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Background

- Adolescents with ADHD and comorbid depression often receive methylphenidate (MPH) and selective serotonin reuptake inhibitors (SSRIs)
- Concurrent use of MPH and SSRIs may increase cardiovascular risks, including arrhythmia
- The causal machine learning method is able to estimate treatment effects on individual patients by calculating average treatment effects.
- This study aims to analyze the treatment effect of concomitant administering SSRIs and MPH on arrhythmia occurrence with a causal forest model

Methods

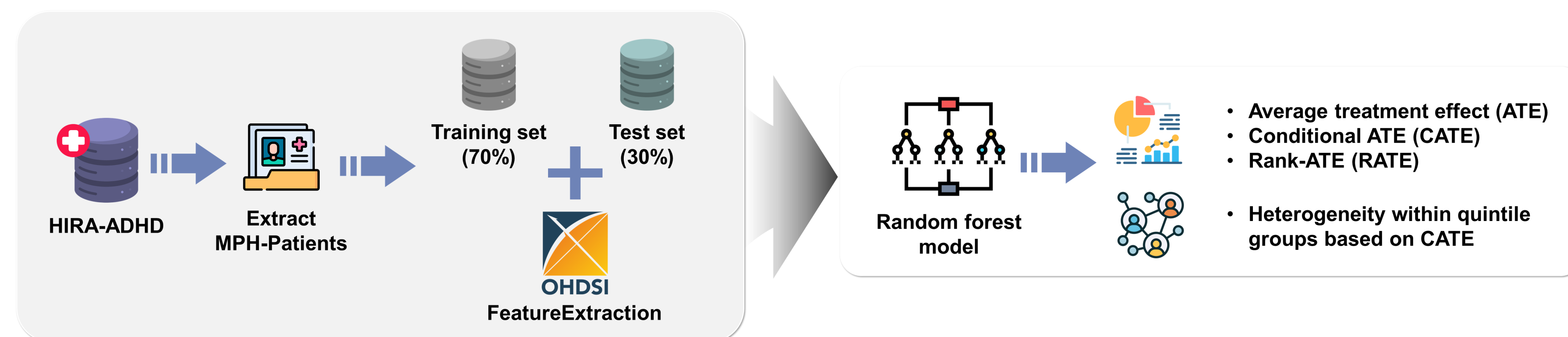


Figure 1. Overall study framework

1. Data collection

- Database: Health Insurance Review and Assessment Service – Attention Deficit/Hyperactivity Disorder (HIRA-ADHD) database which contained ADHD patient data from nationwide claims data
- HIRA-ADHD database was converted to OMOP-CDM
- Data was collected from Jan 1, 2016 to Dec 31, 2020

2. Cohort definition

Target Cohort

- MPH-used patients with an ADHD diagnosis aged between 10 and 19
- Patients with a depression record
- Patients without other anti-ADHD agents and previous antidepressants

Outcome Cohort: Occurrence of arrhythmia

3. Data preprocessing

- Split: 70% for training / 30% for testing, ensuring the same outcome prevalence in both sets
- Extracted patient baseline covariates to employ a large-scale propensity score utilizing the FeatureExtraction
- Initial screening was conducted to exclude rare covariates by 10-fold cross-validation

4. Estimate average treatment effect

- Estimated the average treatment effect (ATE) using constructed causal forest model
- Using rank-ATE (RATE), we estimated treatment heterogeneity based on the quintiles of the test set divided according to CATEs
- We compared the top 5 variables based on variable importance from the causal forest model to identify characteristics of high and low CATE groups

Results

- Among the total of 11,163 MPH-used patients, 7,873 patients were prescribed SSRIs and 58 patients had occurrences of arrhythmia

- Figure 2 shows the ATEs of the quantile groups in increasing order, with values of -0.5, -0.1, 0.1, 0.1, and 0.4
- Among ATE of quantile groups, the ATE of the Q5 group is statistically significant (95% CI: 0.1-0.8).
- The estimated RATE was 0.008 (95% CI: 0.002-0.015), which confirmed the heterogeneity between quantile groups

