Title: Comparison of electronic health records and electronic source data in clinical research trials: a retrospective review

Authors:

Elena A. Christofides, MD, FACE, Amelia Tian, Ada Zhu, Olivia Dennis, and Nicole Mastacouris, MS

Abstract

Accurate documentation of medications and medical history is a critical component in ensuring the integrity of subject data in clinical research trials. With a mandate to use electronic health records (EHR) in healthcare settings, there has been a parallel movement towards integrating EHR and electronic data capture (EDC) software in clinical trials to improve efficiency and accuracy of data entry. However, there is increasing evidence that EHR data tend to be erroneous. The present study is a retrospective review comparing the medications and medical history documented in the EHR versus the EDC of subjects in active, ongoing clinical research studies to assess the validity of the assumption of the utility of using EHR data directly. Our results show significant data deviation from the EHR to the EDC, where 98% of all records were modified for clarity in some capacity. Only 31.3% of all medication records were concordant, and only 45.7% of all medical problem records were concordant. This suggests that principal investigators play a crucial role in parsing out incomplete, inaccurate, and irrelevant information when transferring data from the EHR to the EDC.

Introduction

Electronic health records (EHRs), also known as electronic medical records (EMRs), have been widely established as a means for improving accessibility, availability, and legibility of patient history and information[2]. Parallel to the increased use of EHRs in healthcare, there has been an increase in the use of electronic data capture (EDC) software for storing subject data collected in clinical trials[4].

For many years, clinical trial sponsors have focused on the promise of EHR-to-EDC integration as a means of improving the quality and timeliness of data in the EDC system. For example, TransCelerate's eSource initiative promotes the acceleration of

implementing EHR-to-EDC integrations in CR trials globally[5].
Despite the assurance that EHRs would improve the safety and quality of care, there is growing evidence to suggest that EHR-related errors result in data which is inaccurate, cluttered, redundant, and/or irrelevant[1]. This is unsurprising given that the primary utilization of EHRs is by insurers to review payment strategies. However, crucial areas of data in the EHR are referenced when screening subjects into clinical research (CR) trials. These include common areas of inaccuracy in the EHR like patients' current medications and medical history[2]. This data is often used to determine subject eligibility, or to stratify subjects into discrete cohorts for analysis. However, since there is no current regulatory system in place to monitor the safety and accuracy of the data, EHRs do not have true interoperability.[1] As such, some observers believe that EHR systems at their current state cannot effectively and safely serve patient care.

In clinical research, the Principal Investigator (PI) is responsible for conducting the trial including the collection of reliable data. They are therefore responsible for ensuring the veracity and quality of the data in the EDC[3]. In this study, we will argue that, given the risk of EHR errata and redundancy, direct Principal Investigator review, interpretation and calibration of the EHR data on current medications and medical history is crucial prior to the data being entered into the EDC. Thus, direct EHR to EDC integration without PI intermediation could result in lower quality and reliability of data with increased risks to patient safety through inaccurate eligibility determination.

In this retrospective study, we focused specifically on two elements in the EHR that are foundational to determining subject eligibility for clinical research trials—problem lists and medication history. We then measured concordance between the subject's EHRs at time of screening versus the data entered into the EDC, for the screening visit, in order to assess how accurate and reliable the EHR data was as a basis for clinical trial data entry. This presumes that the EDC data is the true data and the EHR is the variable.

Methods

We solicited five CR trial sites who were conducting active clinical trials. Each site was expected to comply with all applicable legal requirements and responsibilities for obtaining any necessary sponsor or subject clearance. The sites solicited all utilize the CRIO eSource platform, which is an electronic records system that permits sites to configure source templates and capture source data. This establishes the foundational data for each subject as it pertains to that clinical trial. Sites then use this records system for subsequent entry into the EDC system.

Electronic health record data for 72 subjects were submitted. All subjects had been screened and consented into various trials between January 1, 2020 through December 31, 2021 in different therapeutic specialties previously conducted at the solicited sites. Subjects were included provided that, in the course of a subject's screening, the CR site had obtained an up to-date medical record (e.g. medical progress notes, patient portal documentation) which included problems and medication history. Medical history must have been documented in either CRIO eSource or, for visits completed outside the system, in uploaded copies of paper source.

The subjects' medication history and problem list were extracted and reviewed. For each subject, their Screening visit eSource data and EHR data were printed out from CRIO and presented to the medical reviewer as paired documents. In order to ensure confidentiality of the subjects, any PHI (private health information) within the EHR dataset was redacted by site staff before submission to the medical reviewer. Additionally, eSource data utilized in this study only referred to subjects by the subject ID assigned by the site during enrollment.

