A Practical Introduction to Propensity Score Analysis using R

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30 Sept 2020: SPPH, UBC

About this event

- TI Methods Speaker Series page: Therapeutics Initiative
  - Dr. Carole Lunny
- SARGC page: Students and Recent Graduates Committee (SARGC) coordinate activities for the Statistical Society of Canada (SSC)'s student and recent graduate members
  - Md. Erfanul Hoque
  - Janie Coulombe

Assumptions of the webinar

- *Target audience*:
  - Familiar with regression
  - Familiar with R
    - will explain some necessary package / functions / arguments
  - have no/minimal idea about propensity score
- *Topics covered*
  - Not covering any new research
  - Not covering statistical theory
    - implementation being the goal here
  - Not attempting to reach any clinical conclusion

Format of the webinar

- *Presentation format*
  - Rather informal
  - 1 hr vs. 2 hr
  - Q/A at
    - 45 min and
    - at the end
- *Webinar Materials*
  - All reproducible codes provided
    - ehsanx.github.io/SARGC-TIMethods/
  - Necessary references cited in respective slides

Outline

- [1] Data and Regression
  - (Diagnostics)
- [2] Exact matching
  - (motivation)
- [3] Propensity score matching
  - (4 steps)
- [4] Propensity score Reviews in different disease areas
  - (brief)

[1] Right Heart Catheterization (RHC) Dataset

The dataset that we will use today is from Connors et al. (1996).

The effectiveness of right heart catheterization in the initial care of critically ill patients
AF Connors, T Speroff, NV Dawson, C Thomas… - Jama, 1996 - jamanetwork.com
Objective.—To examine the association between the use of right heart catheterization (RHC) during the first 24 hours of care in the intensive care unit (ICU) and subsequent survival, length of stay, intensity of care, and cost of care. Design.—Prospective cohort study. Setting.—Five US teaching hospitals between 1989 and 1994. Subjects.—A total of 5735 critically ill adult patients receiving care in an ICU for 1 of 9 prespecified disease categories. Main Outcome Measures.—Survival time, cost of care, intensity of care, and length of stay in the …
☆ 99 Cited by 2588 Related articles All 11 versions Import into BibTeX

Not secure | biostat.mc.vanderbilt.edu/wiki/pub/Main/DataSets/rhc.html

Swang1	Right Heart Catheterization (RHC)
Sadmdte	Study Admission Date
Dthdte	Date of Death
Lstctdte	Date of Last Contact
Dschdte	Hospital Discharge Date
Death	Death at any time up to 180 Days
Ptid	Patient ID

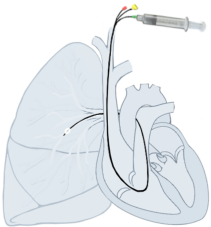
Frank E Harrell Jr
Last modified: Fri Dec 27 16:14:18 EST 2002

Notations

- Outcome `Death` (Y)
  - Death at any time up to 180 Days
- Treatment `swang1` (A: Swan-Ganz catheter)
  - Whether or not a patient received a RHC
- Covariate list: L (`age`, `sex`, `race` , . . .)
- Analysis strategy: matching RHC patients with non-RHC patients

[1] Right Heart Catheterization (RHC) Dataset

- `RHC` is helpful in guiding therapy decision
  - Helps determine the pressures within the heart
  - Popularly beleived that `RHC` is benefitial
  - Conducting RCT is hard (ethical reasons)
  - Benefit of `RHC` was not shown earlier (1996)
- SUPPORT data has 2 phases
  - phase 1: prospective observational study
  - phase 2: cluster RCT
  - Data in this study is combined



[1] Load data

```
# Load the cleaned up data.
# Reproducible codes:
# https://ehsanx.github.io/SARGC-TIMethods/
analytic.data <- readRDS("data/RHC.Rds")
# Data size and number of variables
dim(analytic.data)
```

```
## [1] 4767   23
```

```
# variable names
names(analytic.data)
```

```
##  [1] "age"              "sex"              "race"
##  [4] "Disease.category" "DNR.status"       "APACHE.III.score"
##  [7] "Pr.2mo.survival"  "No.of.comorbidity" "DASI.2wk.prior"
## [10] "Temperature"      "Heart.rate"       "Blood.pressure"
## [13] "Respiratory.rate" "WBC.count"        "PaO2.by.FIO2"
```

