Demonstrating Utility of the Edge Tool Suite through Clinical Trial Emulation

Ruth Kurtycz[1], Wesley Anderson[2], Allan J. Walkey[3], Kerry A. Howard[4], Smith F. Heavner[2,4]
[1] Center for Disease Control and Prevention, [2] CURE Drug Repurposing Collaboratory, Critical Path Institute [3] Chobanian and Avedisian Boston University School of Medicine, [4] Department of Public Health Sciences, Clemson University

Background

Real-world data (RWD) sources, such as electronic health records (EHRs) and claims data, have potential to identify medications previously approved for certain indications to be repurposed for other indications of high unmet need (i.e., drug repurposing).[1] However, these data sources, which can be leveraged to generate real-world evidence, lack standardization across healthcare facilities and organizations. This, along with a lack of data sharing, leads to data silos that make observational research in real-world settings difficult. To address this barrier, common data models have been created to facilitate scalable and reproducible observational research using RWD sources. The Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) is a collaborative data model created by the Observational Heath Data Sciences and Informatics (OHDSI) community. Healthcare institutions that convert their data into a CDM such as OMOP can facilitate an increased ease in both initiating observational research and data sharing, thus breaking free of the limitations of their current data silos.

A drawback to this data sharing process is the time and resources it takes to implement the OMOP CDM, which has previously required thousands of hours of work by a data informatics expert to take a site from no CDM to full implementation. Thus, many healthcare sites with limited size and resources, especially those in disadvantaged areas, are often excluded from implementation of the OMOP CDM. The CURE Drug Repurposing Collaboratory (CDRC), a diverse partnership of stakeholders, aims to provide public access to RWD through the CURE-ID platform by lowering the barrier to convert RWD to the OMOP CDM. This mission led to the development of the Edge Tool suite, which comprises a collection of openly available projects designed to facilitate the conversion of proprietary EHR data into the OMOP CDM.[2] Implementation of this suite of tools has previously been shown to reduce labor costs by up to 90%.[3] The purpose of this work is to look at the potential utility of data extracted and harmonized through the Edge Tool by comparing the results of an observational target trial emulation using data extracted via the Edge Tool to the results of the RECOVERY clinical trial of dexamethasone for COVID-19.

Methods

The Edge Tool enables the extraction, transformation, and loading (ETL) of EHR source data into the OMOP CDM. The suite repository can be found at OHDSI/CureIdRegistry (github.com). Thus far, the CDRC is supporting over thirty healthcare sites in utilizing the Edge Tool suite, with three systems having completed all phases of the ETL process, submitting over 20,000 COVID-19 cases to CURE-ID. This influx of data allows for several potential analyses. To demonstrate utility, an analysis of this data was constructed to emulate the RECOVERY trial, which showed that dexamethasone decreased the risk of 28-day mortality in hospitalized patients, especially those on some level of oxygen support.[4]

A brief analysis was completed with the pilot healthcare site, which contained over 10,000 patient records from between March 2020 and March 2022. A data quality assessment was performed, which evaluated

missingness and plausibility of the extracted EHR data. Outliers in the laboratory values were examined if they fell outside of clinical plausibility rules. Inclusion criteria for patient records included non-missing outcomes, as well as complete demographic and comorbidity information. Patients under the age of 18 were excluded from this study to align with the inclusion criteria of the RECOVERY trial. The RECOVERY trial also excluded pregnant and breastfeeding women; however, due to the limitations of the extracted EHR data, this criterion was unable to be replicated in the trial emulation.

A 2:1 ratio of propensity score matching with replication of controls was used to match patients with any recorded administration of dexamethasone (i.e., treatment group) to patients without any recorded administration of dexamethasone (i.e., control group) within the extracted EHR data. Eleven categorical variables were included in the match; of those, eight were ultimately included in the regression and three were removed and instead used as hard matching criteria due to significant differences that persisted between the groups post-match. The matches were evaluated with Chi-Square tests on each predictor variable to ensure appropriate balance between treatment and control patients. In alignment with the trial analysis, binomial logistic regression and survival analysis using a Cox proportional hazards model were used to assess the effect of dexamethasone administration on 28-day mortality, with the latter also including hospital length of stay (LOS). Both analyses were repeated after stratifying the matched cases and controls by level of oxygen support: invasive mechanical ventilation, oxygen alone, and no oxygen support.

Results

The trial emulation analysis showed that use of dexamethasone was associated with significantly lower 28-day mortality among both those receiving oxygen alone and those on mechanical ventilation when compared to those receiving no respiratory support. This crucial finding aligns with the conclusions drawn from the RECOVERY trial, suggesting that incorporation of medication administration timing by-proxy through inclusion of hospital LOS in the survival analysis is a particularly strong indication for patient mortality. However, this result was not replicated when the stratification by level of oxygen support was removed.

Challenges were noted in the ETL process from the Edge Tool thus far, including difficulty in extracting dosage information related to administered medications, as well as time-of-day information for variables regarding measurements, devices, and administered medications. These limitations may have significantly impacted the results of the analysis.

Conclusion

This study shows the feasibility of utilizing the data extracted with the Edge Tool suite from a RWD source to emulate a clinical trial for an emerging disease. Although there were significant limitations, this analysis shows that extracted EHR data can be used to examine the effectiveness of treatments for emerging diseases such as COVID-19. The goal of increasing the adoption of OMOP into sites with fewer resources and enabling wider participation remains, as the CURE-ID project continues work on expanding the number of healthcare sites that are utilizing the Edge Tool to standardize their data into OMOP. The analysis will be updated in the future as more healthcare sites contribute data.

References

1. Zong, N., Wen, A., Moon, S. et al. Computational drug repurposing based on electronic health records: a scoping review. npj Digit. Med. 5, 77 (2022). https://doi.org/10.1038/s41746-022-00617-6
2. Heavner SF, Anderson W, Kashyap R, Dasher P, Mathé EA, Merson L, Guerin PJ, Weaver J, Robinson M, Schito M, Kumar VK, Nagy P. A Path to Real-World Evidence in Critical Care Using Open-Source Data Harmonization Tools. Crit Care Explor. 2023 Apr 3;5(4): e0893. 10.1097/CCE.0000000000000893.
3. S. F. Heavner, T. Llano, M. Schito, H. Stone, P. Dasher, T. Russel, V. Kumar, B Saeks, M. Cooke, R. Kashyap, M. Robinson, P. Nagy. Lowering the OMOP ETL Barrier for Clinical Registries. OHDSI Symposium, 2022.
4. RECOVERY Collaborative Group, Horby P, Lim W S, Emberson J R, Mafham M, Bell J L, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell L C, Faust S N, Jaki T, … Landray M J. Dexamethasone in Hospitalized Patients with Covid-19. The New England journal of medicine, 2021;384(8), 693–704. https://doi.org/10.1056/NEJMoa2021436