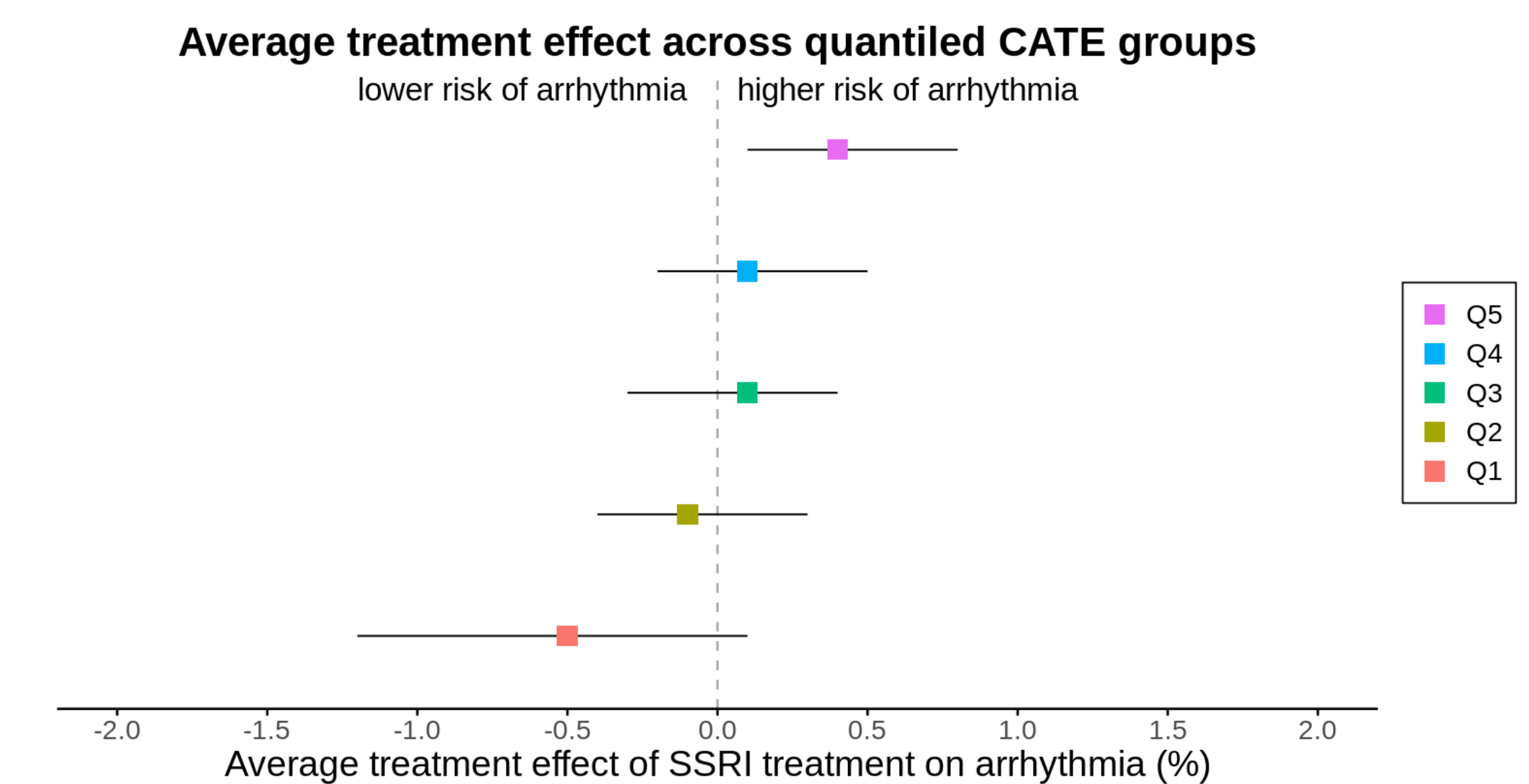


Figure 2. Average treatment effect of quantile groups

- Figure 3 represents the density of top 5 baseline covariates between high and low CATE groups