[1] Inspecting data: Crude

```
require(tableone)
# 2 x 2 table
tab0 <- CreateTableOne(vars = "RHC",
                       data = analytic.data,
                       strata = "Death")
print(tab0, showAllLevels = TRUE)
```

```
##           Stratified by Death
##            level  No           Yes          p      test
##   n                2013         2754
##   RHC (%) No RHC 1315 (65.3)  1268 (46.0)  <0.001
##           RHC     698 (34.7)  1486 (54.0)
```

[1] Inspecting data: Some baseline variables

```
baselinevars <- c("age","sex", "race")
# Table 1
tab1 <- CreateTableOne(vars = baselinevars,
                       data = analytic.data,
                       strata = "Death", includeNA = TRUE,
                       test = TRUE, smd = FALSE)
print(tab1, showAllLevels = FALSE, smd = FALSE)
```

```
##                      Stratified by Death
##                       No            Yes           p      test
##    n                  2013          2754
##    age (%)                                        <0.001
##       [-Inf,50)        713 (35.4)    400 (14.5)
##       [50,60)          351 (17.4)    452 (16.4)
##       [60,70)          426 (21.2)    789 (28.6)
##       [70,80)          382 (19.0)    750 (27.2)
##       [80, Inf)        141 ( 7.0)    363 (13.2)
```

[1] Crude regression

```
# adjust the exposure variable (primary interest)
fit0 <- glm(I(Death=="Yes")~RHC,
            family=binomial, data = analytic.data)
require(Publish)
publish(fit0)
```

```
##  Variable  Units OddsRatio       CI.95 p-value
##       RHC No RHC       Ref
##              RHC      2.21 [1.96;2.49]  <1e-04
```

[1] Adjusted regression

```
# adjust the exposure variable + demographics
fit1 <- glm(I(Death=="Yes")~RHC + age + sex + race,
            family=binomial, data = analytic.data)
publish(fit1)
```

```
##  Variable     Units OddsRatio       CI.95     p-value
##       RHC    No RHC       Ref
##               RHC      2.71 [2.38;3.08]     < 1e-04
##       age [-Inf,50)       Ref
##            [50,60)      3.56 [3.01;4.20]     < 1e-04
##            [60,70)      0.74 [0.64;0.87]   0.0001274
##            [70,80)      1.33 [1.15;1.54]     < 1e-04
##          [80, Inf)      1.06 [0.93;1.21]   0.3633526
##       sex      Male       Ref
##             Female      0.49 [0.43;0.56]     < 1e-04
##      race     white       Ref
##             black      1.10 [0.93;1.31]   0.2666157
```

[1] Why adjust?

Continuous outcome (Y)

- treated group $A = 1$ (`RHC`)
- control group $A = 0$ (`no RHC`)

Treatment effect $= E[Y|A = 1]$ vs. $E[Y|A = 0]$

- Would only work if 2 groups are comparable / exchangeable / ignorable treatment assignment
- Randomization with enough sample size is one

Binary outcome (Y)

Treatment effect $= prob[Y = 1|A = 1]$ vs. $prob[Y = 1|A = 0]$

[1] Why adjust?

In absence of randomization,

$E[Y|A = 1] - E[Y|A = 0]$

includes

- Treatment effect
- Systematic differences in 2 groups ('confounding')
  - Doctors may prescribe tx more to frail and older age patients.
  - In here, L = age is a confounder.

[1] Why adjust?

In absence of randomization, if age is a known issue

Causal effect for young

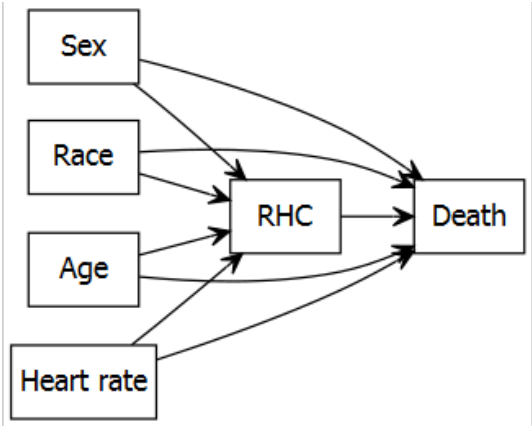
- $E[Y|A = 1, L = \texttt{younger age}]$ - $E[Y|A = 0, L = \texttt{younger age}]$

Causal effect for old

- $E[Y|A = 1, L = \texttt{older age}]$ - $E[Y|A = 0, L = \texttt{older age}]$

Conditional exchangeability; only works if L is measured

[1] Why adjust?



