Large-scale evaluation of treatment effect heterogeneity in hypertension

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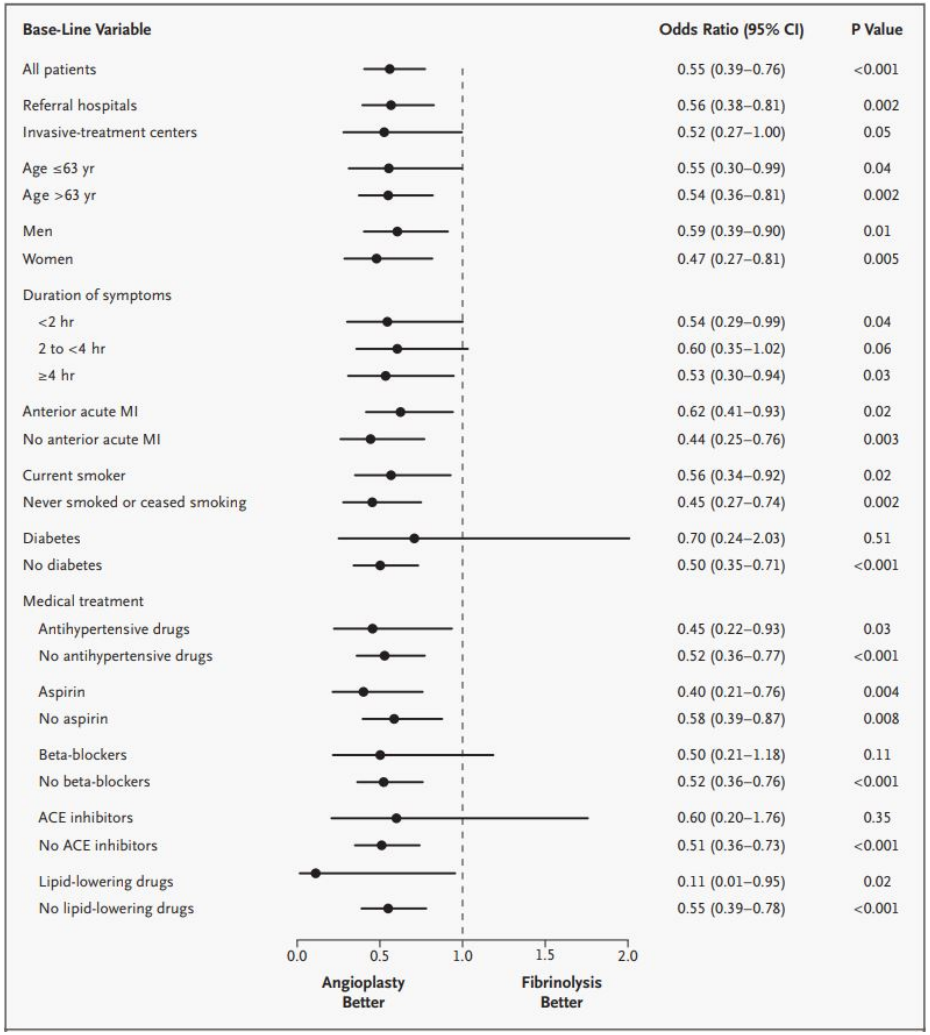
Heterogeneity of treatment effect

Heterogeneity of treatment effect (HTE) is the non-random explainable variability in the direction and/or magnitude of treatment effect

Main goals:

