RWD157

Challenges and Opportunities of Using Electronic Health Records in Multi-Country Studies

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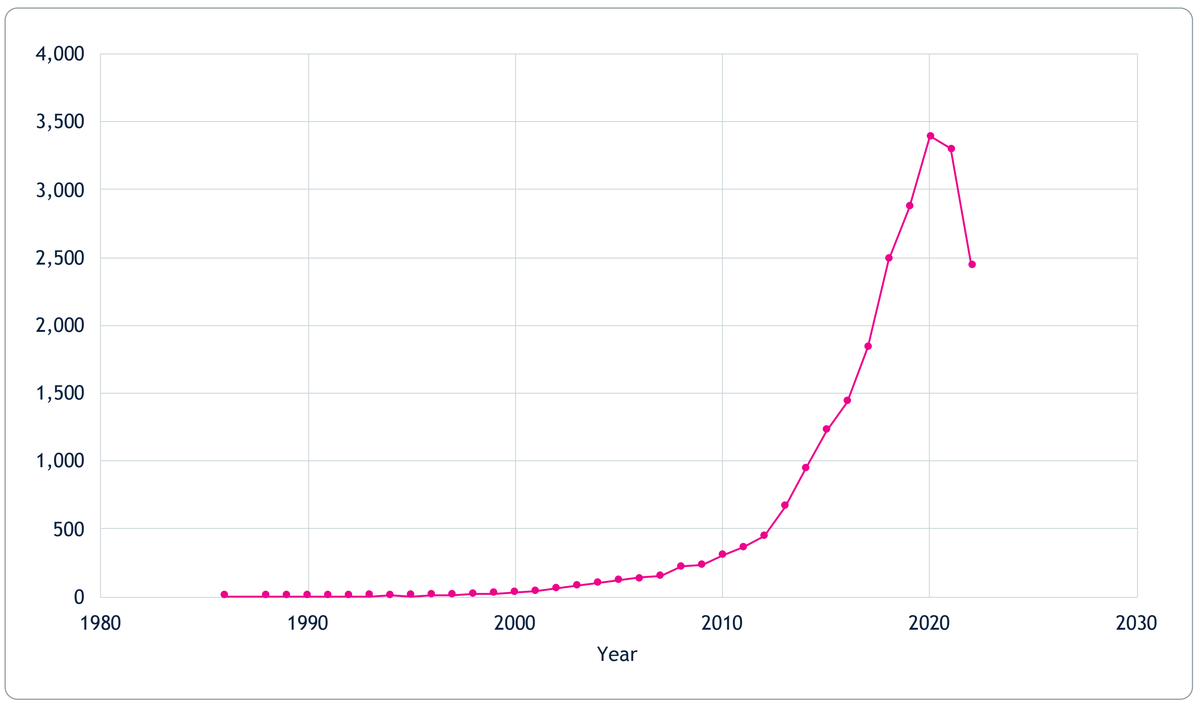
INTRODUCTION

Over the past decade, there has been a substantial increase in the acceptance of real-world evidence, further amplified with the COVID-19 pandemic. This has led to an increase in observational multi-country studies, allowing for the generalisability of real-world findings beyond specific geographic borders.

Figure 1. Number of PubMed hits for multi-country observational studies by calendar year



Note: PubMed search run on 07 Oct 2022 on : ((“multicountry”[All Fields] OR “Multi-country”[All Fields] OR “international”[All Fields]) AND (“observational“[All Fields] OR “real-world”[All Fields] OR “real-world “[All Fields] OR “non-interventional”[All Fields]) AND (“study”[All Fields] OR “cohort”[All Fields])

OBJECTIVES

- To assess the methodological challenges and opportunities for observational multi-country studies based on electronic health records (EHRs).