This was not a completely randomized data; some observational data was combined.

[1] Adjusted regression (v2)

```
# adjust the exposure variable + adjustment variables
baselinevars <- c("age","sex", "race","Disease.category",
                  "DNR.status", "APACHE.III.score",
                  "Pr.2mo.survival","No.of.comorbidity",
                  "DASI.2wk.prior","Temperature",
                  "Heart.rate", "Blood.pressure",
                  "Respiratory.rate", "WBC.count",
                  "PaO2.by.FIO2","PaCO2","pH",
                  "Creatinine","Albumin","GComa.Score")
out.formula <- as.formula(paste("I(Death=='Yes')", "~ RHC +",
                                paste(baselinevars,
                                      collapse = "+")))
out.formula
```

```
## I(Death == "Yes") ~ RHC + age + sex + race + Disease.category +
##     DNR.status + APACHE.III.score + Pr.2mo.survival + No.of.comorbidity
##     DASI.2wk.prior + Temperature + Heart.rate + Blood.pressure +
```

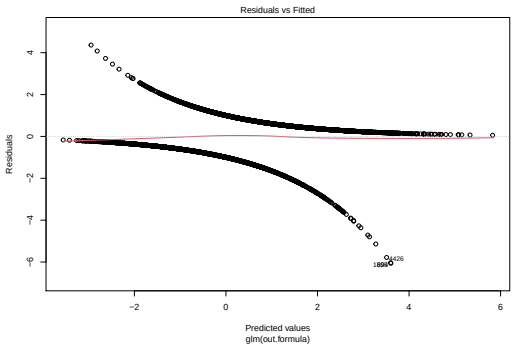
[1] Adjusted regression (v2)

```
fit2 <- glm(out.formula,
            family=binomial, data = analytic.data)
publish(fit2)
```

```
##            Variable     Units OddsRatio       CI.95     p-value
##                 RHC    No RHC       Ref
##                            RHC      2.55 [2.18;2.97]     < 1e-04
##                 age [-Inf,50)       Ref
##                       [50,60)      1.70 [1.39;2.07]     < 1e-04
##                       [60,70)      0.77 [0.65;0.91]   0.0019296
##                       [70,80)      1.18 [1.01;1.38]   0.0396871
##                   [80, Inf)        1.13 [0.98;1.30]   0.0957860
##                 sex      Male       Ref
##                        Female      0.43 [0.38;0.50]     < 1e-04
##                race     white       Ref
##                         black      1.14 [0.94;1.38]   0.1917093
##                         other      0.91 [0.67;1.24]   0.5634739
```

[1] Adjusted regression (v2)

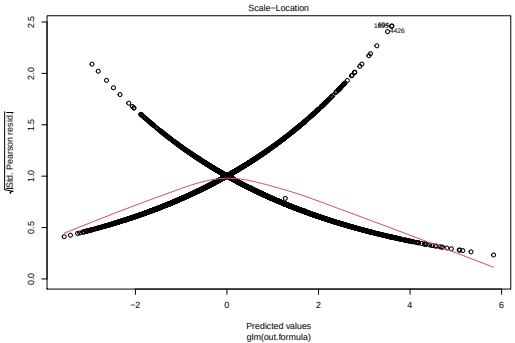
```
plot(fit2, which =1)
```



- curvilinear trends?
  - logistic regression IS curvilinear by nature

[1] Adjusted regression (v2)

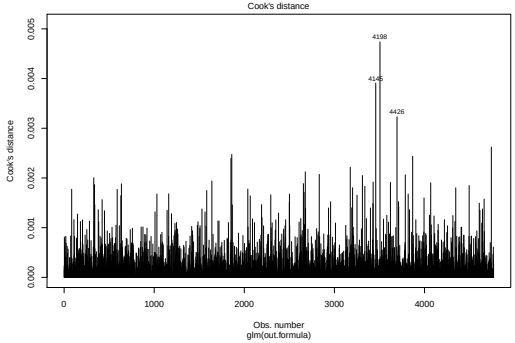
```
plot(fit2, which =3)
```



- red line is approximately horizontal?
- points have approximately equal spread around the red line?
  - more about detecting heteroscedasticity?

[1] Adjusted regression (v2)

```
plot(fit2, which =4)
```



- Cook's D estimates the influence of data points

[2] Alternate to Regression

How sure are you about the model-specification?

