Real-World Evaluation of Systematic Bias and Balance of Overall Patient Characteristics of Propensity Score Matching Versus Cardinality Matching

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Background

- Propensity score matching (PSM) is subject to limitations, especially in studies of small sample size:
    1. Susceptible to substantial bias due to limited overlap in covariate distributions
    2. Potential model overparameterization due to limited degrees of freedom
- Cardinality matching (CM) uses integer programming to find the largest matched sample meeting a set of prespecified balance criteria.
- CM overcomes the limitations of PSM by matching directly on the marginal distribution of covariates
- Prior research has shown large-scale CM achieves superior patient retention and comparable systematic bias as compared to large-scale PSM; however, large-scale methods may not be applicable in the setting of small sample sizes.

Study Objectives: To compare the performance of PSM and CM in the context of a study of new users of new users of angiotensin-converting enzyme inhibitor (ACEI) and β-blocker monotherapy at small sample sizes

Methods

Study Design: Comparative new user cohort study
Data Source: Data were from the IBM® MarketScan® Commercial Claims and Encounters database
Study Population: New users of ACEI and β-blocker monotherapy between 10-01-2014 to 01-01-2017 with a history of hypertension (index = first drug exposure)
Covariates
- **Matching covariates** – covariates included in the PS model and CM – included patient demographics (i.e., age, sex, race, ethnicity, year) and clinical characteristics (i.e., comorbidities comprising the Charlson Comorbidity Index; and the Hospital-Frailty Risk Score)
- **Observed covariates** included patient demographics, and all conditions, drug exposures and other health-service-use-behaviors observed 30 and 365 days prior to index

Statistical Analysis
- PSM was conducted through greedy matching (1:1 match, caliper=0.15)
- CM performed through 1:1 matching with the following prespecified balance criteria: max SMD=0.00, max SMD=0.01, max SMD=0.05 and max SMD=0.10

Subsample Groups
- Developed 10% and 0.25% sample groups consisting of 5 and 200 subsample draws, respectively
    - Subsample draws randomly sampled from study population without replacement

Evaluation of CM and PSM
- Post-match sample size
    - Average sample size across all subsample draws within each sample group
- Post-match matching covariate and observed covariate balance
    - Evaluated using SMDs where an absolute SMD ≤0.10 was considered balanced
    - Assessed post-match SMDs of all matching covariates and observed covariates across all subsample draws within each sample group
- Post-match residual bias
    - Performed a total of 105 negative control outcome experiments for each sample group
    - Due to the low frequency of negative control outcomes, negative control outcome experiments were conducted across a pooled sample consisting of matched patients identified across all subsample draws for each sample group
    - Assessed using the expected absolute systematic error (EASE) of the empirical null distribution of negative control outcome experiments

Results

Pre-match:
- A total of 186,233 (β-blocker: 56,871; ACEI: 129,362) patients met the study criteria
- 18,576 (β-blocker: 5,675; ACEI: 12,901) and 465 (β-blocker: 142; ACEI: 323) patients were included in each subsample draw of the 10% and 0.25% sample groups, respectively
- Average 35,458 and 8,566 observed covariates in the 10% and 0.25% sample groups, respectively