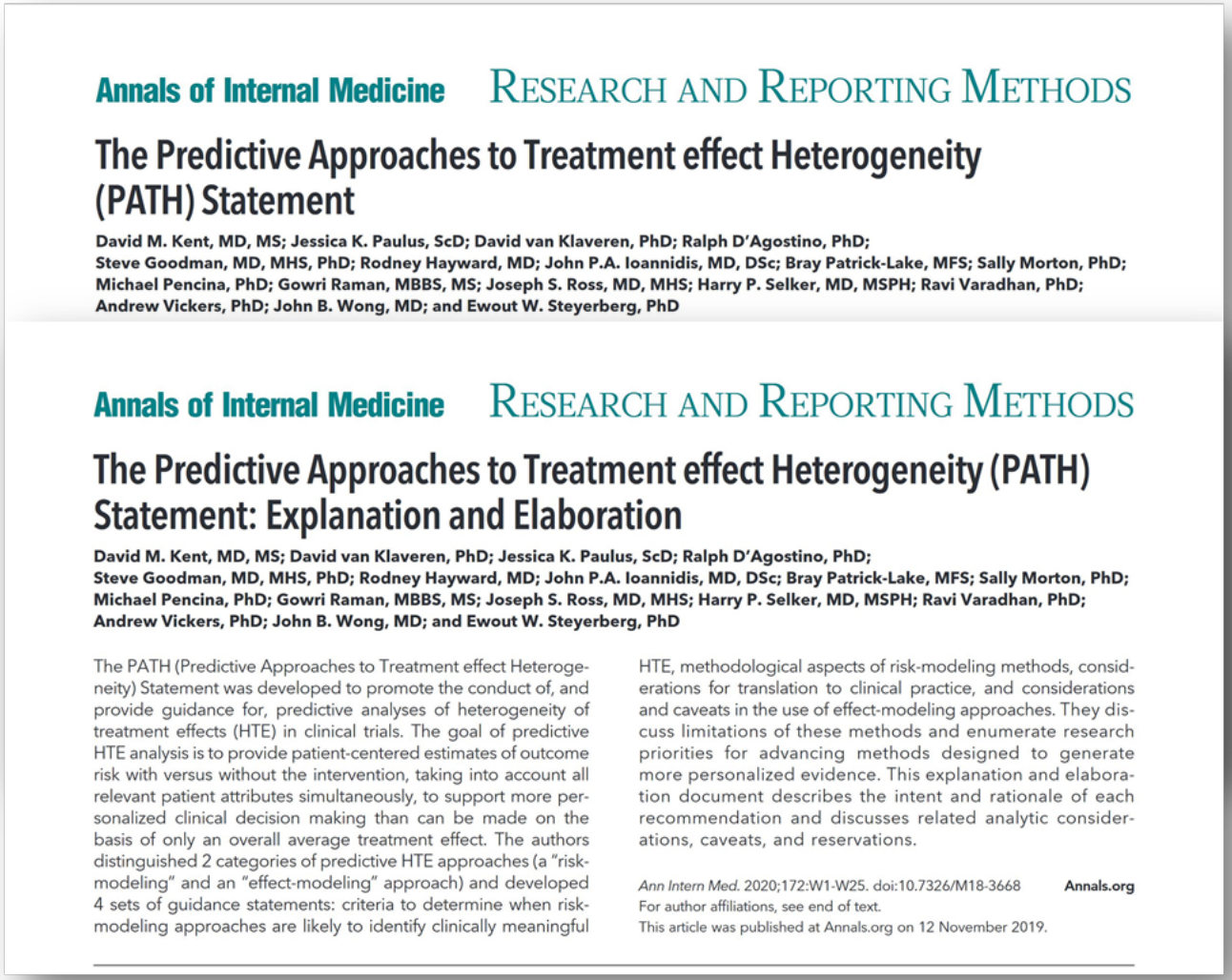
- Estimation of treatment effects in clinically relevant patient subgroups
- Prediction of individual benefit (or harm) from treatment
- Aid stakeholders make informed decisions

Forest plot of the DANAMI-2 RCT



Andersen HR, Nielsen TT, Rasmussen K et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003; 349: 733-742