- Interaction?
- Polynomial?
- Potential solution?
  - Exact Matching

[2] Exact Matching: 2 variables

```
var.comb <- do.call('paste0',
                    analytic.data[, c('race', 'sex')])
length(table(var.comb))
```

```
## [1] 6
```

```
table(var.comb)
```

```
## var.comb
## blackFemale   blackMale otherFemale   otherMale whiteFemale   whiteMale
##         331         404         113         140        1340        2439
```

```
table(analytic.data$RHC,var.comb)
```

```
##         var.comb
##          blackFemale blackMale otherFemale otherMale whiteFemale whiteMa
##   No RHC         161       239          50        61          667       14
```

[2] Exact Matching: 2 variables

```r
require(MatchIt)
# exact match by sex and race
m.out = matchit (RHC=="RHC" ~ sex + race,
                 data = analytic.data,
                 method = "exact")
m.out
```

```
##
## Call:
## matchit(formula = RHC == "RHC" ~ sex + race, data = analytic.data,
##     method = "exact")
##
## Exact Subclasses: 6
##
## Sample sizes:
##           Control Treated
## All          2583    2184
```

[2] Exact Matching: 3 variables

```
var.comb <- do.call('paste0',
                    analytic.data[, c('race', 'sex', 'age')])
length(table(var.comb))
```

```
## [1] 30
```

```
table(analytic.data$RHC,var.comb=="otherMale[80, Inf)")
```

```
##
##           FALSE TRUE
##   No RHC  2580    3
##   RHC     2183    1
```

```
table(analytic.data$RHC,var.comb=="otherFemale[80, Inf)")
```

```
##
##           FALSE TRUE
```

[2] Exact Matching: 3 variables

```
# exact match by age, sex and race
m.out = matchit (RHC=="RHC" ~ age + sex + race,
                 data = analytic.data,
                 method = "exact")
m.out
```

```
##
## Call:
## matchit(formula = RHC == "RHC" ~ age + sex + race, data = analytic.data
##     method = "exact")
##
## Exact Subclasses: 29
##
## Sample sizes:
##           Control Treated
## All          2583    2184
## Matched      2581    2184
```

[2] Exact Matching: 3 variables

```
matched.data <- match.data(m.out)
dim(matched.data)
```

```
## [1] 4765   25
```

```
nrow(analytic.data)-nrow(matched.data) # subjects deleted
```

```
## [1] 2
```

```
# Not taking into account of matched sets
fit1m <- glm(I(Death=="Yes")~RHC,
             family=binomial, data = matched.data)
publish(fit1m)
```

```
##  Variable  Units OddsRatio       CI.95 p-value
##       RHC No RHC       Ref
##               RHC      2.21 [1.96;2.49]  <1e-04
```

[2] Exact Matching: many categorical variables

```
m.out = matchit (RHC=="RHC" ~ age + sex + race +
                   Disease.category + DNR.status,
                 data = analytic.data,
                 method = "exact")
m.out
```

```
##
## Call:
## matchit(formula = RHC == "RHC" ~ age + sex + race + Disease.category +
##     DNR.status, data = analytic.data, method = "exact")
##
## Exact Subclasses: 137
##
## Sample sizes:
##           Control Treated
## All          2583    2184
## Matched      2524    2150
```

[2] Exact Matching: many categorical variables

```
matched.data <- match.data(m.out)
dim(matched.data)
```

```
## [1] 4674   25
```

```
fit2m <- glm(I(Death=="Yes")~RHC,
             family=binomial, data = matched.data)
publish(fit2m)
```

```
##  Variable  Units OddsRatio       CI.95 p-value
##       RHC No RHC       Ref
##               RHC      2.23 [1.98;2.51]  <1e-04
```

[2] Exact Matching: including a continuous variable

```
m.out = matchit (RHC=="RHC" ~ age + sex + race +
                   Disease.category + DNR.status+
                   Heart.rate, # continuous
                 data = analytic.data,
                 method = "exact")
m.out
```

```
##
## Call:
## matchit(formula = RHC == "RHC" ~ age + sex + race + Disease.category +
##     DNR.status + Heart.rate, data = analytic.data, method = "exact")
##
## Exact Subclasses: 504
##
## Sample sizes:
##           Control Treated
## All          2583    2184
```

[2] Exact Matching: including more continuous variables

```
m.out = matchit (RHC=="RHC" ~ age + sex + race +
                   Disease.category + DNR.status+
                   Heart.rate + Blood.pressure +
                   Temperature,
                 data = analytic.data,
                 method = "exact")
m.out
```

```
##
## Call:
## matchit(formula = RHC == "RHC" ~ age + sex + race + Disease.category +
##     DNR.status + Heart.rate + Blood.pressure + Temperature, data = analy
##     method = "exact")
##
## Exact Subclasses: 3
##
## Sample sizes:
```