Given that the source data is considered the "source of objective truth" for clinical trials, we assumed that eSource served as the true record in our comparisons of EHR vs. eSource. Records were therefore deemed incomplete, irrelevant, and/or inaccurate when comparing EHR to eSource. The medical reviewer analyzed each medication in the EHR and denoted them as "in source" (indicating complete conformity between EHR and eSource), "not in source", or "modified to source" (indicating modification of any kind between EHR and eSource). Next, the eSource medication list for that subject's screening visit was analyzed to find medications which were "not in EHR".

The medical reviewer used criteria defined *a priori* to determine concordance between EHR and eSource data.

Medication History:

Upon comparing medication history records in the EHR and source, the medical reviewer categorized each record as concordant, incomplete, irrelevant, or inaccurate. A **concordant** record was a medication that was listed in both the EHR and eSource. Under the discretion of the medical reviewer, concordant records included records that were deemed "modified to source" as long as the medication was listed in the same dosage, formulation, and start/end date. Spelling errors and conversions of medication names (e.g. from brand name to generics or vice versa) were not considered when determining discordance. The definition used for an **incomplete** record was a single medication not listed in the EHR that was listed in

the eSource. An **irrelevant** record is a single medication listed in the EHR which was not listed in the eSource and deemed immaterial for the trial (e.g. the medication listed was a duplicate, the subject did not report taking the medication at screening, or the medication was completely irrelevant to study parameters). Finally, the definition used for an **inaccurate** record was one that included errors that compromised the veracity of data (e.g. incorrect dosing, start/end date).

Problem Lists:

The definitions of incompleteness, irrelevancy, and inaccuracy utilized in analysis of the medication history were similarly applied in analysis of problem lists. An **incomplete** record was a single problem (including symptoms, conditions, disease, diagnosis, etc.) not listed in the EHR that was listed in the eSource. An **irrelevant** record is a single problem listed in the EHR which was not listed in the eSource and deemed immaterial for the trial. An **inaccurate** record was one which included errors that compromised the veracity of data (e.g. number of years since the subject was first diagnosed with a condition). When comparing problems which were pulled from EHR to eSource verbatim, spelling errors were not counted as inaccuracies.

Similar to medication records, a **concordant** problem record was one that was listed accurately in both EHR and eSource. However, concordant problem records were classified further to account for **mappability** of concordant problem records that were deemed "modified in source". For these terms that were not verbatim transferred from EHR to eSource, we had to consider how much concordance there was between EHR and eSource data after investigator interpretation. If there was not a word-for-word match between a problem in EHR and the associated eSource, the medical reviewer allowed for **consolidation**, **disintegration**, and **term modification** of problems to still be deemed concordant.

The definition of an incomplete record stipulated that the absent information was critical in providing full context on the subject's illness or the nature of the disease. Pursuant to that, non verbatim mismatches in problems between EHR and corresponding eSource were allowed as long as the problems reliably mapped to each other. As an example of allowing for **consolidation**, the inclusion of "coughing" and "runny nose" in an EHR problem list would not be considered irrelevant if they were left out of the eSource as long as a problem those two symptoms collectively map to, such as "common cold", was included in eSource. Similarly, as an example of allowing for **disintegration**, the problem "GERD" in EHR was considered equivalent to the problems "acid reflux" and "regurgitation of food" in eSource. Finally, another consideration of mappability was that of **term modification**. Two equivalent problems which were worded differently between EHR and eSource were not counted as inaccurate (e.g. "chest pain" in EHR and "angina" in eSource data was

forgiven).

Data Analysis

For medication history, descriptive statistics were generated to calculate the average number of records in source which were accurately present in both EHR and eSource (concordant), not present in EHR (incompleteness), average number of records in EHR which were not present in source (irrelevancy), and average number of records with modifications (inaccuracy).

For problem lists, descriptive statistics were generated to calculate the average number of records in source which were accurately present in both EHR and eSource (concordant) not present in EHR (incompleteness), average number of records in EHR which were not present in source (irrelevancy), and average number of discordant records (inaccuracy). We then measured the percentage of EHR records which were in full concordance.

For our secondary endpoint, when reviewing a subject's EHR vs. eSource, the medical reviewer tallied each case of consolidation, disintegration, and term modification (collectively referred to as "**allowed records**"). The average number of allowed records were calculated, as well as the percentage of concordant EHRs which contained allowed records. These statistics served as a measure for how much PI intervention—even in concordant EHRs in—was required in order to adjust EHR terminology to study-appropriate verbiage.