PATH statement



Annals of Internal Medicine RESEARCH AND REPORTING METHODS

The Predictive Approaches to Treatment effect Heterogeneity (PATH) Statement

David M. Kent, MD, MS; Jessica K. Paulus, ScD; David van Klaveren, PhD; Ralph D'Agostino, PhD; Steve Goodman, MD, MHS, PhD; Rodney Hayward, MD; John P.A. Ioannidis, MD, DSc; Bray Patrick-Lake, MFS; Sally Morton, PhD; Michael Pencina, PhD; Gowri Raman, MBBS, MS; Joseph S. Ross, MD, MHS; Harry P. Selker, MD, MSPH; Ravi Varadhan, PhD; Andrew Vickers, PhD; John B. Wong, MD; and Ewout W. Steyerberg, PhD

Annals of Internal Medicine RESEARCH AND REPORTING METHODS

The Predictive Approaches to Treatment effect Heterogeneity (PATH) Statement: Explanation and Elaboration

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The PATH (Predictive Approaches to Treatment effect Heterogeneity) Statement was developed to promote the conduct of, and provide guidance for, predictive analyses of heterogeneity of treatment effects (HTE) in clinical trials. The goal of predictive HTE analysis is to provide patient-centered estimates of outcome risk with versus without the intervention, taking into account all relevant patient attributes simultaneously, to support more personalized clinical decision making than can be made on the basis of only an overall average treatment effect. The authors distinguished 2 categories of predictive HTE approaches (a "risk-modeling" and an "effect-modeling" approach) and developed 4 sets of guidance statements: criteria to determine when risk-modeling approaches are likely to identify clinically meaningful HTE, methodological aspects of risk-modeling methods, considerations for translation to clinical practice, and considerations and caveats in the use of effect-modeling approaches. They discuss limitations of these methods and enumerate research priorities for advancing methods designed to generate more personalized evidence. This explanation and elaboration document describes the intent and rationale of each recommendation and discusses related analytic considerations, caveats, and reservations.