[2] Exact Matching: including more continuous variables

```
matched.data <- match.data(m.out)
dim(matched.data)
```

```
## [1]  6 25
```

```
nrow(analytic.data)-nrow(matched.data) # subjects deleted
```

```
## [1] 4761
```

```
fit3m <- glm(I(Death=="Yes")~RHC,
             family=binomial, data = matched.data)
publish(fit3m)
```

```
##  Variable  Units OddsRatio        CI.95 p-value
##       RHC No RHC       Ref
##               RHC      1.00 [0.03;29.81]       1
```

[3] Propensity Score

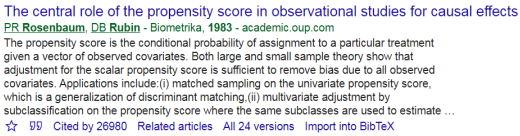
Defining Propensity score (PS)

- Conditional Probability of getting treatment, given the observed covariates
- Prob(treatment: `A` $= 1$ | baseline or pre-treatment covariates: `L`)
  - Prob(`RHC` = treated/RHC group | age, sex, race, etc.)
  - f(L) = Prob(A=1|L)

```
baselinevars
```

```
##  [1] "age"              "sex"              "race"
##  [4] "Disease.category" "DNR.status"       "APACHE.III.score"
##  [7] "Pr.2mo.survival"  "No.of.comorbidity" "DASI.2wk.prior"
## [10] "Temperature"      "Heart.rate"       "Blood.pressure"
## [13] "Respiratory.rate" "WBC.count"        "PaO2.by.FIO2"
## [16] "PaCO2"            "pH"               "Creatinine"
## [19] "Albumin"          "GComa.Score"
```

[3] Propensity Score


The central role of the propensity score in observational studies for causal effects
PR Rosenbaum, DB Rubin - Biometrika, 1983 - academic.oup.com
The propensity score is the conditional probability of assignment to a particular treatment given a vector of observed covariates. Both large and small sample theory show that adjustment for the scalar propensity score is sufficient to remove bias due to all observed covariates. Applications include:(i) matched sampling on the univariate propensity score, which is a generalization of discriminant matching,(ii) multivariate adjustment by subclassification on the propensity score where the same subclasses are used to estimate ...
☆ 99 Cited by 26980 Related articles All 24 versions Import into BibTeX

Theoretical result

Rosenbaum, Rubin (1983) showed:

- For potential outcomes (Y^0, Y^1), if you have sufficient observed covariate list L to reduce confounding ('strong ignoribility'): A being treatment assignment here:
  - i.e., if $(Y^0, Y^1) \perp\!\!\!\perp A|L$ (Note that is this NOT $Y \perp\!\!\!\perp A|L$)
- then
  - $(Y^0, Y^1) \perp\!\!\!\perp A|PS$ and
  - $A \perp\!\!\!\perp L|PS$

[3] Propensity Score

Assumptions

- no unmeasured confounding
- positivity ($ 0 < \text{PS} < 1 $)
- well-defined treatment
- sufficient overlap
- model-specification

[3] Propensity Score

Variable selection for **propensity score** models
MA Brookhart, S Schneeweiss… - American journal of …, 2006 - academic.oup.com
Despite the growing popularity of **propensity score** (PS) methods in epidemiology, relatively little has been written in the epidemiologic literature about the problem of **variable selection** for PS models. The authors present the results of two simulation studies designed to help …
☆ 99 Cited by 1550 Related articles All 18 versions Import into BibTeX

The design *versus* the analysis of observational studies for causal effects: parallels with the design of randomized trials
DB Rubin - Statistics in medicine, 2007 - Wiley Online Library
For estimating causal effects of treatments, randomized experiments are generally considered the gold standard. Nevertheless, they are often infeasible to conduct for a variety of reasons, such as ethical concerns, excessive expense, or timeliness. Consequently, much of our knowledge of causal effects must come from non-randomized observational studies. This article will advocate the position that observational studies can and should be designed to approximate randomized experiments as closely as possible. In particular, observational …
☆ 99 Cited by 896 Related articles All 6 versions Import into BibTeX

