EquiSCAT: Strategies for Equity Considerations in Synthetic Control Arm Design

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INTRODUCTION

- RCT - gold standard for measuring any intervention's efficacy
- Representativeness/Equity in RCTs has become a national priority
- Synthetic Controls incorporate RWD into RCT and creates a hybrid trial population and has shown great potential to produce more effective and accurate studies

RESEARCH AIMS

Design methods for creating hybrid trials with synthetic controls -

- accurately estimates generalized treatment effect on a target population
- produce a representative/equitable trial (e.g., target and trial populations match) potentially using less concurrent controls

DATA

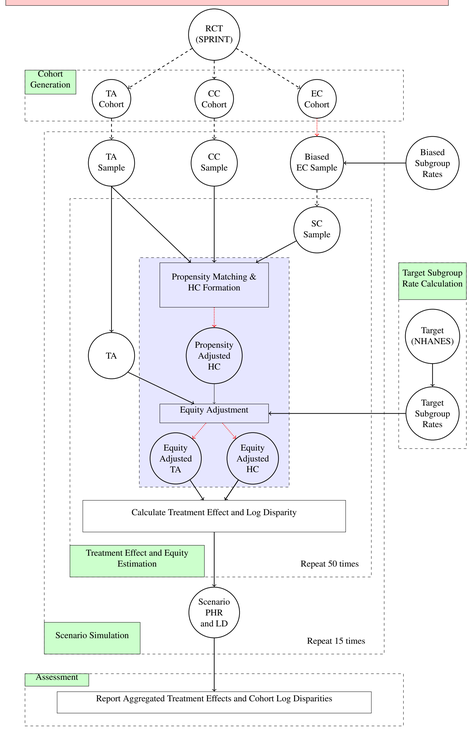
- RCT: SPRINT (Systolic Blood Pressure Intervention Trial)
- Target: NHANES (National Health and Nutrition Examination Survey), Hypertensive, 2015-2016
- Protected Attributes: Age Group (40-59, 59+), Gender (Male, Female), Race/Ethnicity (NH Asian, NH Black, NH White, Hispanic, Other)
- Other Attributes: Educational status, Is smoker, Fasting glucose level, Total cholesterol, Average of 3 sitting Systolic BP, Has clinical or subclinical CVD, Framingham risk score, Serum creatinine, Estimated GFR within past 6 months

METHOD

- Five main functions –
  - Cohort Generation, Scenario Simulation, Target Subgroup Rates Calculation, Treatment Effect and Equity Estimation, Assessment
- Standard Propensity Score Matching method -
  - reduces distributional differences between selected synthetic controls and RCT data
- Weighting by Inverse odds of Trial Participation [2] method -
  - adjusts the hybrid trial data to make it representative of the target population
- EquiSCAT is a modular framework
  - allows using different methods for propensity and equity adjustment

FRAMEWORK

EquiSCAT: Strategies for Equity Considerations in Synthetic Control Arm Design



Legend

TA = Treatment Arm
CC = Concurrent Controls
EC = External Controls
SC = Synthetic Controls
HC = Hybrid Controls
PHR = Population Hazard Ratio
LD = Log Disparity

- Random Sampling
- Sample Adjustment
- Standard input/output
- Data
- Process
- EquiSCAT Functions

Adjustment Methods

1. **CC Only:** No SC, No Propensity or Equity adjustment
2. **HC + Propensity:** Use both CC and SC, Only Propensity Adjustment
3. **HC + NC Matching:** Use both CC and SC, use NC Matching
4. **HC + Equity:** Use both CC and SC, Only Equity Adjustment
5. **HC + Propensity + Equity:** Use both CC and SC, both Propensity and Equity Adjustment **(method shown in figure)**

Notes

1. Any Matching and Weighting methods can be used in Treatment Effect and Equity Estimation
2. Any RCT, RWD, and Target data can be used in Cohort Generation, Scenario Simulation, and Target Subgroup Rate Calculation
3. Any endpoint or metric can be used for Assessment

Measure Treatment Effect:

- Hazard Ratio is used as the indicator of the treatment effect

Measure Equity/Representativeness:

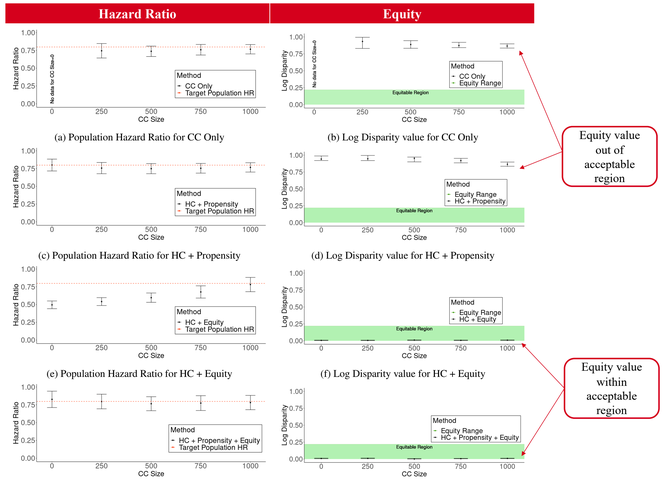
- The degree of representativeness is measured by Log Disparity (LD) ($0 \leq LD \leq 0.22$ is considered representative) [1]
- Equivalent to the ratio of enrollment odds of subjects of the protected group in the observed cohort to the odds of the protected subjects in the ideal cohort [1]

RESULTS

Table 1: Comparison of Population Hazard Ratio and Log Disparity across different methods. TA (n=1000), CC (n=500). Bold (*) symbol in Hazard Ratio column indicates estimated HR being significantly different ($p < 0.05$) from Target PHR. Bold (†) symbol in Log Disparity column indicates measured Log Disparity not being within equitable range. (LD > 0.22).

Biased EC Cohort	Control Population	Adjustment Method	Hazard Ratio [95% Confidence Interval]	Log Disparity [95% Confidence Interval]
High Risk	**CC**	**None**	0.725 [0.655, 0.804]	**0.905 [0.416, 1.394]†**
	HC	**Propensity**	0.738 [0.670, 0.814]	**0.887 [0.519, 1.254]†**
	HC	**NC Matching**	0.748 [0.679, 0.824]	**0.893 [0.833, 0.960]†**
	HC	**Equity**	**0.575 [0.519, 0.632]***	0.013 [0.009, 0.017]
	HC	**Propensity + Equity**	0.741 [0.655, 0.826]	0.010 [0.004, 0.016]
Veterans	**CC**	**None**	0.725 [0.655, 0.804]	**0.905 [0.416, 1.394]†**
	HC	**Propensity**	0.742 [0.676, 0.816]	**0.745 [0.308, 1.183]†**
	HC	**NC Matching**	0.717 [0.649, 0.793]	**0.881 [0.834, 0.959]†**
	HC	**Equity**	0.789 [0.713, 0.865]	0.012 [0.007, 0.016]
	HC	**Propensity + Equity**	0.756 [0.682, 0.831]	0.014 [0.011, 0.017]
Unbiased	**CC**	**None**	0.726 [0.655, 0.804]	**0.905 [0.416, 1.394]†**
	HC	**Propensity**	0.730 [0.670, 0.796]	**0.912 [0.428, 1.396]†**
	HC	**NC Matching**	0.758 [0.687, 0.835]	**0.865 [0.809, 0.955]†**
	HC	**Equity**	0.730 [0.661, 0.800]	0.011 [0.006, 0.017]
	HC	**Propensity + Equity**	0.729 [0.658, 0.801]	0.013 [0.008, 0.017]
Target PHR	**All Controls**	**Equity**	0.757 [0.740, 0.773]	0.031 [0.022, 0.040]

Figure 1: PHR and equity for varying CC sample sizes using "High Risk" cohort as biased External Controls. Log Disparity is shown for Gender=Female subgroup only.



(a) Population Hazard Ratio for CC Only
(b) Log Disparity value for CC Only
(c) Population Hazard Ratio for HC + Propensity
(d) Log Disparity value for HC + Propensity
(e) Population Hazard Ratio for HC + Equity
(f) Log Disparity value for HC + Equity
(g) Population Hazard Ratio for HC + Propensity + Equity
(h) Log Disparity value for HC + Propensity + Equity

DISCUSSION

- Failure to perform equity adjustment led to inequitable trials for all three biased EC cohorts and significantly different PHR estimate in case of "High Risk Cohort"
- Combining propensity and equity adjustment achieved an accurate estimation of PHR with a representative trial population in all cases
- Performing no equity adjustment always leads to inequitable trials for all varying CC sizes
- Equity adjustment alone produces incorrect PHR estimations ("High Risk" cohort), but improves with increasing CC Size
- Performing both propensity and equity adjustment leads to accurate PHR estimations and achieves acceptable equity for all CC sizes

CONCLUSION

- Identified and defined the issue of equity in hybrid RCTs
- Developed EquiSCAT framework and compare several equitable HCA construction methods
- Empirically demonstrated the necessity of both propensity and equity adjustments

FUTURE WORK

- Explore multiple propensity and equity adjustment methods
- Examine empirical results with other RCT data and Target data
- Investigate performance with other types of outcome variables
- Conduct additional theoretical exploration and analysis
- Work with real RWD data
- Working on an advanced framework named FRESCA
- Open to possible future collaborations

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