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For author affiliations, see end of text.
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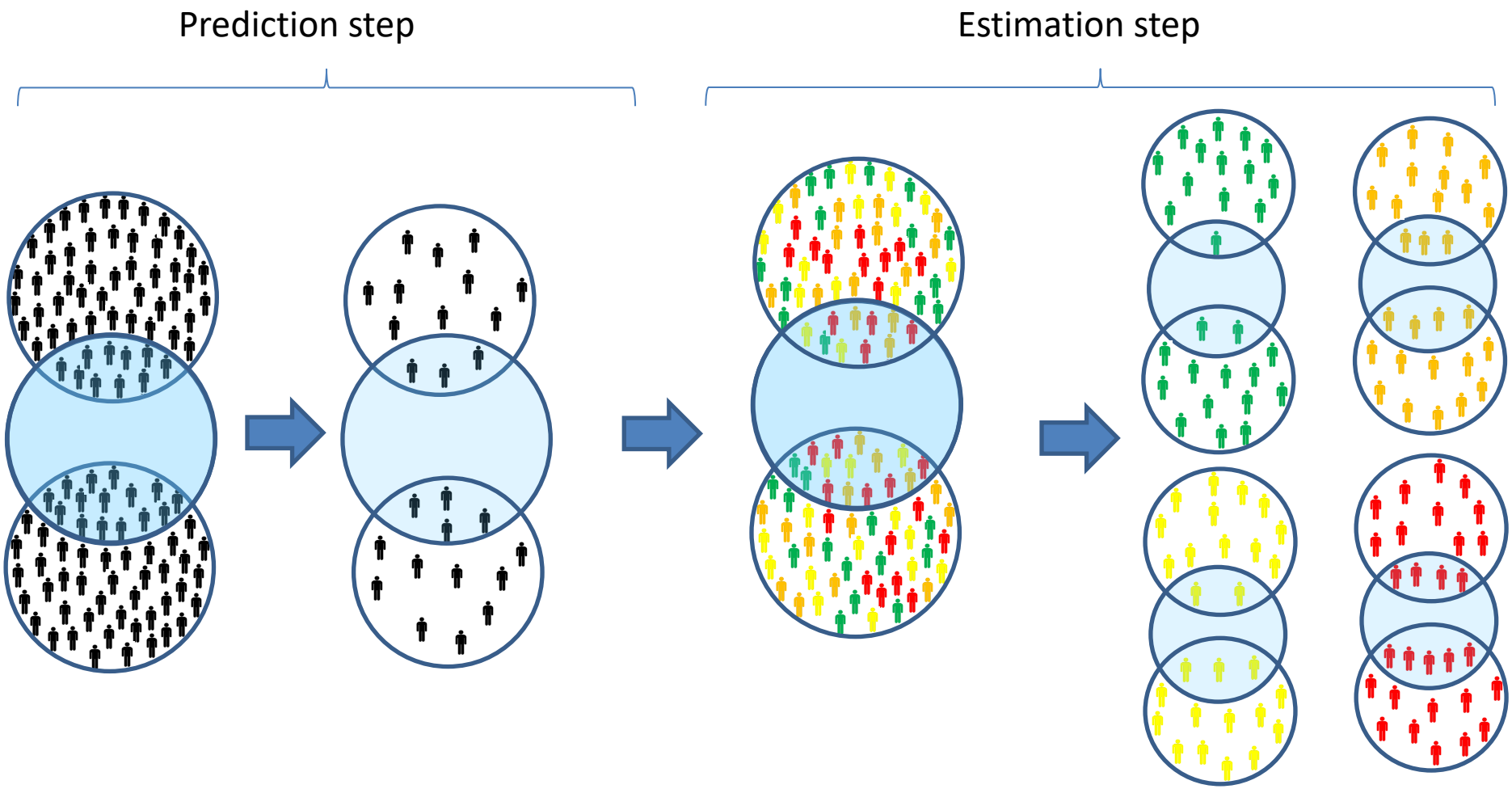
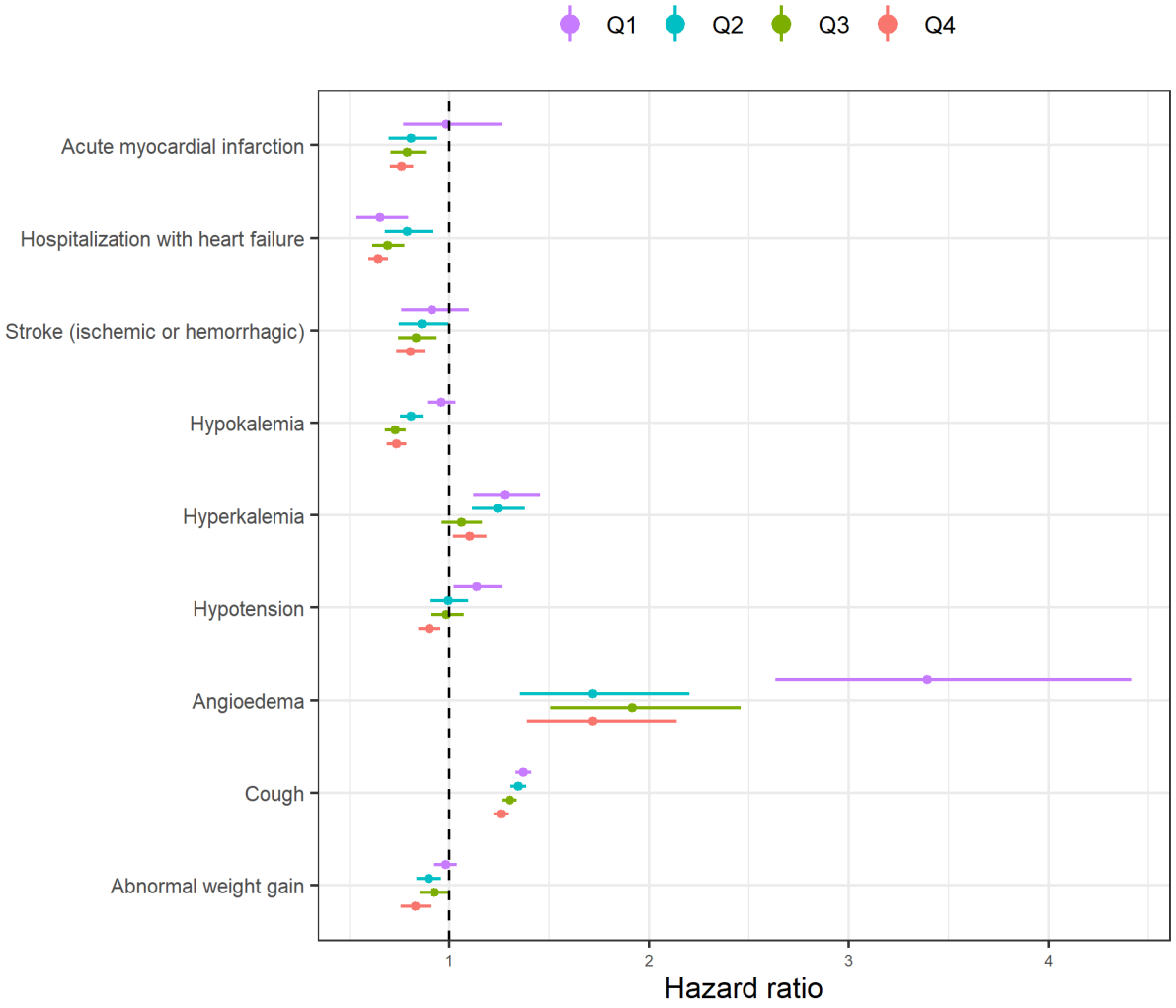
OHDSI framework for risk-based HTE