- Observed covariates are used to fix design
- Which covariates should be selected:
  - known to be a confounder (causes of `Death` and `RHC`)
  - known to be a cause of the outcome (risk factors of `Death`)
  - avoid known instruments or noise variables: **SE suffers**
  - mediating factors should be avoided (total effect = goal)
- Stepwise (p-value or criterion based) not recommended
  - depending on sample size, different values can get selected
  - may select variables highly associated with A

[3] Propensity Score

Many ways to use propensity scores (PS) in the analysis

- **PS matching** [our focus today: intuitive!]
- PS weighting
- PS stratification
- PS used as a covariate

[3] Propensity Score Matching

A tutorial and case study in **propensity score** analysis: an application to estimating the effect of in-hospital smoking cessation counseling on mortality
PC **Austin** - Multivariate behavioral research, **2011** - Taylor & Francis
Propensity score methods allow investigators to estimate causal treatment effects using observational or nonrandomized data. In this article we provide a practical illustration of the appropriate steps in conducting propensity score analyses. For illustrative purposes, we use ...
☆ 99 Cited by 304 Related articles All 13 versions Import into BibTeX

Propensity score matching has 4 steps

- Stage 1: exposure modelling: $PS = Prob(A = 1|L)$
- Stage 2: Match by PS
- Stage 2: Assess balance and overlap (PS and L)
- Stage 4: outcome modelling: $Prob(Y = 1|A = 1)$

[3] Propensity Score Matching

An introduction to **propensity score** methods for reducing the effects of confounding in observational studies

PC **Austin** - Multivariate behavioral research, **2011** - Taylor & Francis

The propensity score is the probability of treatment assignment conditional on observed baseline characteristics. The propensity score allows one to design and analyze an observational (nonrandomized) study so that it mimics some of the particular characteristics ...

☆ 99 Cited by 5235 Related articles All 15 versions Import into BibTeX

- Assessment of Balance in the whole data
  - balance = similarity of the covariate distributions
  - d or $SMD > 0.1$ can be considered as imbalance

$$d = \frac{(\overline{x}_{treatment} - \overline{x}_{control})}{\sqrt{\frac{s^2_{treatment} + s^2_{control}}{2}}}$$

$$d = \frac{(\hat{p}_{treatment} - \hat{p}_{control})}{\sqrt{\frac{\hat{p}_{treatment}(1 - \hat{p}_{treatment}) + \hat{p}_{control}(1 - \hat{p}_{control})}{2}}}$$

```
tab1e <- CreateTableOne(vars = baselinevars,
                        data = analytic.data, strata = "RHC",
                        includeNA = TRUE,
```

[3] Propensity Score Matching

```
print(tab1e, smd = TRUE)
```

```
##                                  Stratified by RHC
##                                   No RHC          RHC             SMD
##   n                                 2583            2184
##   age (%)                                                         0.181
##      [-Inf,50)                       573 (22.2)      540 (24.7)
##      [50,60)                         432 (16.7)      371 (17.0)
##      [60,70)                         638 (24.7)      577 (26.4)
##      [70,80)                         603 (23.3)      529 (24.2)
##      [80, Inf)                       337 (13.0)      167 ( 7.6)
##   sex = Female (%)                   878 (34.0)      906 (41.5)    0.155
##   race (%)                                                        0.098
##      white                          2072 (80.2)     1707 (78.2)
##      black                           400 (15.5)      335 (15.3)
##      other                           111 ( 4.3)      142 ( 6.5)
##   Disease category (%)                                            0.557
```

[3] Propensity Score Matching

Step 1: PS estimation

Specify the propensity score model to estimate propensity scores, and fit the model

```
ps.formula <- as.formula(paste("I(RHC == 'RHC')", "~",
                               paste(baselinevars, collapse = "+")))
ps.formula
```

```
## I(RHC == "RHC") ~ age + sex + race + Disease.category + DNR.status +
##     APACHE.III.score + Pr.2mo.survival + No.of.comorbidity +
##     DASI.2wk.prior + Temperature + Heart.rate + Blood.pressure +
##     Respiratory.rate + WBC.count + PaO2.by.FIO2 + PaCO2 + pH +
##     Creatinine + Albumin + GComa.Score
```

- Coef of PS model fit is not of concern
- Model can be rich: to the extent that prediction is better
- But look for multi-collinearity issues
  - SE too high?

