to look at that and pull it in to a better framework.

5. Is it easy to make a contract with a hospital, particularly in Europe?

It's not easy, which is why we typically go with a company like Flatiron or Ciox who already have agreements in place in the US. We haven't attempted to replicate this in Europe yet.

6. Does uni-centre make more sense than multi-centre?

It makes more sense however what I am seeing at the moment is that an EHR approach is used more in rare populations, which requires more centres, therefore this is dependent on the therapeutic area.

7. What do you do in the instance of missing data?

It depends what data is missing. Typically, we find what you are missing in one area you usually gain in another, as long as you are not missing the end-point data that is. Our approach uses the longitudinal data in order to look at trends and modelling and it is important to note there is a big difference to looking at clinical trial data where you need full completeness vs EHR data, which is generally used to supplement evidence generation. EHR enables you to have an overview of the entire population, in order to understand treatment patterns and then you also have the option to utilise machine learning and modelling to see where the trend is leading. As an example, at the University of San Francisco they have been looking into patient journeys for Multiple Sclerosis. This involved a lot of missing data but they were able to look at patterns.

8. Do you see any challenges for oncology studies?

The biggest challenge with oncology studies is where they are looking for the omics data, e.g., genomics, transcriptomics, proteomics, and metabolomics data. Where centres haven't done this before, you will need to set up the agreements.

9. Are there any types or phases of clinical trials where EHR data is more beneficial?

I've seen two use cases. Firstly, in rare populations, because you can't get the patients for a control arm so you can use a retrospective control group as a synthetic control area. The bigger attraction is in the more straight forward therapeutic areas where the endpoints are easy to collect, e.g., cholesterol lowering, where there is an established treatment pattern, where everyone is doing it more or less the same way.

10. What countries are we limited to if we are dependent on companies like Flatiron?

Currently these studies are primarily done in the US, it's a little bit easier to get centres around the US to work in a similar way (as they have a similar origin to meet payer requirements) but it becomes more of a challenge to replicate this across centres in Europe, where there are different rules and different legislation. However, there are pockets of great data across Europe.

11. Which countries have the best high-quality data?

A few of the Scandinavian countries have a more robust, disciplined approach, which it may be worth exploring. Equally Asia-Pacific (APAC) could be a great area to explore, but the native language could complicate the extraction.

12. When it is more economic to consider EHR data?

This is a different data pool; the advantages are to compare data with the payor data to get that complete picture of the patient. You are looking at it in a more complete way. It is not currently being viewed as a replacement for RCTs, therefore I haven't seen a cost analysis on that.

13. Where EHR data has been used to compliment RCTs data, what's the feedback you've had from the FDA?

The FDA are very open to EHR data, particularly for rare disease and they are also including this in the INFORMED database they are producing. There is a big push and a big understanding of how EHRs can be used as evidence to support FDA submissions.

14. Do you know how many studies have utilised EHR data to date?

Generally speaking, we still are in the early days. Big pharma are seriously looking into this and are actively building their data management and data analytics groups, likewise a few of the smaller biotech's in novel areas are also interested because they need access to this data. There is a tendency to start with the assumption that it is cheaper to do this, but that is generally not the case, however it can be quicker.

15. Could AI push for integration?

It might, but AI may just be a quicker implementation technique because you still need to know what you want. We are limited by the number of AI programmers that know what we are looking for and set up the trial properly within the Pharmaceutical Clinical Trial environment. AI may help us get to the results quicker and more efficiently.

Final comments from Francis Kendall

I think it's great the eDigital team are starting to look at this and it's the right time to do it. I recommend that you consider that this is not RCT data but EHR data, so you need to think differently to get the most value rather than to try to shoehorn it into common approaches. EHR data helps to bring a new perspective either retrospectively or in real time on patients in the real world. It's a whole new data management technique and you have a great opportunity here to set the landscape.

Final thoughts from the eDigital team

We had these initial discussions on EHR integration in 2019, however in light of the pandemic we are publishing our considerations now because it is increasingly important to consider how we might innovate around the current challenges in order to continue to support the advancement of drug therapies so that we can improve the quality of life of patients all over the world. We have all had to adapt our studies and utilize new technology and we believe EHR has the potential to become a rich source of data for building a more complete picture of patients in the real world.

There may be ongoing effects from COVID which may change how we plan our clinical trials and the wealth of data available in the healthcare setting could reduce the need for additional on-site patient visits. If we could find a way to make EHR data more accessible and less costly, it has the ability to allow us to continue in a way that is more patient friendly whilst also providing the vital link for real world evidence data as evidence to payees.

The conversations we have held in the eDigital team to date have been encouraging as to the growing accessibility for this data and we will continue to review how our industry rises to the challenges outlined above with a view of determining whether we believe our community is ready to integrate EHR data.

References:

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