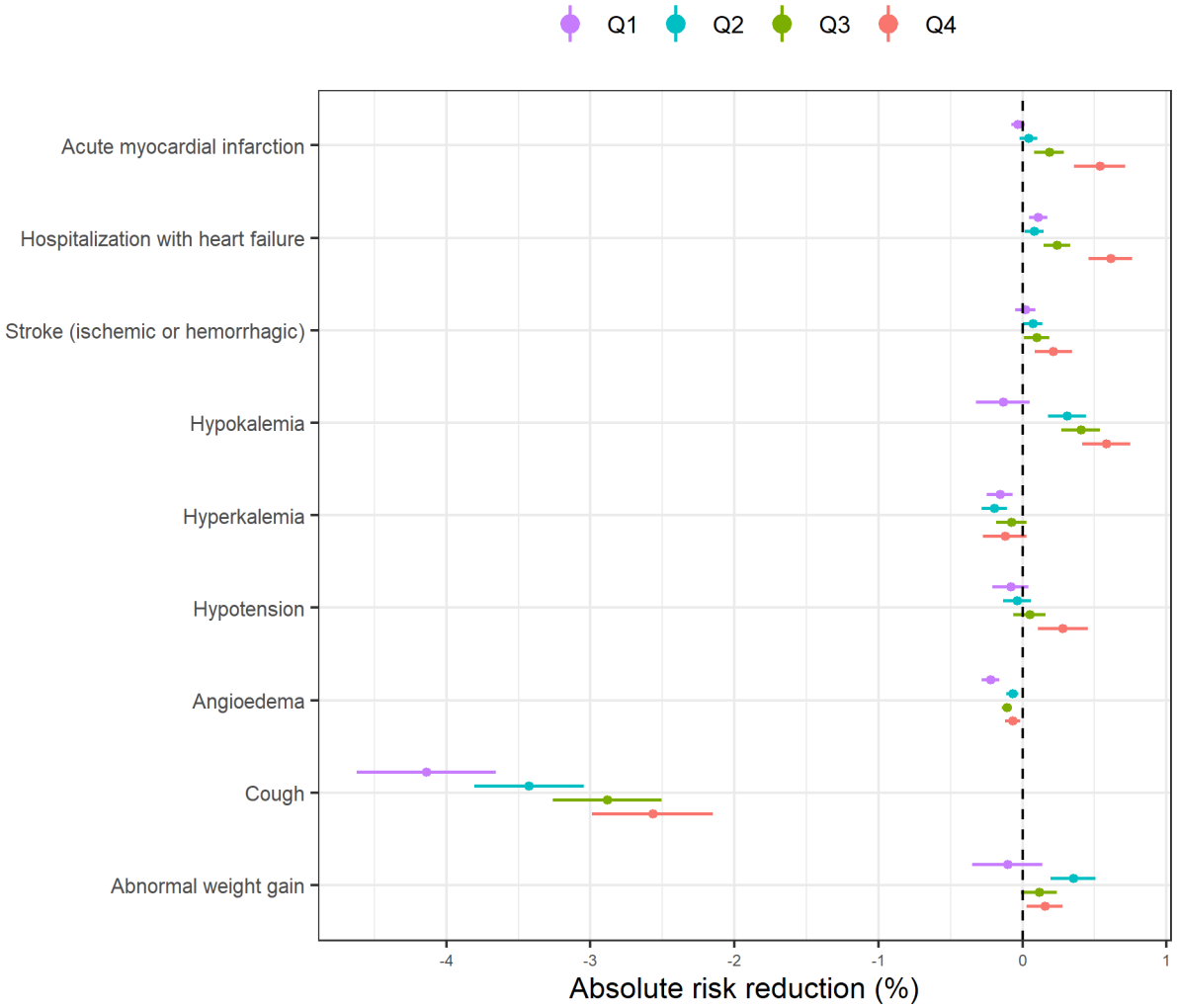
Application in hypertension treatment

- We compare ACE-inhibitors to beta blockers
- Databases: CCAE, MDCD, MDCR
- Main outcomes
  - Acute myocardial infarction
  - Hospitalization with heart failure
  - Stroke
- Safety outcomes:
  - Hypokalemia
  - Hyperkalemia
  - Hypotension
  - Angioedema
  - Cough
  - Abnormal weight gain

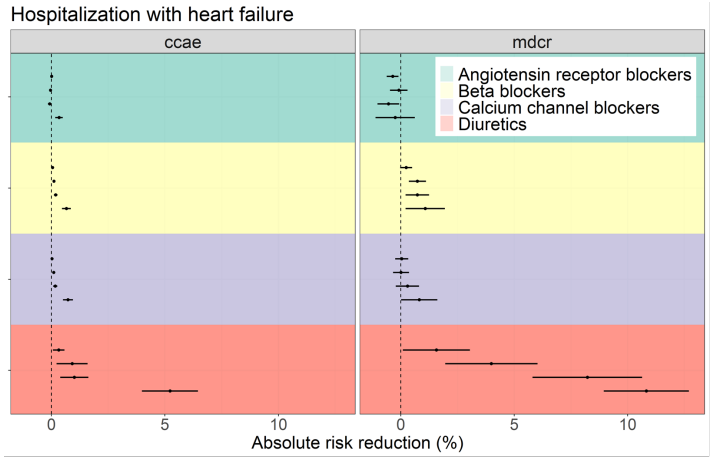
Results

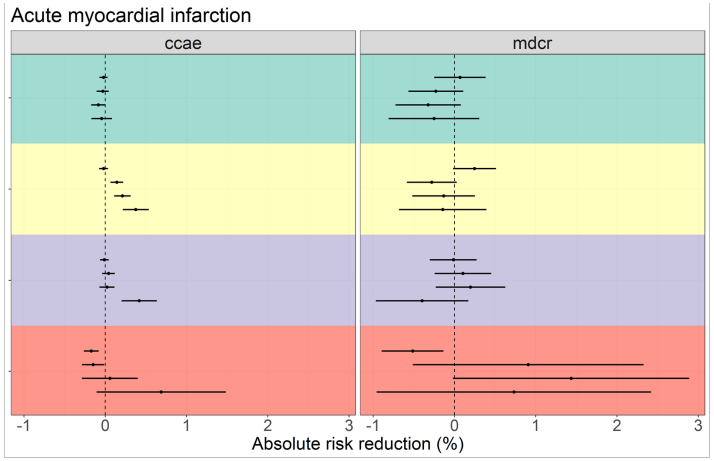

Q1
Q2
Q3
Q4
Acute myocardial infarction
Hospitalization with heart failure
Stroke (ischemic or hemorrhagic)
Hypokalemia
Hyperkalemia
Hypotension
Angioedema
Cough
Abnormal weight gain
1
2
3
4
Hazard ratio