[3] Propensity score Matching

While PS has balancing property, PS is unknown and needs to be estimated:

```
# fit logistic regression to estimate propensity scores
PS.fit <- glm(ps.formula,family="binomial",
              data=analytic.data)
# extract estimated propensity scores from the fit
analytic.data$PS <- predict(PS.fit,
                            newdata = analytic.data, type="response")
```

- Other machine learning alternatives are possible to use instead of logistic regression.
  - tree based methods have better ability to detect non-linearity / non-additivity (model-specification aspect)
  - shrinkage methods - lasso / elastic net may better deal with multi-collinearity
  - ensemble learners / super learners were successfully used
  - shallow/deep learning!

[3] Propensity score Matching

- Don't loose sight that better *balance* is the ultimate goal for propensity score
- Prediction of A is just a means to that end (as true PS is unknown).
- May attract variables highly associated with A

Improving propensity score estimators' robustness to model misspecification using super learner
R Pirracchio, ML Petersen… - American journal of …, 2015 - academic.oup.com
The consistency of propensity score (PS) estimators relies on correct specification of the PS model. The PS is frequently estimated using main-effects logistic regression. However, the underlying model assumptions may not hold. Machine learning methods provide an alternative nonparametric approach to PS estimation. In this simulation study, we evaluated the benefit of using Super Learner (SL) for PS estimation. We created 1,000 simulated data sets (n= 500) under 4 different scenarios characterized by various degrees of deviance from …
☆ 99 Cited by 98 Related articles All 9 versions Import into BibTeX

Should a propensity score model be super? The utility of ensemble procedures for causal adjustment
S Alam, EEM Moodie, DA Stephens - Statistics in medicine, 2019 - Wiley Online Library
In investigations of the effect of treatment on outcome, the propensity score is a tool to eliminate imbalance in the distribution of confounding variables between treatment groups. Recent work has suggested that Super Learner, an ensemble method, outperforms logistic regression in nonlinear settings; however, experience with real-data analyses tends to show overfitting of the propensity score model using this approach. We investigated a wide range of simulated settings of varying complexities including simulations based on real data to …
☆ 99 Cited by 6 Related articles All 5 versions Import into BibTeX

[HTML] Propensity score estimation: machine learning and classification methods as alternatives to logistic regression
D Westreich, J Lessler, MJ Funk - Journal of clinical epidemiology, 2010 - ncbi.nlm.nih.gov
Objective Propensity scores for the analysis of observational data are typically estimated using logistic regression. Our objective in this Review was to assess machine learning alternatives to logistic regression which may accomplish the same goals but with fewer assumptions or greater accuracy.
☆ 99 Cited by 47 Related articles All 4 versions Import into BibTeX

Can we train machine learning methods to outperform the high-dimensional

[3] Propensity score Matching

Step 1

```
# summarize propensity scores
summary(analytic.data$PS)
```

```
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## 0.009182 0.268112 0.454924 0.458150 0.640362 0.975476
```

```
# summarize propensity scores by exposure group
tapply(analytic.data$PS, analytic.data$RHC, summary)
```

```
## $`No RHC`
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## 0.009182 0.184909 0.330687 0.357838 0.504012 0.974095
##
## $RHC
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
```

[3] Propensity Score Matching

Step 2: PS matching

```
logitPS <-  -log(1/analytic.data$PS - 1)
# logit of the propensity score
.2*sd(logitPS) # suggested in the literature
```

```
## [1] 0.2382708
```

```
0.1*sd(logitPS) # we are using this
```

```
## [1] 0.1191354
```

```
# choosing too strict PS has unintended consequences
```

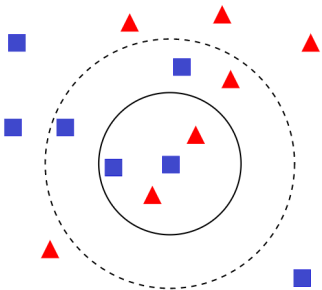
[PDF] Why **propensity scores should not** be **used** for **matching**
G King, R Nielsen - Copy at http://j. mp/1sexgVw Download ..., 2016 - gking.harvard.edu
We show that propensity score matching (PSM), an enormously popular method of preprocessing data for causal inference, often accomplishes the opposite of its intended goal—thus increasing imbalance, inefficiency, model dependence, and bias. The weakness ...
☆ 99 Cited by 620 Related articles All 12 versions Import into BibTeX »

[3] Propensity Score Matching

Step 2

Match using estimates propensity scores

- nearest-neighbor (NN) matching
- without replacement
- with caliper = .1*SD of logit of propensity score
- with 1:1 ratio (pair-matching)



