PyRRHiC: Pharmaceutical Benefits Scheme Replication and Harmonisation Challenge using Australian dispensing data

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Background

- Replicability of study findings by different research teams is of fundamental importance to pharmacoepidemiology research but may be challenging in practice.
- Researchers make different, apparently minor, technical choices during data preparation and analysis that can lead to different results.
- In 2021, OHDSI embarked on a reproducibility challenge, where nine teams aimed to reproduce the cohort logic for the target, comparator and outcome cohorts. That study found that only the simplest criteria were easy to reproduce and on average, the teams did not reproduce 60% of the criteria.
- Using this challenge as our inspiration, we aimed to conduct our own replicability study (PyRRHiC) to inform research practices using a medicine dispensing research dataset available in Australia (PBS10% sample). Four sites in the Medicines Intelligence Centre of Research Excellence (MI-CRE) participated. Each site completed the HARmonized Protocol Template to Enhance Reproducibility (HARPER) protocol.2

Our study aimed to:

1. Identify variation in data preparation and analysis for drug utilisation studies and measure its impact on replicability;
2. Develop guidance on data preparation and analysis for drug utilisation studies;
3. Develop documentation standards.

Methods

- Each site accessed the same simple protocol based on an existing treatment dynamics study. Each site independently produced a detailed protocol using the HARPER template. Analysis was then conducted separately at each site in a variety of languages (SAS, Python and R).

Results

<table>
<thead>
<tr>
<th>Site</th>
<th>Cohort size (N)</th>
<th>Sex Male (%)</th>
<th>Age (Median (IQR))</th>
<th>Concession* (%)</th>
<th>Died (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site 1</td>
<td>32 (57-71)</td>
<td>48.9±43.2</td>
<td>63 (52-71)</td>
<td>93.9±44.9</td>
<td>0.9±0.5</td>
</tr>
<tr>
<td>Site 2</td>
<td>42 (57-71)</td>
<td>48.9±43.1</td>
<td>63 (52-71)</td>
<td>94.4±44.7</td>
<td>2.5±0.5</td>
</tr>
<tr>
<td>Site 3</td>
<td>54 (39-66)</td>
<td>48.9±43.2</td>
<td>63 (52-71)</td>
<td>83.8±42.6</td>
<td>3.1±0.3</td>
</tr>
<tr>
<td>Site 4</td>
<td>55 (39-66)</td>
<td>48.9±43.1</td>
<td>63 (52-71)</td>
<td>83.8±42.3</td>
<td>5.1±0.3</td>
</tr>
</tbody>
</table>

A similar number of patients were included during each study period with comparable demographic profiles for sex and age, indicated by a rating of ‘good’.

Conclusions

What we learnt

- Data curation and preparation differs across sites.
- Different approaches used to calculate exposure duration and to define outcomes.
- Starting from the same dataset and basic protocol does not guarantee replicability.

How OHDSI will help?

- Using a shared mapping of PBS item codes to Australian Medicines Terminology (AMT) and RxNorm will allow for a standardized approach to estimation of exposure duration across Australia.
- Consistent definitions of outcomes (discontinuation, switching, intensification) will be developed using validated phenotypes.
- Application of OHDSI tools will facilitate standardized analytics overcoming potential differences introduced when a variety of statistical software is used.

Final thoughts

Drug utilisation studies are difficult to implement consistently but are critical in Australia where a universal medicines subsidy framework is used. These data are important for our medicines subsidy committee, PBAC, to ensure that robust cost-effectiveness estimates are available for their decision making. Collaborating to create harmonized approaches will ensure rigor and build trust in those estimates. Understanding how minor changes in data curation and preparation, as well as definitional and analytical differences, impact on results is critical to generalizability and interpretability. In addition to this, careful sensitivity analyses are needed to ensure results adequately reflect true analytical uncertainty.

References


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