Results

At the individual record level, 98% of the 1506 total problem and medication records were modified in some capacity.

Figure 1 shows the percentage of the total medication records which were modified in source in some capacity. Including concordant records, only 5 records, or less than 1%, of the 764 total medication records were deemed "in source" and not modified in any capacity.

Figure 1: Number of Medication Records Modified to Source vs. Not Modified (In Source)

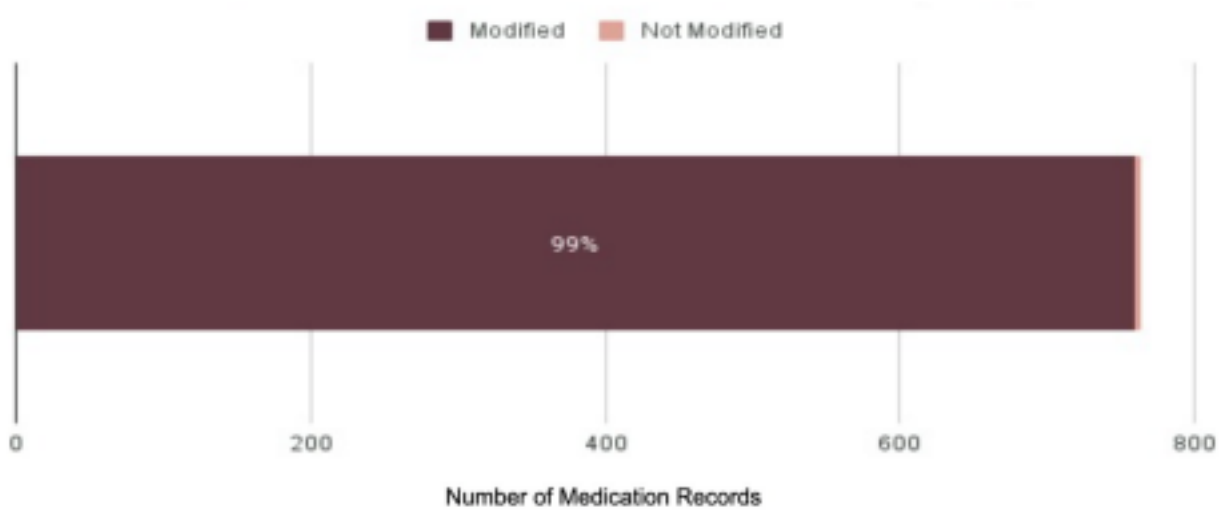


Figure 2 shows the percentages of the total medication records reviewed which were concordant, incomplete, irrelevant, or inaccurate. Of the 764 total medication records, 31.3% were concordant, 37.8% were incomplete, 20.7% were irrelevant, and 10.2% were inaccurate.

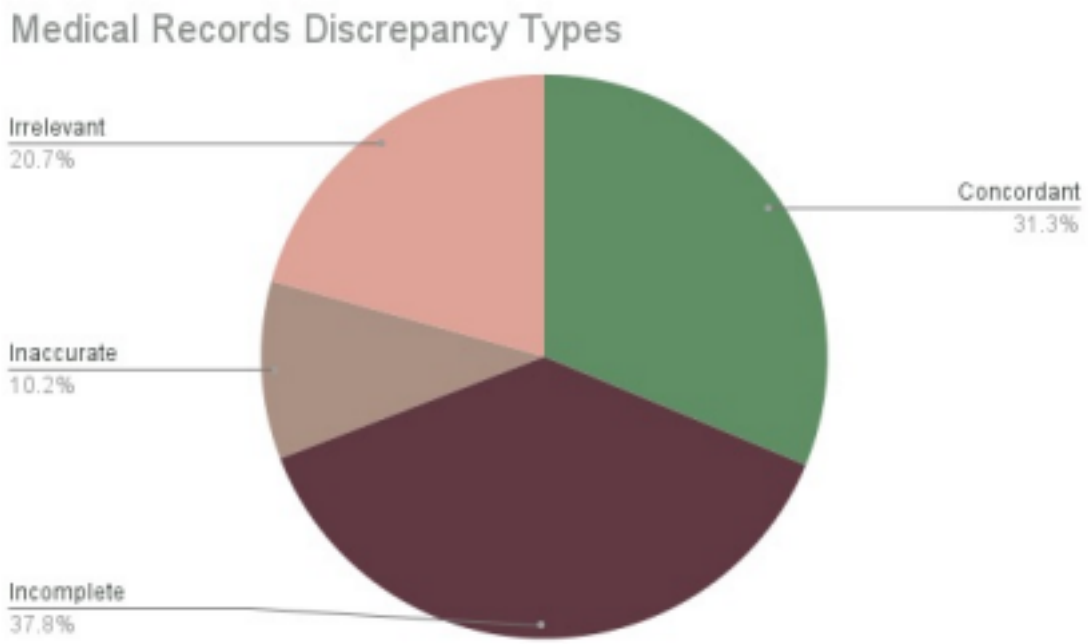


Figure 2: Percentages of Concordant, Incomplete, Irrelevant, and Inaccurate Medication Records

Figure 3 shows the percentage of the total problem records which were

modified in source in some capacity. Including concordant records, only 31 records or 4% of the 742 total medication records were deemed “in source” and not modified in any capacity.

