Assessing heterogeneity of hypertension treatment effects

A risk modeling approach

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Background

- The Large-scale Evidence Generation and Evaluation in a Network of Databases (LEGEND) study compared classes of hypertension drugs for their relative treatment effect on multiple outcomes
- The absolute treatment effect (absolute risk reduction) of one drug class versus another often depends on baseline outcome risk
- We performed a risk-based re-analysis of the LEGEND study, comparing the absolute risk difference of angiotensin-converting enzyme (ACE) inhibitors versus beta blockers for multiple outcomes
- The analyses were performed with regard to baseline 2-year risk of total cardiovascular disease (CVD) risk

Methods

- For our analyses we considered the following databases:
  - IBM MarketScan® Multi-State Medicaid Database (MDCD)
  - IBM MarketScan® Medicare Supplemental Database (MDCR)
  - IBM MarketScan® Commercial Database (CCAE)
- We predicted personalized CVD risk using LASSO logistic regression on the combined ACE-inhibitor and beta blocker cohorts
- We estimated propensity scores using LASSO logistic regression within quartiles of predicted CVD risk
- We used inverse probability of treatment weighting to balance covariates within quartiles of predicted CVD risk
- We estimated absolute risk reduction for each LEGEND outcome from the difference of the weighted treatment-specific (ACE-inhibitors vs beta blockers) Kaplan-Meier estimators within quartiles of predicted CVD risk

Results

Absolute risk reduction estimates (ACE-inhibitors vs beta blockers) for each LEGEND outcome can be found in Figure:

- High CVD risk quartile hypertensive patients (top)
- Low CVD risk quartile hypertensive patients (bottom)

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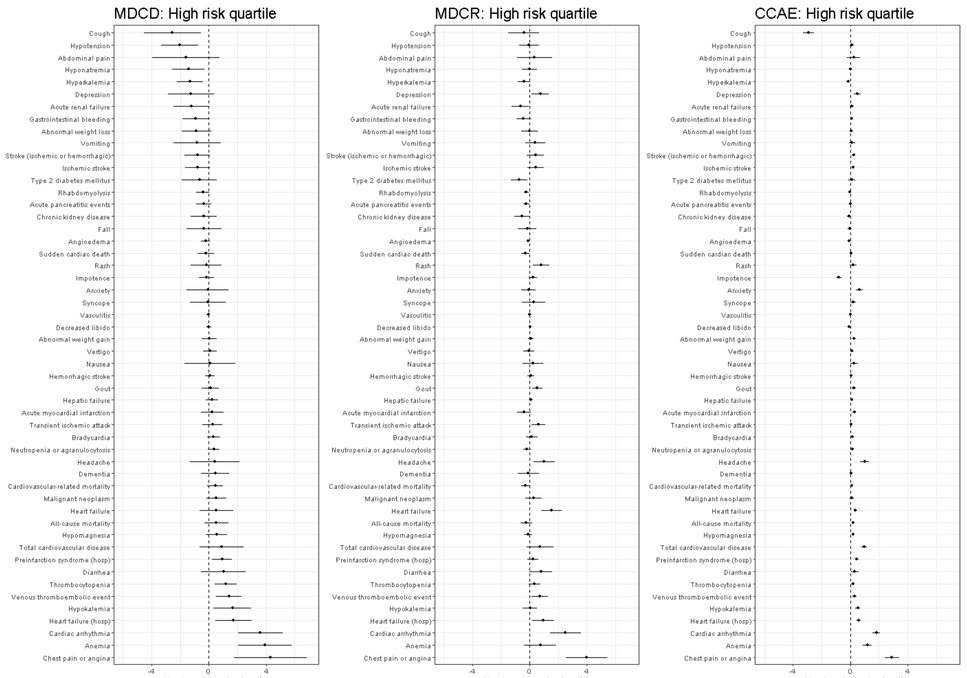

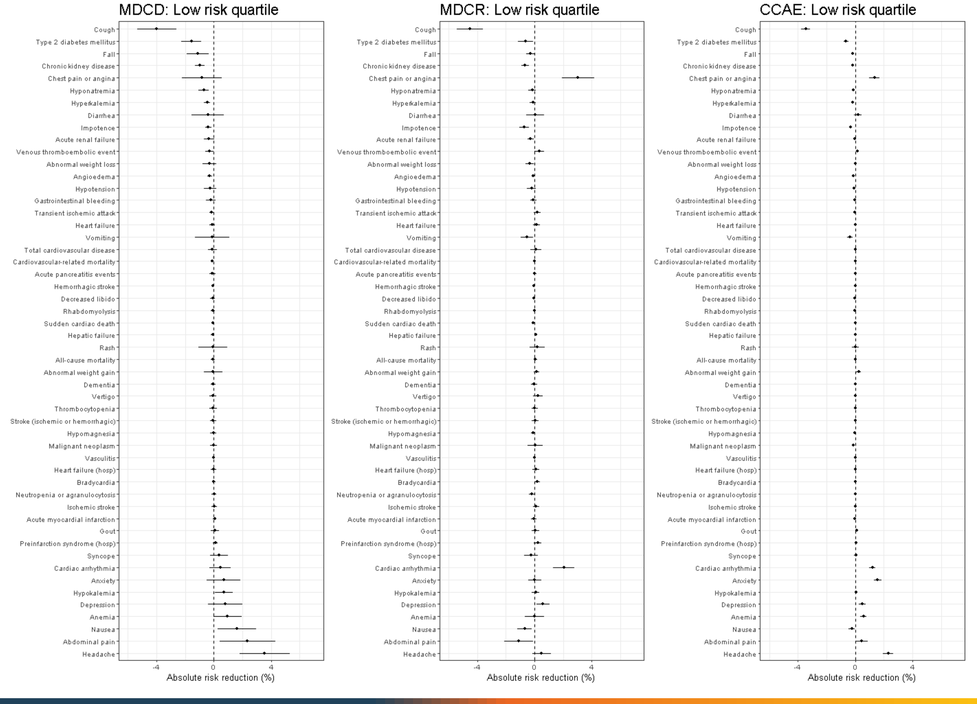

Conclusions

When comparing ACE inhibitors vs beta blockers:

- Patients at high CVD risk receive substantially more absolute benefit in terms of CVD related outcomes (total CVD, heart failure, arrhythmia) than patients at low CVD risk
- The magnitude of harms (cough, hyperkalemia) does not increase with CVD risk

CVD risk should be considered when deciding between ACE inhibitors and beta blockers

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