Comparing IRB Review of OHDSI Network Studies: Sharing Experience and Guidance

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Background

While the importance of proactively vetting research activities to ensure that patient safety, privacy, and institutional ethics are protected cannot be understated, it is also important for researchers to understand and be able to effectively collaborate with the local IRB process so that impactful research can be executed and disseminated at an efficiency that does not limit the potential for progress in healthcare delivery. This is particularly true in observational health research, where the rate of data acquisition, preparation, and analysis used to be the rate limiting step. Progress in data standardization and the adoption of common data models like OMOP have enabled observational study execution times to go from months to a matter of days.[1] With these robust studies becoming the norm rather than remarkable achievements, it is imperative that informatics faculty and observational health researchers work to optimize their processes for working with the IRB. OHDSI network studies are still a relatively new phenomenon to the larger health research community. With the unfamiliarity of this methodology from data governance boards and IRB reviewers, the sheer number of considerations involved with ensure patient safety and privacy, sharing experience across the OHDSI community to develop an effective process for collaboration with IRBs and clear communication of OHDSI network study protocols.

Methods

This project involved the collation experience and identification of important considerations for IRB review of OHDSI network studies. Individual experiences with the submission of OHDSI network study protocols for IRB review were shared amongst clinical research teams at Johns Hopkins. Feedback and guidance from data governance board members and IRB reviewers were examined across different projects and common issues and unique considerations were summarized. Common information required for IRB application was compared with publicly shared IRB protocols on the OHDSI website. Key language around important points identified by IRB reviewers were compiled to proactively address requests for more information in future protocol submissions.

Results

As was expected with IRB review of observational research, the most common request from IRB reviewers was around the degree of data deidentification. At JHU, the OMOP data resources are available as separate projections with three distinct levels of patient health information (PHI). The minimum level of deidentification applied to the data being used in each project is as follows:

- *Fully identifiable projection of the OMOP CDM. This CDM does not contain any direct identifiers such as MRN, or patient names, but does contain fields such as date of birth and encounter dates.*
- *OMOP CDM which has been determined by the Core for Clinical Research Data Acquisition to meet criteria for a HIPAA limited dataset.*
- *Aggressively deidentified OMOP CDM; which has been determined by the Core for Clinical Research Data Acquisition to meet criteria for a limited dataset and has had sensitive data removed to further prevent reidentification.*

Examining four different IRB applications for leading or participating in OHDSI network studies submitted for review at Johns Hopkins University by distinct clinical study teams in the last six months, each study had unique considerations that were of importance to data governance board and IRB reviewers. The key framing language for each study is summarized in Table 1. None of the protocols were deemed eligible for "exempt" review status. Removing the variance in time added for clarifying information, the primary rate determining factor was the assignment of applications to either "expedited" or "convened" IRB review. Expedited review is assigned to research that presents no more than minimal risk to the participants and does not require full IRB Committee review (convened review).[2] The expedited review process generally moves more quickly than a full, committee convened review. Two of the studies were assigned to a convened review while the other two were considered eligible for expedited review. The specific study features that crossed the threshold for requirement of convened IRB review were evaluation of drug efficacy and utilization of the patient-level predication algorithm.

Table 1. Overview of three different OHDSI networks studies from an IRB's perspective

OHDSI Network Study	Key IRB Framing Summary	Unique Considerations	Review Type
Study A	• Fully identifiable OMOP projection; • Lead site for a network study; • Characterization via executing CohortDiagnostics and Phevaluator	Use of the patient-level prediction algorithm in the Phevaluator package raised concerns about FDA regulations around software as a medical device	Full Review
Study B	• Aggressively deidentified OMOP projection; • Lead site for a network study; • Patient-level prediction study of adverse drug events	Use of the patient-level prediction algorithm prompted requests for more information around FDA software as a medical device regulations Evaluation of adverse drug events for a broad category of drugs	Expedited Review
Study C	• Aggressively deidentified OMOP; • Data partner for an external network study; • Population-level effect estimation	Evaluation of a drug efficacy requires full IRB review; the specificity of drug evaluation was also a difference between Study B	Full Review

Study D	• Aggressively deidentified OMOP projection; • Characterization of comorbidities	Single site study; descriptive analysis only	Expedited Review

Conclusions

The specific language for describing HIPAA compliance among OMOP data projections will vary between institutions. Many institutions consider the removal of all identifiers, minimum cell count rules, and application the shift-and-truncate method to obscure elements of date sufficient to consider a dataset "fully deidentified" rather than a limited dataset.[3] The takeaway point is the importance of being very detailed and clear about the extent of data deidentification and sensitive data removal applied to the OMOP projection being used in a project, as that is a primary concern when IRBs review observational studies using secondary data.

The convened review requirement for evaluation of drug efficacy is due to an exception to research that would otherwise be considered exempt if it involves a drug, biologic, or complementary and alternative medicine.[2] The convened review assignment for the study utilizing the patient-level prediction algorithm is due to consideration of the FDA's recent regulatory changes regarding software as a medical device and is likely a relevant consideration for any institution as IRBs evolve their processes to meet current FDA regulations.[4-6] The ability to provide source code for all OHDSI analysis packages is an asset to investigators and IRB reviews considering these FDA regulations around software, and this highlights the importance of clear and detailed communication of how OHDSI analysis packages will be used and for what purpose.

This work serves as a supportive resource for researchers getting started with OHDSI and a base for developing a more standardized process for dealing with the diversity in IRBs and data governance across the real-world data landscape. It is vital that the OHDSI community continues to support each other in optimizing our collaborations with local IRB review processes by continuing to share knowledge and experience in this domain to facilitate steps towards improving health care delivery.

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