Figures 1-3. Average post-match sample size (left panel); post-match matching covariate and observed covariate balance (middle panel); and post-match EASE (right panel)
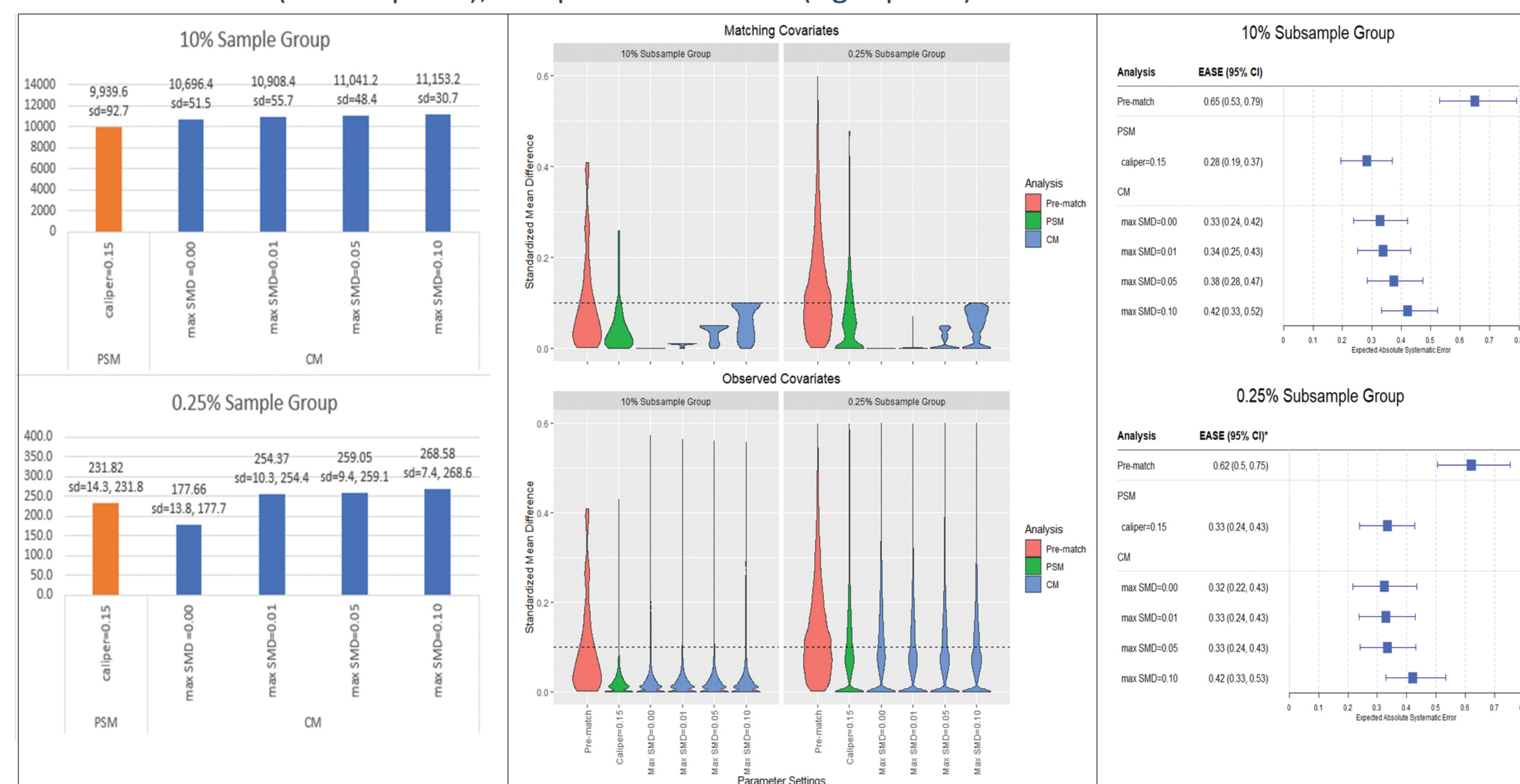
Post-match sample size:
- As shown in **Figure 1**, CM was associated with increased average post-match sample size except for analyses in the 0.25% sample group with a tightest balance criterion of (max SMD=0.00)

Post-match covariate balance:
- CM achieved balance on all matching covariates; PSM failed to achieve balance in both sample groups
- In the 10% sample group, PSM achieved improved observed covariate balance as compared to CM
- In the 0.25% sample group, as compared to PSM, observed covariate balance was improved with CM at tighter balance criteria and similar at looser balance criteria

Post-match residual confounding:
- As compared to CM, PSM was associated with improved EASE in the 10% sample group and similar EASE in the 0.25% sample group
- CM achieved improved EASE with tighter balance criteria

Conclusions

CM found the largest matched sample meeting a set of prespecified balance criteria. At smaller sample sizes, PSM and CM achieved comparable balance in overall patient characteristics and reductions in systematic bias albeit CM had improved performance at more stringent prespecified balance criteria (i.e., SMD <0.05). Improved indirect covariate balance and reductions in EASE were observed with PSM at larger sample sizes as compared to CM. We recommend CM as an alternative to PSM in studies of small sample size.

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