Comparison of cardinality matching and propensity score matching for population-level estimation in observational studies

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BACKGROUND

- Propensity score matching (PSM), a mainstay of population-level estimation, is subject to limitations:
  1. Substantial bias and variance of estimates due to limited overlap of covariate distributions
  2. Model overparameterization due to limited degrees of freedom or observations per covariate
- Cardinality matching (CM) uses integer programming to find the largest matched sample meeting a set of prespecified balance criteria thereby overcoming limitations of PSM by directly matching on the original covariates

Study Objectives: To describe the performance of PSM and CM within the context of a study of new users of angiotensin-converting enzyme inhibitor (ACEI) and thiazide or thiazide-like diuretic monotherapy

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 ACEI and thiazide or thiazide-like diuretic monotherapy between 10-01-2014 to 01-01-2017 with a history of hypertension (index = first drug exposure)

Covariates

- Covariate candidates included patient demographics, and all conditions, drug exposures and other health-service-use-behaviors observed 30 and 365 days prior to index
- Covariate candidates considered in propensity model limited to those with frequency >0.1%
  - Due to memory constraints of CM, frequency >2% required for CM in the full study population
- Matching covariates defined as covariates with non-zero beta coefficients in the propensity model

Statistical Analysis

- Large-scale PSM was conducted through greedy matching (1:1 match, caliper=0.10 and 0.20)
- CM performed through 1:1 matching with the following prespecified balance criteria: exact marginal distributional balance (e.g., max SMD=0), max SMD=0.01, max SMD=0.05 and max SMD=0.10

Evaluation of CM and PSM

- Post-match sample size
- Post-match covariate candidate and matching covariate balance
  - Assessed using standardized mean differences (SMD); absolute SMD ≤0.10 considered balanced
- Post-match residual bias
  - Assessed using the expected systematic error (ESE) of the empirical null distribution of negative control outcome experiments
  - Identified a total of 105 negative control outcomes, and estimated the hazard ratio of each negative control outcome using unconditional Cox models

Subsample Group Analyses

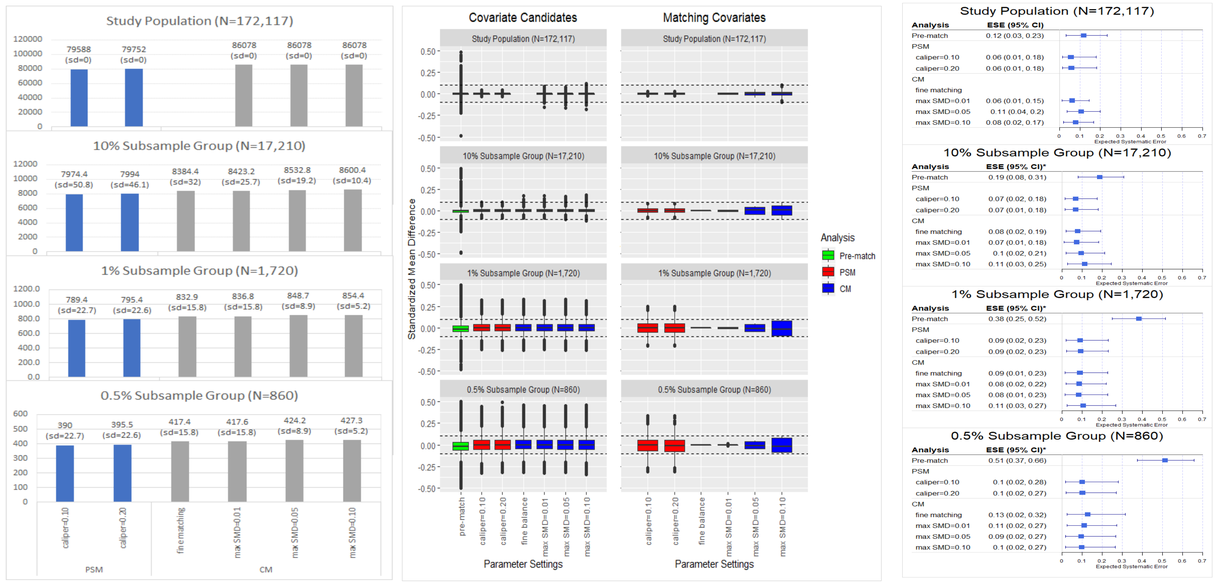
- Developed 10%, 1% and 0.5% subsample groups with 5, 50 and 100 subsample draws, respectively, randomly sampled from the study population
- Empirical selection of matching covariates, matching and negative control experiments performed independently across all subsample draws
- Post-match covariate balance and residual bias evaluated across all subsample draws within each subsample group considered jointly

RESULTS

Table 1 shows the average pre-match sample size, and number of covariate candidates and matching covariates. We identified 172,117 (ACEI: 129,078; thiazide: 43,039) patients meeting the study criteria.

	Sample size, n	Covariate Candidates, n (sd)	Matching Covariates, n (sd)
Study population	172,117	50,391	1,237 (PSM); 717 (CM)
10% Subsample Group	17,210	26,696 (467)	210.6 (43.7)
1% Subsample Group	1,720	11,644 (442)	42.0 (19.6)
0.5% Subsample Group	860	8,581 (436)	23.2 (9.3)

Figure 1. Evaluation of CM and PSM; average post-match sample size (left panel); post-match covariate candidate and matching covariate balance (middle panel); and post-match ESE (right panel)



- **Post-match Sample Size:** CM requiring fine matching failed to converge to a matched sample within the full study population, but was otherwise associated with improved patient retention
- **Post-match Covariate Balance:** PSM achieved improved covariate candidate balance at larger sample sizes. Similar covariate candidate balance between CM and PSM was achieved at smaller sample sizes. PSM achieved balance on all matching covariates in the full study population but failed at smaller sample sizes. CM achieved balance on all matching covariates at all sample sizes.
- **Post-match residual bias:** ESE was similar between CM and PSM at all sample sizes. Improvements in ESE as compared to the pre-match sample were most pronounced at smaller sample sizes.

CONCLUSIONS

CM found the largest matched sample meeting prespecified balance criteria while achieving similar covariate candidate balance and residual confounding. While matching covariate balance was consistently achieved with CM, PSM resulted in imbalance at smaller sample sizes. We recommend CM as an alternative to PSM in studies where PSM cannot achieve balance of matching covariates.

CONFLICT OF INTEREST STATEMENT

The authors are full time employees of Janssen Research and Development, a unit of Johnson and Johnson. The work on this study was part of their employment. They also hold pension rights from the company and own stock and stock options.

IRB STATEMENT: The use of IBM data sets was reviewed by the New England Institutional Review Board (IRB) and was determined to be exempt from broad IRB approval, as this research project did not involve human subject research.