Figure 3: Number of Problem Records Modified to Source vs. Not Modified (In Source)

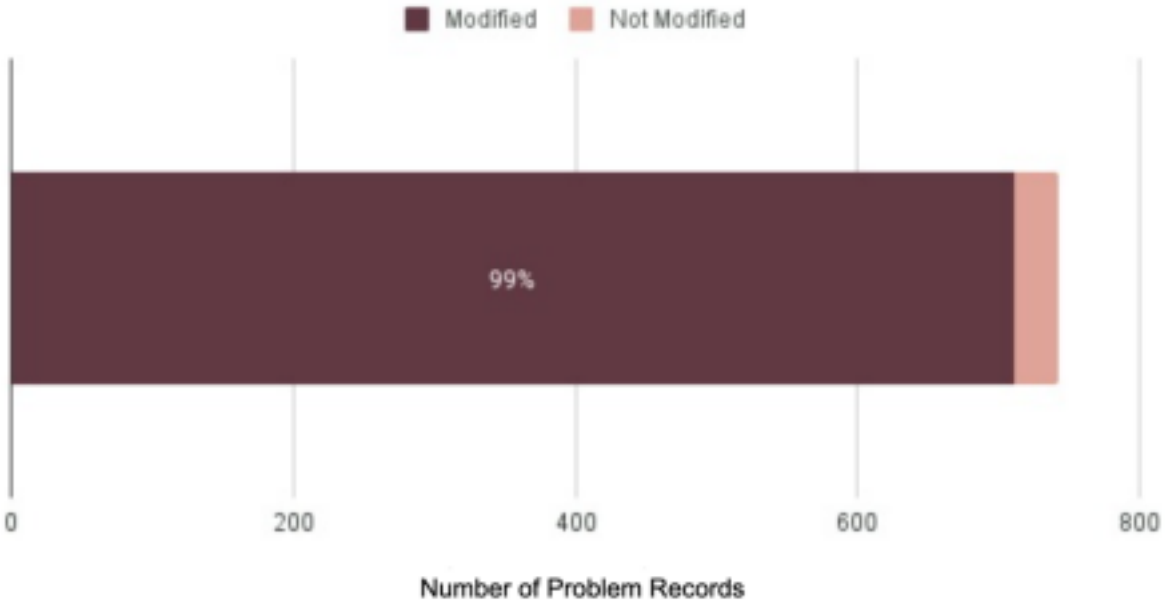
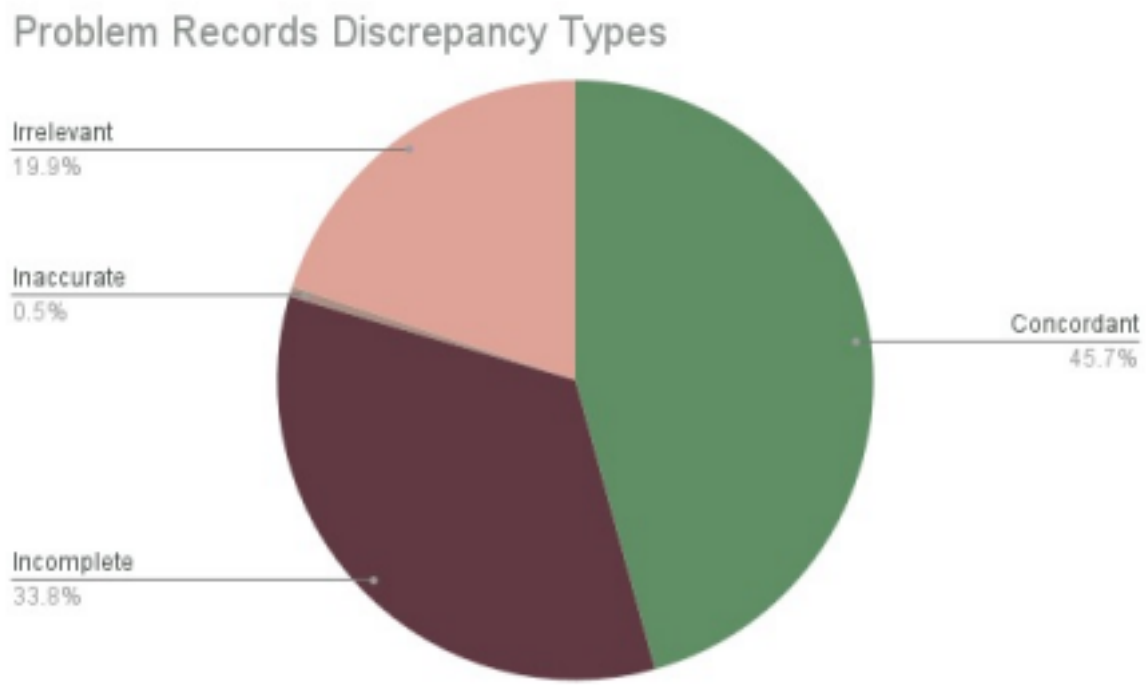


