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Presentation type (s):	**Software Demonstration**

Large Scale Risk Identification System for Proactive Safety Surveillance

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Abstract

Large patient-level datasets offer unprecedented opportunities for evidence generation at scale. Thanks to computing advances in massively parallel processing database platforms and the OHDSI methods library, researchers no longer need to constrain themselves to custom-selecting one piece of evidence at a time. This requires a standardized, systematic approach and tools to interrogate, evaluate and synthesize all of the diverse evidence that is generated to guide decision-making.

Introduction

The U.S. Food and Drug Administration (FDA) Amendments Act of 2007 mandated that the FDA develop a system for using automated health care data to identify risks of marketed drugs and other medical products. [1] A vision for a tool for large-scale risk identification was described at the 2013 OMOP Symposium[2] named **HOMER**: **H**ealth **O**utcomes and **M**edical **E**vidence **R**esearch. HOMER's objective is to take a data source converted to the OMOP common data model (CDM) and produce summary statistics aligned to the Sir Austin Bradford Hill's criteria for determining association or casual relationships for all drug-outcome pairs. In this software demonstration, we aim to posit an initial framework and tooling for HOMER based on work done for proactive safety surveillance initiatives at Janssen Research & Development.

Software Demonstration Topics

- Describe the process for generating a 'large scale' cohort characterization data set. Current capabilities consist of generating characterization information across domains of interest (demographics, conditions, drugs, procedures, measurements and observations) for all new-drug users and hospitalization-outcome cohorts. Cohorts are further organized using cohort sets to group related cohorts of interest.
- Leveraging the OHDSI methods libraries for new-user cohort and self-controlled cohort designs to execute analyses across the full set of drug and outcome cohorts. In the case of a new user cohort design, comparators are configured and defined as part of the analysis. In both designs, a set of standardized diagnostics are produced and a set of negative controls are used for empirical calibration.
- User interface segmented into two roles for reviewing evidence: publishers and viewers. Publishers can review the full set of characterization and estimation evidence generated and create reports to disseminate results. Reports include all drug-outcome pairs that have been reviewed including all diagnostic information generated by the methods libraries. Viewers are restricted by the system and can only review cohort characterization statistics and download reports generated by publishers.

Target: abiraterone with metastatic castration-resistant prostate cancer and concomitant prednisone
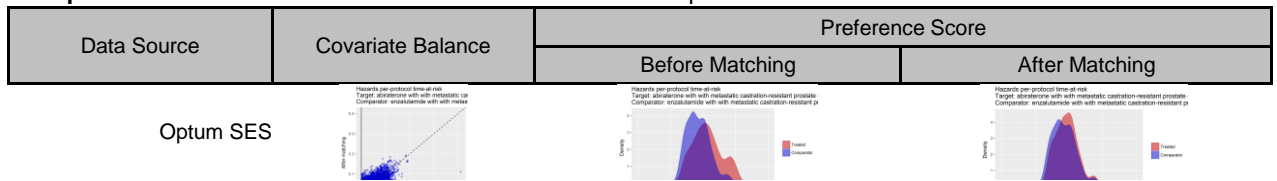**Comparator:** enzalutamide with metastatic castration-resistant prostate cancer

Data Source	Covariate Balance	Preference Score	
		Before Matching	After Matching
Optum SES			

Figure 1. User-defined report including diagnostic information

- Publishers have the ability to review specific drug-outcome pairs in order to evaluate any potential safety signals. In addition, they can also review all outcomes using a dashboard that provides the ability to filter results along specific dimensions:
  - Estimate: The amount of evidence suggesting a positive association. Low = 0 database, Medium = at least 1 and High = all databases.
  - Incidence: Based on the CIOMS III working group categorization of adverse reaction frequency: Very Common ($\geq$ 10%), Common ($\geq$ 1% and < 10%), Uncommon ($\geq$ 0.1% and < 1%), Rare ($\geq$ 0.01% and < 0.1%) and Very rare (< 0.01%)
  - Seriousness: A relative measure of severity of the disease based on health service utilization before and after incident outcome.
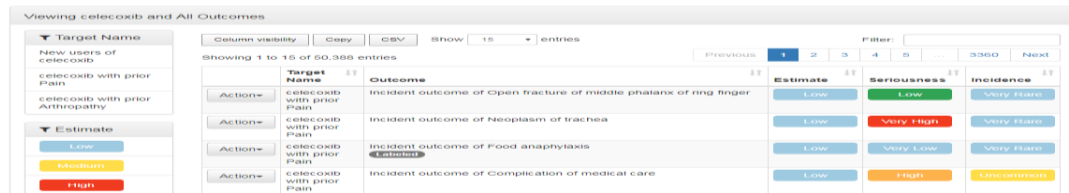

Figure 2. Evidence evaluation dashboard

- Browsing evidence supports the ability to leverage the OMOP vocabulary to focus on a specific concept and use its ancestors/descendants to explore potential signals in a selected disease context.
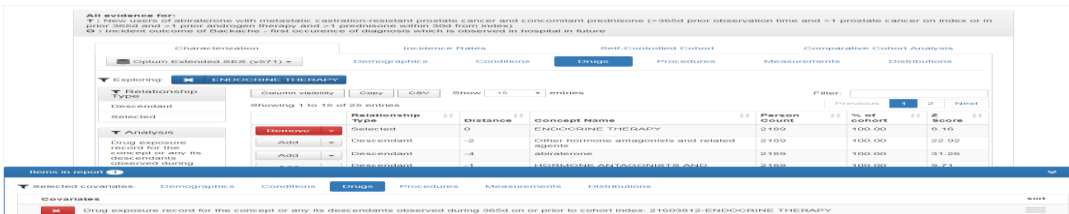

Figure 3. Browsing covariates for a selected drug-outcome pair using the OMOP vocabulary.

Conclusion

The OMOP CDM coupled with the OHDSI suite of open-source analytics tools provides the underpinnings for a large scale risk identification system for proactive safety surveillance. This tool for evaluating and synthesizing evidence is an initial attempt to initiate further discussion around HOMER amongst the OHDSI collaborative.

References

1. Stang, P. E., et al. Advancing the science for active surveillance: rationale and design for the Observational Medical Outcomes Partnership. Ann Intern Med 2010 153(9): 600-606.
2. PB Ryan, OMOP's Vision of Risk Identification. Oral presentation at OMOP Symposium; November, 2013; Washington, DC. http://omop.org/node/649