

A standardized framework for risk-based assessment of heterogeneity of treatment effect

Alexandros Rekkas^{1,2}, Peter R. Rijnbeek¹, David M. Kent³, Ewout W. Steyerberg^{2,4}, David van Klaveren^{4,3}

¹Department of Medical Informatics, Erasmus Medical Center, Rotterdam, The Netherlands

²Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands

³Predictive Analytics and Comparative Effectiveness Center, Tufts Medical Center, Boston, USA

⁴Department of Public Health, Erasmus Medical Center, Rotterdam, The Netherlands

Background: The Observational Health Data Sciences and Informatics (OHDSI) collaborative has established an international network of databases mapped to the Observational Medical Outcomes Partnership (OMOP) Common Data Model [1], enabling large-scale analyses.

Aim: Development of a framework for risk-based assessment of heterogeneity of treatment effect (HTE) within the OHDSI setting of analysis of observational data.

Methods: The steps required for the standardized analysis are: 1) definition of the problem, i.e. the treatment, the comparator and the outcome(s) of interest; 2) identification of the database(s) in which the framework will be applied; 3) development of the prediction model for the outcome(s) of interest from a propensity score matched sub-population of merged treatment and comparator cohorts, using a large set of standardized predictor variables including demographics, conditions, drugs, measurements procedures and observation concepts; 4) estimation of the propensity scores within strata of predicted risk using large-scale regularized regression, selecting from the same large set of candidate variables; 5) estimation of relative and absolute treatment effects within risk strata—matching or stratification on the propensity score or inverse probability of treatment weighting can be applied.

Results: We compared angiotensin-converting enzyme (ACE) inhibitors (treatment) to beta blockers (comparator) with regard to a set of 9 outcomes in patients with hypertension across three observational databases.

Conclusions: Reproducible risk-based assessment of HTE in observational data is made possible. The standardized nature of the process allows its implementation at scale, while the common data model enables collaboration across multiple sites with access to different databases.

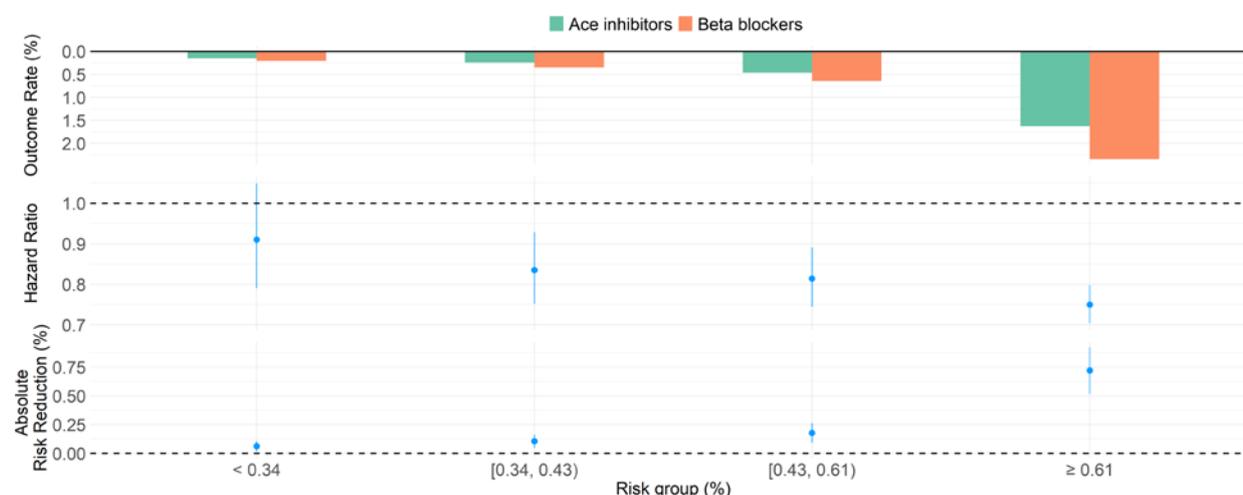


Figure 1: Application in Truven MarketScan Commercial Claims and Encounters (CCA) database containing enrollees in US employer-sponsored insurance health plans. Patients are divided into quarters of predicted risk of hospitalization with heart failure. Observed event rates by risk quarter are given (top). The hazard ratios—estimated using stratification on the propensity score—show a decreasing trend in favor of ACE inhibitors (middle). The benefits of ACE inhibitors increase strongly at the absolute scale with increasing hospitalization risk (bottom, absolute risk reduction increases from 0.06% to 0.72%).

Keywords

heterogeneity of treatment effect, prediction, observational data, framework, electronic health records

References

[1] Overhage JM, Ryan PB, Reich CG, Hartzema AG, Stang PE. Validation of a common data model for active safety surveillance research. *J Am Med Inform Assoc* 2012;19(1):54–60.