Large-scale evaluation of treatment effect heterogeneity is feasible

INTRODUCTION
In the presence of a truly effective treatment, effect heterogeneity should always be anticipated on some scale, as baseline risk is bound to vary across the study population.

METHODS
- We translated existing RCT guidelines to the observational setting.
- We created an open-source software package for the application of our framework.
- **Hypertension**: We compared ACE inhibitors to beta blockers with regard to 3 main outcomes (acute myocardial infarction-MI, hospitalization with heart failure, and stroke) and 6 safety outcomes (abnormal weight gain, angioedema, cough, hyperkalemia, hypokalemia, and hypotension) in IBM MarketScan Commercial Claims and Encounters (CCAE), IBM MarketScan Medicaid (MDCD), and IBM MarketScan Medicare Supplemental Beneficiaries (MDCR).
- **Osteoporosis**: We compared the effect of teriparatide to oral bisphosphonates in female patients over the age of 50, diagnosed with osteoporosis in CCAE, Optum De-Identified Electronic Health Record Dataset (Optum-EHR), and Optum De-Identified Clininformatics Data Mart Database-Date of Death (Optum-DOD).

RESULTS
**Hypertension**
- With increasing acute MI risk we observed increasing absolute benefits in terms of acute MI and hospitalization with heart failure with ACE inhibitors.
- We also observed large cough risk increase with ACE inhibitors across all acute MI risk strata.

**Osteoporosis**
- Strong evidence of residual confounding limits our ability to draw conclusions.