METHODS

- A review of publications from selected networks at the forefront of multi-country collaborative research studies:
  - The European Health and Evidence Network (EHDEN) www.ehden.eu
  - The European Medical Information Framework (EMIF) www.emif.eu
  - Observational Health Data Sciences and Informatics (OHDSI) www.ohdsi.org
  - The SIGMA Consortium https://sigmaconsortium.eu

RESULTS

Our review found that the increase in observational multi-country studies is being driven by:

- **Generalisability:** the need to demonstrate the safety and effectiveness of treatment across multiple geographies,[1] describe the epidemiology of diseases and their burden in multiple countries,[2] and evaluate associations between risk factors and outcomes in multiple settings.[3]
- **Replicability:** the need to understand sources of heterogeneity in real-world settings and replicate findings from one study into another context.[4]
- **Sample size:** the need to pool samples to increase the size of the study population.[5]

Despite the opportunities that multi-country observational studies afford in generating multi-country evidence, they also involve significant challenges, including:

- **Different structure and coding terminology:** EHRs in different countries are structured in multiple ways and may employ different coding terminologies (e.g., ICD-9/10, SNOMED CT, ICPC).
- **Differences in healthcare systems:** There are inherent differences in healthcare systems which are organised to serve specific populations. This can introduce heterogeneity and may in some instances limit the validity of multi-country studies.
- **Data completeness:** There is also an emerging literature on biases introduced by EHR and claims database studies which emphasises limitations related to representativeness, data availability and interpretation, missing measurement, and missing visits.[6]

ADDRESSING CHALLENGES

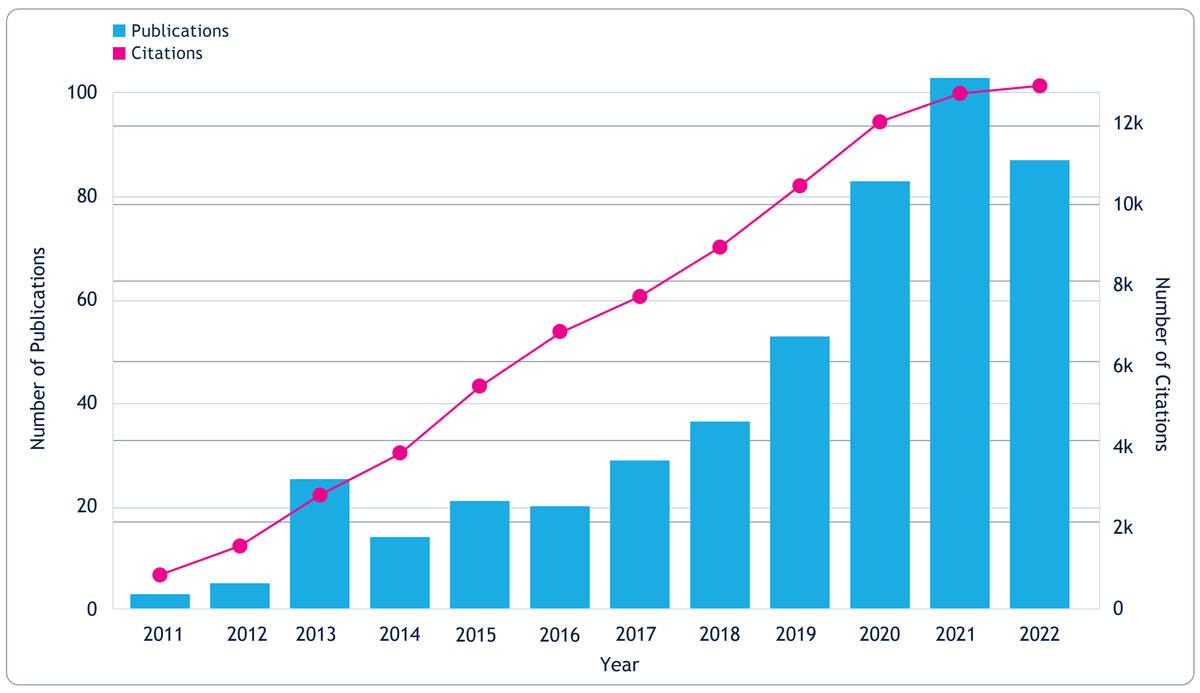
Nevertheless, the review also found that standardisation techniques are emerging to address these challenges, including:

1. The adoption of standards for study development, including Post Authorisation Safety Study Protocol (PASS) Template and European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENcEPP) registration.
2. Ongoing initiatives to catalogue existing data sources and collect metadata information to inform researchers on the most suitable databases for their research study with:
   - The ENCePP catalogue of databases set to be replaced in late 2023 by a Catalogue of Data Sources, including information on extensive metadata developed by the DARWIN consortium following recommendations of the HMA/EMA Big Data Task Force.
   - The continuous expansion of the EHDEN network and the development of the EHDEN Catalogue.
3. Recognised statistical methods for data comparison, such as negative case control, and data pooling, including meta-analytical techniques.
4. The continued use and development of a Common Data Model (e.g., EHDEN and OMOP) for data extraction and analysis in which raw data are standardised to a common structure, format and terminology independently from any particular study, in order to allow a combined analysis across several datasets.[7]
   - The advantages of a Common Data Model are:
     - Rapid (real-time) access to real-world data systems which is accessible to a community of researchers.
     - Privacy is protected with de-identification.
     - Data sources retain ownership and control of patient data.

The rise in database networks underlines the opportunities ahead for performing multi-database studies.

- OHDSI/OMOP is the largest and most successful networking collaboration. The OHDSI network currently includes 2,367 collaborators spread across 74 countries.
- In Europe, the EHDEN network has grown rapidly since its launch in 2018 and currently includes 166 data partners from 27 countries.
- These networks have enabled rapid international collaboration to emerge to answer research questions of interest (see Figure 2), especially for COVID-19 research.

Figure 2. OHDSI publications and cumulative citations



(Reproduced from http://dash.ohdsi.org/publication_dashboard).
PubMed Publication Tracking highlights scholarship generated using the OMOP Common Data Model, OHDSI tools, or the OHDSI network.

CONCLUSIONS

- Researchers seeking accurate answers to research questions across geographic borders need to consider the potential benefits and drawbacks of observational multi-country studies. However, we believe we are entering an era where emerging standardisation techniques afford greater opportunities to generate rapid and robust multi-country evidence based on EHRs.
- As industry professionals and researchers, we must advocate for the use of a standardised methodology for multi-country studies to ensure the reporting of reliable, valid and generalisable findings.

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REFERENCES

1. Prats-Uribe A, Sena AG, Lai LYH, et al. Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study [published correction appears in *BMJ*. 2021 May 21;373:n1277]. *BMJ*. 2021;373:n1038. Published 2021 May 11. doi:10.1136/bmj.n1038.
2. Kostka K, et al. Unraveling COVID-19: a large-scale characterization of 4.5 million COVID-19 cases using CHARYBDIS. *Clin Epidemiol*. 22 Mar 2022;14: 369-384. doi:10.2147/CLEP.S323292.
3. Harshfield EL, Pennells L, Schwartz JE, et al. Association Between Depressive Symptoms and Incident Cardiovascular Diseases. *JAMA*. 2020;324(23):2396-2405. doi:10.1001/jama.2020.23068.
4. Gonçalves BP, Hall M, Jassat W, et al. An international observational study to assess the impact of the Omicron variant emergence on the clinical epidemiology of COVID-19 in hospitalised patients. *Elife*. 2022;11:e80556. Published 2022 Oct 5. doi:10.7554/eLife.80556.
5. Gaggiano C, Vitale A, Tufan A, et al. The Autoinflammatory Diseases Alliance Registry of monogenic autoinflammatory diseases. *Front Med (Lausanne)*. 2022;9:980679. Published 2022 Sep 9. doi:10.3389/fmed.2022.980679.
6. Gianfrancesco MA, Goldstein ND. A narrative review on the validity of electronic health record-based research in epidemiology. *BMC Med Res Methodol*. 2021;21(1):234. Published 2021 Oct 27. doi:10.1186/s12874-021-01416-5.
7. Garza M, Del Fiol G, Tenenbaum J, Walden A, Zozus MN. Evaluating common data models for use with a longitudinal community registry. *J Biomed Inform*. 2016;64:333-341. doi:10.1016/j.jbi.2016.10.016.

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