REal World Assessment and Research of Drugs Benefits (REWARD-B): A Technical implementation that aids the identification of unexpected benefits

James P. Gilbert, PhD[1], Rachel E. Teneralli, PhD[1] Christopher A. Knoll BSc[1], David M. Kern PhD[1], M Soledad Cepeda MD, PhD[1], Patrick B. Ryan, PhD[1]
[1]Janssen Research and Development, Titusville NJ

Abstract

Research Category Software application

Introduction

The use of real-world evidence in the context of signal detection for the potential of hazards in medication has been well studied (1). Previous work has shown the potential for self-controlled cohort analysis to detect previously unknown benefits of medications in the context of Parkinsonism (2) and Alzheimer's disease (3) by assessing incidence risk ratios (IRRs) of all medications with these disease outcomes. That work leveraged the REal World Assessment and Research of Drugs Benefits (REWARD-B) platform. Here, we present the REWARD-B platform and its capabilities in detail. REWARD-B is an application built on top of the OHDSI HADES software suite that utilises observational data to generate novel hypotheses for drug repurposing and drug target identification.

Methods: Building on the common data model

The use of the CDM allows REWARD-B to be deployed at scale to evaluate the effect estimates of exposure-outcome pairs across multiple datasets. A high-level system overview of REWARD-B is shown in Figure 1. The design can be broken into 3 components: The administration of cohorts with both automated SQL and ATLAS defined definitions, the statistical analysis of cohorts created from CDM data with self-controlled cohort designs, and the visualization and exploration of results in the RShiny tool.

Negative controls (4) are required to model systematic bias and are typically hand-curated, a process not feasible in large scale evidence dissemination. Consequently, controls are selected through a fully automated process for the assessment of known evidence between target outcome-pairs, building on previous work in the Common Evidence Model (CEM) (5) and standard vocabulary. Combined with the empirical calibration of p-values and confidence intervals (6,7) this allows for a robust source for the evaluation of effect estimates.

Results: visualizations and data exploration in RShiny

As with many applications developed under the OHDSI banner and building upon the extensive R software ecosystem, REWARD-B provides an easy to use, rapid deployment option for the exploration of data. Figure 2 shows a screenshot of Shiny dashboard for data filtering effect estimates (IRRs) and a forest plot of calibrated and uncalibrated results.

Conclusion

This software demonstration presents REWARD-B, an open source software application that builds on top of the CDM and CEM to provide a reusable platform for the assessment of medications in the context of unknown benefits. The software package provides automated empirical calibration of effect estimates, convenient deployment into an existing open-source OHDSI platform and ease of exploration and visualization of results.

In the future, we aim to explore methods to improve the selection of cohorts and integrate with other OHDSI platforms to provide "one-click" cohort characterization and improved visualization of large number of effect estimates. We also aim to include more study designs such as the increasingly used self-controlled case-series design. Whilst this work presents a valuable tool for the exploration of real-world data, it should be noted that this is a hypothesis generating step in the long process of finding potential targets for drug repurposing or novel drug target identification.

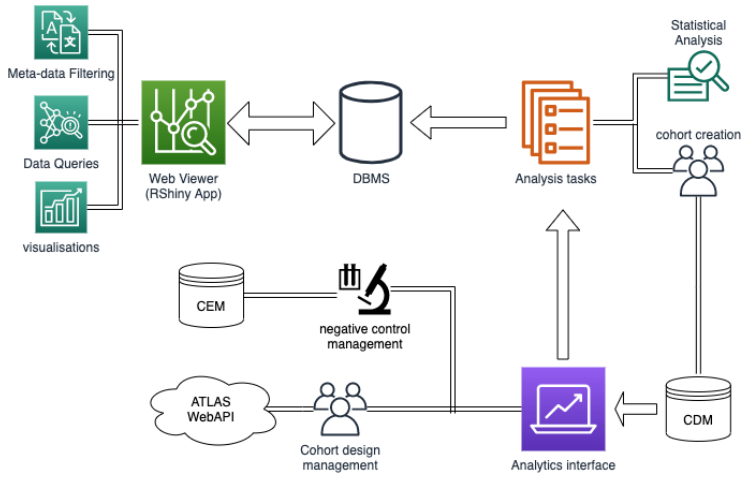

Figure 1. High-level systems overview of the REWARD-B software package. Building on top of the Common Data Model (CDM), Common Evidence Model (CEM) and the OHDSI communities software utilities, REWARD-B provides the means to perform statistical analysis, data-capture, exploration and visualisation of results within the RShiny web application.

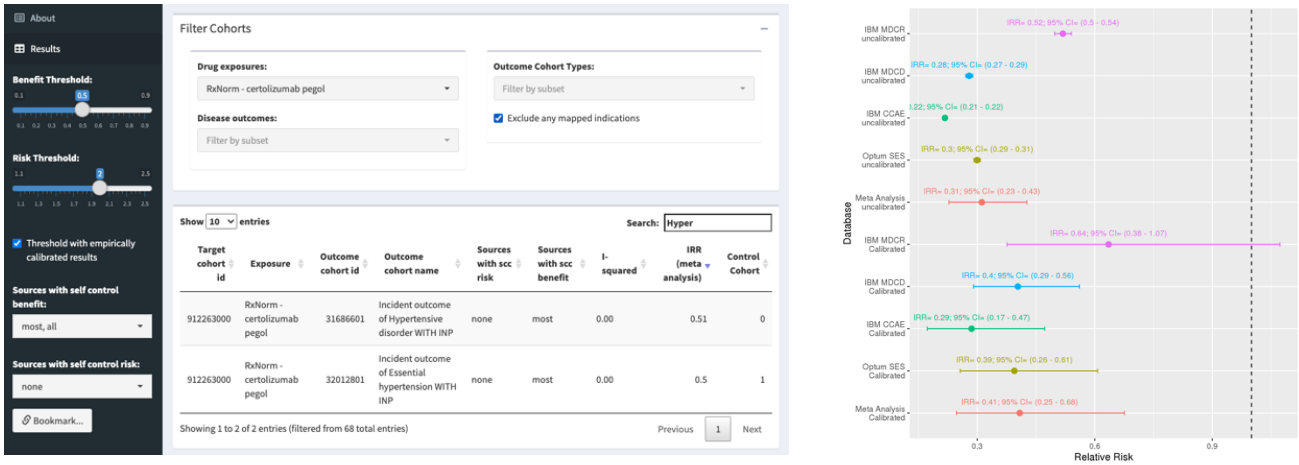

Figure 2. Screenshots of visualization and exploration of data in the REWARD-B Shiny application. Filtering of results by thresholding risk ratios (left) can be used to find significant relationships between target-outcome parings. Results shown are taken with a meta-analysis from 4 datasets following the OMOP CDM, cohorts are generated with the self-controlled cohort design. Filtering for results that do no present any risk at a threshold of IRR < 2.0 and show a benefit in at least 2 databases with an IRR < 0.5. The forest plot (right) shows confidence intervals for calibrated and uncalibrated effect estimates.

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