A standardized framework for risk-based assessment of treatment effect heterogeneity in observational healthcare databases

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# Abstract

One of the aims of the Observational Health Data Sciences and Informatics (OHDSI) initiative is population-level treatment effect estimation in large observational databases. Since treatment effects are well-known to vary across groups of patients with different baseline risk, we aimed to extend the OHDSI library of open-source tools with a framework for risk-based assessment of treatment effect heterogeneity. The proposed framework consists of five steps: 1) definition of the problem, i.e. the population, the treatment, the comparator and the outcome(s) of interest; 2) identification of relevant databases; 3) development of a prediction model for the outcome(s) of interest; 4) estimation of relative and absolute treatment effect within strata of predicted risk, after adjusting for observed confounding; 5) presentation of the results. We demonstrate our framework by evaluating heterogeneity of the effect of angiotensin-converting enzyme (ACE) inhibitors versus beta blockers on 3 efficacy and 6 safety outcomes across three observational databases. Patients at low risk of acute myocardial infarction (MI) received negligible absolute benefits for all 3 efficacy outcomes, though they were more pronounced in the highest risk quarter, especially for hospitalization with heart failure. The substantial risk increase of cough and angioedema with ACE inhibitors across all risk strata suggests that beta blockers provide a viable alternative to patients at low risk of acute MI. The proof of concept study demonstrates its feasibility in large observational data. Further insights may arise by application to safety and effectiveness questions across the global data network.

**Keywords**: observational data, heterogeneity of treatment effect, risk stratification, subgroup analysis

# 1 Introduction

The Observational Health Data Science and Informatics (OHDSI) collaborative has established a global network of data partners and researchers that aim to bring out the value of health data through large-scale analytics by mapping local databases to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) [1,2]

# 2 References

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2 Overhage JM, Ryan PB, Reich CG *et al.* Validation of a common data model for active safety surveillance research. *Journal of the American Medical Informatics Association* 2012;**19**:54–60. doi:[10.1136/amiajnl-2011-000376](https://doi.org/10.1136/amiajnl-2011-000376)