Figure 4 shows the percentages of the total problem records reviewed which were concordant, incomplete, irrelevant, or inaccurate. Of the 752 problem records reviewed, 33.8% were incomplete, 19.9% were irrelevant, and 0.5% were inaccurate.



Of the remaining 45.7% concordant problem records, 17% still required investigator interpretation through mapping.

Figure 4: Percentages of Concordant, Incomplete, Irrelevant, and Inaccurate Problem Records

Discussion

In this present analysis, we measured concordance between the subjects' EHRs, specifically medication lists and problem lists, at the time of screening versus the eSource data, which served as a proxy for data entered into the EDC. Despite EHRs' promise to decrease the frequency of medical documentation errors, our results contribute to an increasing body of evidence detailing the prevalence of inaccuracy, incompleteness, and irrelevance present in EHR data[1,2]. Of the 764 medication records reviewed, only 31.3% were concordant while 37.8% were incomplete, 20.7% were irrelevant, and 10.2% were inaccurate. Of the 752 problem records reviewed, only 45.7% were concordant while 33.8% were incomplete, 19.9% were irrelevant, and 0.5% were inaccurate.

The discordance identified in the present study is notable in that it potentially affects the quality and veracity of data entered into the EDC. For instance, out of all of the medication and problem records analyzed, 98% of the records were modified in some capacity, either modified from EHR to eSource, not included in eSource, or added to eSource when not present in the EHR.
Notably, even for concordant records, 17% of those records demonstrated some degree of investigator intervention in parsing through and consolidating related symptoms listed in EHR into conditions in eSource, disintegrating EHR conditions into separate problem entries in eSource, or modifying terms where appropriate. These decisions made by investigators when reviewing EHR and entering data into eSource are critical in providing a full context of the nature of the subject's disease(s).

Our results reveal a significant schism between the ideal EHR-EDC integration, in which data could flow directly from EHR into EDC, and the practical reality in which investigator intervention is required to audit and interpret EHR data into source data before it is ultimately transferred to EDC.

Conclusion

Our findings suggest that investigator review and intervention is crucial in parsing out inaccurate and incomplete EHR entries, ultimately mitigating the risk of errors being transcribed to EDC. Given the relatively small sample size of the present study, a large-scale study may be beneficial in the future to obtain more information with differentiation between different therapeutic specialties.

Bibliography

1. Bowman S. Impact of electronic health record systems on information integrity: quality and safety implications. Perspect Health Inf Manag. 2013;10(Fall):1c. Published 2013 Oct 1.
2. Hong CJ, Kaur MN, Farrokhyar F, Thoma A. Accuracy and completeness of electronic medical records obtained from referring physicians in a Hamilton, Ontario, plastic surgery practice: A prospective feasibility study. Plast Surg (Oakv). 2015;23(1):48-50. doi:10.4172/plastic-surgery.1000900
3. Mosa, Abu Saleh Mohammad, et al. "Online Electronic Data Capture and Research Data Repository System for Clinical and Translational Research." *Missouri Medicine*, Journal of the Missouri State Medical Association, 2015, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6170092/.

4. Mosa AS, Yoo I, Parker JC. Online electronic data capture and research data repository system for clinical and translational research. Mo Med. 2015;112(1):46-52. 5. Parab AA, Mehta P, Vattikola A, et al. Accelerating the Adoption of eSource in Clinical Research: A Transcelerate Point of View. Ther Innov Regul Sci. 2020;54(5):1141-1151. doi:10.1007/s43441-020-00138-y