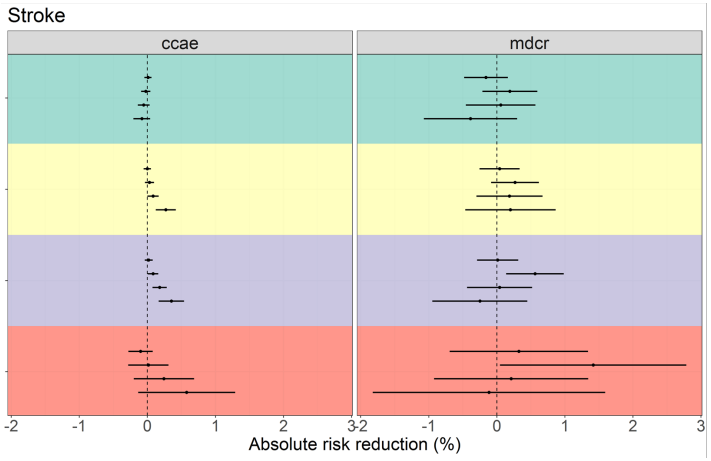
Results

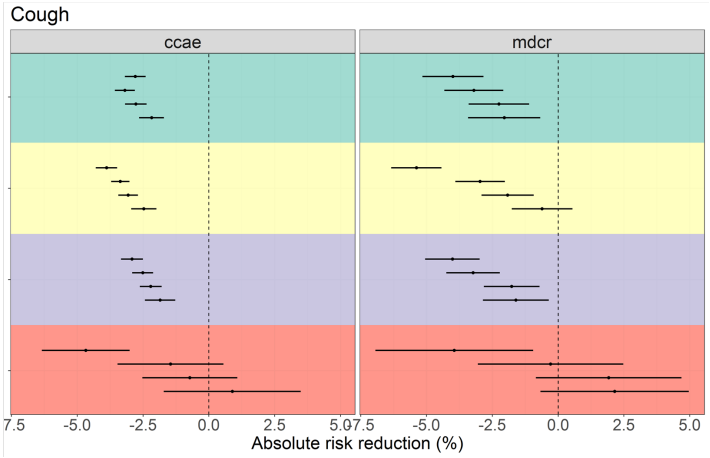

Q1
Q2
Q3
Q4
Acute myocardial infarction
Hospitalization with heart failure
Stroke (ischemic or hemorrhagic)
Hypokalemia
Hyperkalemia
Hypotension
Angioedema
Cough
Abnormal weight gain
-4
-3
-2
-1
0
1
Absolute risk reduction (%)

Results


Hospitalization with heart failure
ccae
mdcr
Angiotensin receptor blockers
Beta blockers
Calcium channel blockers
Diuretics
0
5
10
Absolute risk reduction (%)


Acute myocardial infarction
ccae
mdcr
-1
0
1
2
3
Absolute risk reduction (%)


Stroke
ccae
mdcr
-2
-1
0
1
2
3
Absolute risk reduction (%)


Cough
ccae
mdcr
-7.5
-5.0
-2.5
0.0
2.5
5.0
Absolute risk reduction (%)

Useful links

- R-package: RiskStratifiedEstimation

https://github.com/OHDSI/RiskStratifiedEstimation

- Shiny application:

https://data.ohdsi.org/AceBeta9Outcomes/

- Framework preprint:

https://arxiv.org/abs/2010.06430

Thank you

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