Propensity score methods to ensure fair comparisons between treatment groups in observational studies

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Contents

Motivation

- Randomised clinical trials (RCTs): gold standard for studying the efficacy of interventions or treatments.
- Observational studies: differences between groups ⟶ could confound the association between exposure and outcome.
- Ensure fair comparisons ⟶ control for confounding.
- Several studies compare different COVID-19 waves ⟶ no matching or adjustment procedures.

Statistical aim

To compare standard and propensity score methodologies in R that ensure fair comparisons between groups.

Methods

Model estimation

- Compare effect of dichotomous variable (intervention/exposure) Z in a dichotomous outcome Y
- 5-way strategy:
  - Raw logistic regression model
  - Full adjusted logistic regression model
  - Logistic regression model adjusted by the propensity score value
  - Propensity matching logistic regression model
  - Inverse probability weighting (IPW) logistic regression model

Raw model

First approach: Raw logistic regression model

Logistic regression model with intervention as a covariate

$$\ln\left(\frac{\mathrm{P}(Y_i = 1)}{1 - \mathrm{P}(Y_i = 1)}\right) = \alpha + \gamma Z_i$$

$i = 1, \ldots, n$ where n is the number of subjects of analysis

Full adjusted model

Second approach: Full adjusted logistic regression model

Logistic regression model with intervention and all baseline variables as covariates

$$\ln\left(\frac{\mathrm{P}(Y_i = 1)}{1 - \mathrm{P}(Y_i = 1)}\right) = \alpha + \gamma Z_i + \beta_1 X_{i1} + \cdots + \beta_k X_{ik}$$

PS models

Propensity score computation

- Logistic regression model
  - **Outcome**: Exposure
  - **Adjustment variables**: Baseline variables
  - **Result**: Probability of exposure

$$\ln\left(\frac{\mathrm{P}(Z_i = 1)}{1 - \mathrm{P}(Z_i = 1)}\right) = \alpha + \beta_1 X_{i1} + \cdots + \beta_k X_{ik}$$

Z_i indicator of exposure, $X_i = X_{i1}, \ldots, X_{ik}$ is the vector of baseline variables

- Prediction for each patient ⟶ Propensity score

$$\mathrm{ps}(X_i) = \mathrm{P}(Z_i = 1 | X = X_i)$$

PS adjusted model

Third approach: Logistic regression model adjusted by the propensity score value

- Logistic regression model
  - **Outcome**: Event of interest
  - **Adjustment variables**: Intervention and propensity score

$$\ln\left(\frac{\mathrm{P}(Y_i = 1)}{1 - \mathrm{P}(Y_i = 1)}\right) = \alpha + \gamma Z_i + \beta\,\mathrm{ps}(X_i)$$

PSM model

Fourth approach: Propensity matching logistic regression model

- Match patients according to propensity score
  - Distance: propensity score
  - Nearest neighbour matching
  - Caliper 0.2 standard deviations
- Compare matching
- Logistic regression model with matched cohorts and intervention as covariate

R packages and functions

- MatchIt: `matchit()`
- cobalt: `bal.tab()`, `love.plot()`
- survey: `svyglm()`

IPW model

Fifth approach: Inverse probability weighting (IPW) logistic regression model

- Weight patients according to propensity score
  - $1/\mathrm{ps}(X_i)$ for patients in exposure group
  - $1/(1-\mathrm{ps}(X_i))$ for patients in non-exposure group
- Compare weighted cohorts
- Logistic regression model with weighted cohorts and exposure as covariate

R packages and functions

- WeightIt: `weightit()`
- cobalt: `bal.tab()`, `love.plot()`
- survey: `svyglm()`

Aim

Clinical aim

To compare in-hospital mortality between first and successive waves of COVID-19

- Y_i: in-hospital mortality (Yes/No)
- Z_i: wave (1st wave vs waves 2-3-5)
- $X = (X_1, \ldots, X_k)$: baseline variables

MetroSud cohort

- Patients admitted to hospital with a proven SARS-CoV-2 infection
- Adult patients (aged 18 years or older)
- Full available information in a set of key variables
- Data collected during 4 waves of the pandemic ⟶ Recoded in wave 1 vs waves 2/3/5

Methods - Model definition

Model definition

- **Outcome:** In-hospital mortality
- **Variable of interest:** Wave (1st vs others)
- **Adjustment variables**
  - Demographic: age, sex, race, body mass index (BMI), long-term facility
  - Comorbidities: diabetes mellitus, chronic obstructive pulmonary disease (COPD), heart failure, hypertension, renal insufficiency, dyslipidemia, coronary heart disease, hematological neoplasm, solid neoplasm, organ transplantation, immunosuppressive treatment, chronic complex patient/patients with advanced chronic disease
  - Laboratory data: Dimer, C-reactive protein, leukocytes, hemoglobin, lymphocytes
  - Other: Pneumonia severity index (PSI), FiO2 and oxygen support

Methods - Missing imputation

Missing imputation

- Missing data in important variables $\longrightarrow$ Multiple imputation
  - Identify variables with missings (8 variables, 5% to 25% of missings)
  - Chained equations to impute missing values with complete variables
    - Continuous variables: Predictive mean matching
    - Binary variables: Logistic regression
  - $n = 5$, iterations=25 $\longrightarrow$ 5 completed datasets (convergence)
  - R package: mice