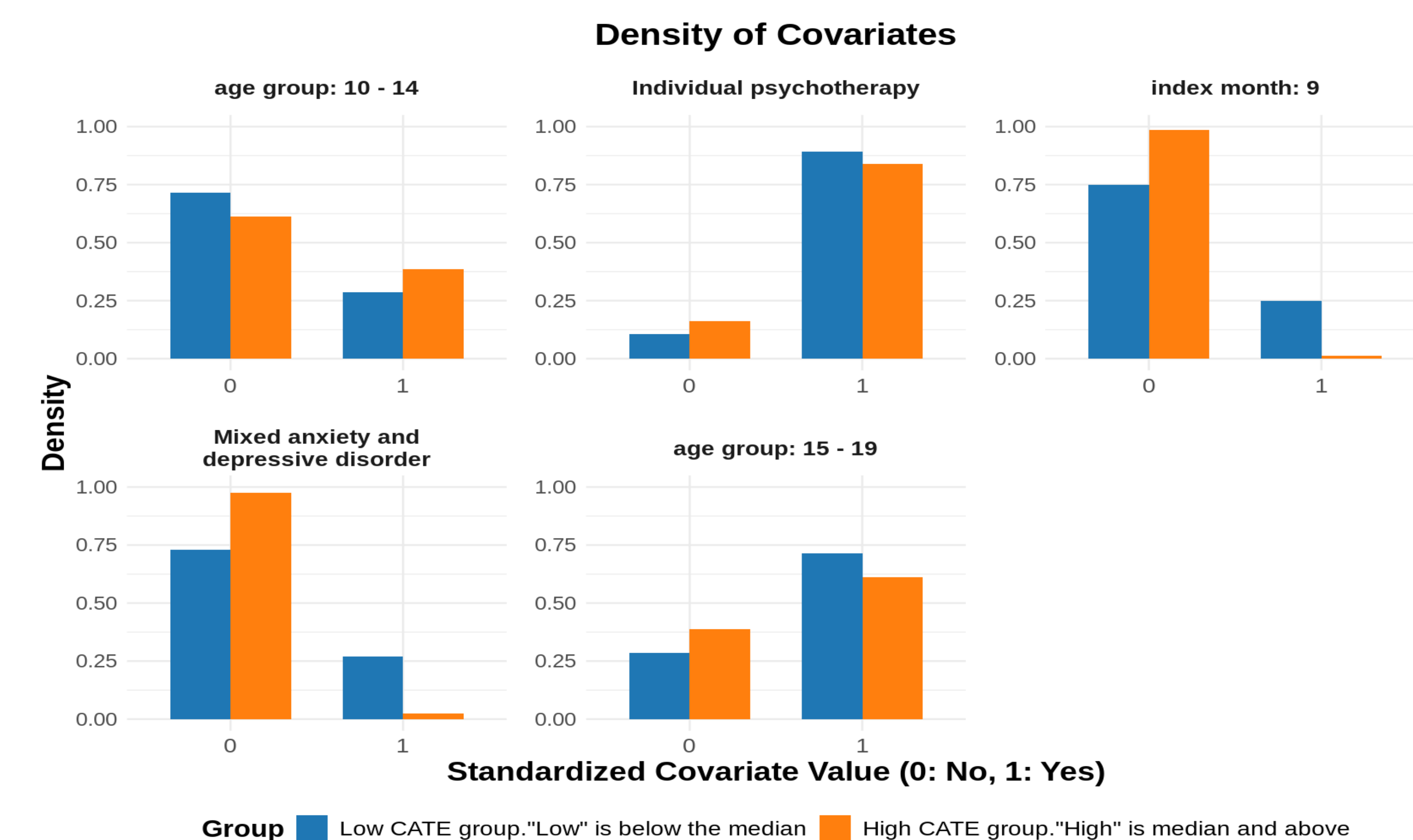


Figure 3. Density of top 5 covariates

Conclusions

- This study suggests that while SSRI treatment did not significantly affect arrhythmia
- Individualized treatment rule accounting for this heterogeneity could modify guidelines for concurrent use of MPH and SSRIs

Acknowledgements

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