R packages and functions

- MatchThem: `matchthem()`, `weightthem()`

Methods - Results reporting

- Rubin rules to adjust variability between imputations
- Pool five models for each strategy ⟶ Five final models
- Graphical comparison of OR and 95% CI

R packages and functions

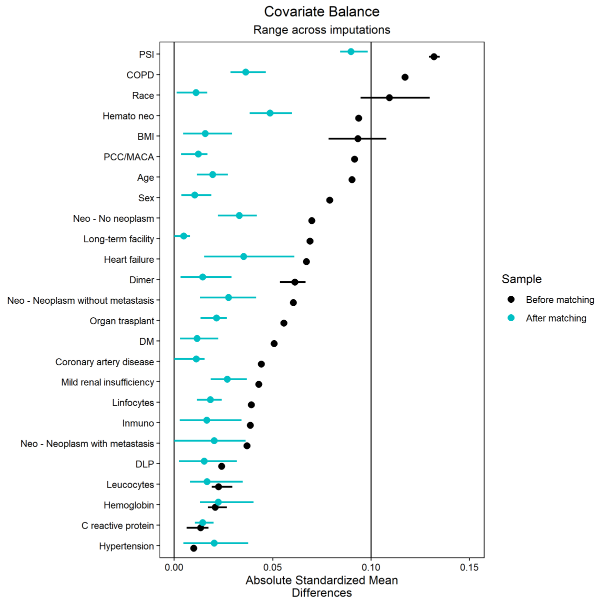
- gtsummary: `tbl_regression()`
- ggplot2: `ggplot()`

Included patients

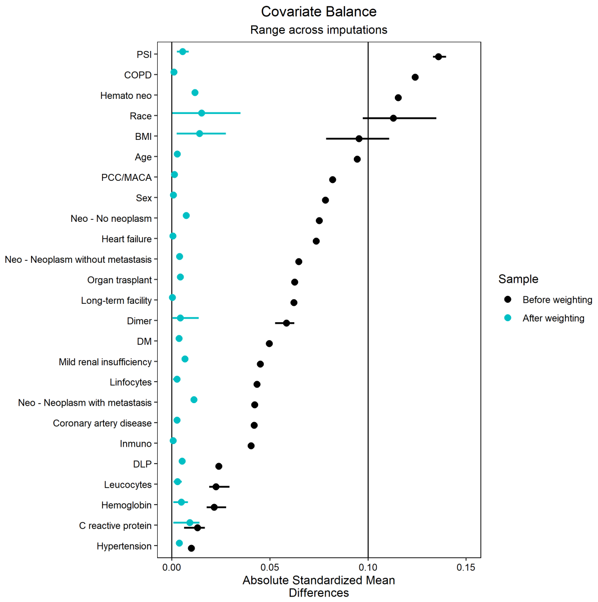
	Wave 1 **N=2074**	**Wave 2-3-5** **N=1906**
Age (years)	59.00 [49.00; 69.00]	59.00 [46.00; 69.00]
Women	854 (41.18%)	712 (37.36%)
BMI	28.90 [25.86; 32.15]	29.41 [26.45; 32.99]
Unknown	636	352
COPD	274 (13.21%)	337 (17.68%)
Heart Failure	50 (2.41%)	70 (3.67%)
Hematological neoplasm	12 (0.58%)	35 (1.84%)
Race		
Caucasian	1206 (78.06%)	1264 (72.90%)
Other	339 (21.94%)	470 (27.10%)
Unknown	529	172
Dimer D	566.50 [314.00; 1,050.00]	450.50 [255.00; 840.00]
Unknown	488	176
C-reactive protein	79.70 [34.00; 149.00]	81.90 [39.40; 139.90]
Unknown	161	120

Median [Q1; Q3]; n (%)

Graphical comparison propensity matching (N=3484)

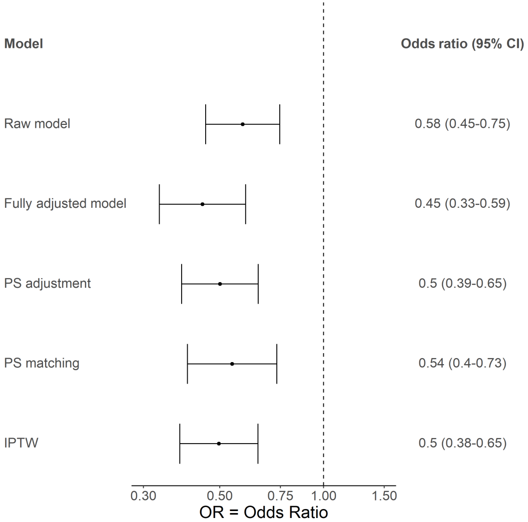


Graphical comparison propensity weighting (N=3980)



Models

OR and 95%CI for the pool logistic models for each strategy



Discussion

- All adjustment methods corrected raw OR
- Full adjusted model
  - Allows the measurement of each covariate risk
  - Overfitting when small number of events or large number of covariates
- Propensity matching
  - Perfect covariate balance
  - Reduces sample size
- Propensity weighting
  - Retains all sample size
  - Unstable with extreme weights

- Limitations: residual confounding

Conclusions

- Same statistical conclusion regardless of the strategy used (in this cohort)
- PS matching and weighting result in similar distribution of baseline variables
- PS methods reduce a set of confounders into a single variable
- R has a range of functions to adjust for confounders in observational studies
- These functions are adapted for missing data scenarios

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Thank you for your attention!

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