[3] Propensity Score Matching

Step 2

Match using estimates propensity scores

```
set.seed(123)
match.obj <- matchit(ps.formula, data = analytic.data,
                     distance = analytic.data$PS,
                     method = "nearest", replace=FALSE,
                     caliper = .1*sd(logitPS), ratio = 1)
# see matchit function options here
# https://www.rdocumentation.org/packages/MatchIt/versions/1.0-1/topics/ma
analytic.data$PS <- match.obj$distance
summary(match.obj$distance)
```

```
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## 0.009182 0.268112 0.454924 0.458150 0.640362 0.975476
```

[3] Propensity Score Matching

Step 2

```
match.obj
```

```
##
## Call:
## matchit(formula = ps.formula, data = analytic.data, method = "nearest",
##     distance = analytic.data$PS, replace = FALSE, caliper = 0.1 *
##         sd(logitPS), ratio = 1)
##
## Sample sizes:
##           Control Treated
## All          2583    2184
## Matched      1519    1519
## Unmatched    1064     665
## Discarded       0       0
```

[3] Propensity Score Matching

Step 2

Step 1 and 2 can be done together by specifying `distance`

```
match.obj <- matchit(ps.formula, data = analytic.data,
                     distance = 'logit',
                     method = "nearest",
                     replace=FALSE,
                     caliper = .1*sd(logitPS),
                     ratio = 1)
analytic.data$PS <- match.obj$distance
summary(match.obj$distance)
```

```
##      Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
## 0.009182 0.268112 0.454924 0.458150 0.640362 0.975476
```

[3] Propensity Score Matching

Step 2: Taking a closer look at the matches

```
# Ref: https://lists.gking.harvard.edu/pipermail/matchit/2013-October/0005
matches <- as.data.frame(match.obj$match.matrix)
colnames(matches)<-c("matched_unit")
matches$matched_unit<-as.numeric(
  as.character(matches$matched_unit))
matches$treated_unit<-as.numeric(rownames(matches))
matches.only<-matches[!is.na(matches$matched_unit),]
head(matches.only)
```

```
##    matched_unit treated_unit
## 5           438            5
## 10         2385           10
## 12         4177           12
## 13         4429           13
## 17         5228           17
```

[3] Propensity Score Matching

Step 2: Taking a closer look at the matches (1st pair)

```
analytic.data[analytic.data$ID %in%
                as.numeric(matches.only[1,]),]
```

```
##           age  sex  race Disease.category DNR.status APACHE.III.score
## 5     [60,70) Male white             MOSF        Yes               72
## 438 [80, Inf) Male white              ARF        Yes               93
##     Pr.2mo.survival No.of.comorbidity DASI.2wk.prior Temperature Heart.r
## 5        0.43699980                0       21.05078    34.79688
## 438      0.01399994                2       15.95312    34.89844
##     Blood.pressure Respiratory.rate WBC.count PaO2.by.FIO2 PaCO2       p
## 5               65               27 29.699219     478.0000    17 7.22949
## 438             46                0  8.699219     138.0938    82 7.01953
##     Creatinine  Albumin GComa.Score    RHC Death  ID        PS
## 5     3.599609 3.500000          41    RHC   Yes   5 0.4213309
## 438   3.500000 2.799805         100 No RHC   Yes 438 0.4125774
```

[3] Propensity Score Matching

Step 2: Taking a closer look at the matches (2nd pair)

```
analytic.data[analytic.data$ID %in%
                as.numeric(matches.only[2,]),]
```

```
##            age    sex  race Disease.category DNR.status APACHE.III.score
## 10   [-Inf,50) Female white              ARF         No               48
## 2385   [70,80) Female white              ARF         No               30
##      Pr.2mo.survival No.of.comorbidity DASI.2wk.prior Temperature Heart
## 10         0.6689453                1       23.25781        38.5
## 2385       0.6219997                1       18.35156        36.5
##      Blood.pressure Respiratory.rate WBC.count PaO2.by.FIO2 PaCO2
## 10               73               40 20.597656      68.0000    30 7.3490
## 2385             67                9  3.199707     168.5625    34 7.4290
##      Creatinine Albumin GComa.Score    RHC Death   ID        PS
## 10     0.500000     2.5           0    RHC    No   10 0.6565211
## 2385   1.599854     3.5           0 No RHC    No 2385 0.6292985
```

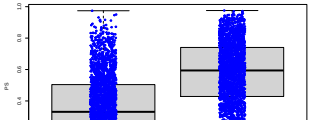
[3] Propensity score Matching

Step 3: Assessing balance and overlap

Balance is more important than prediction!

- Criteria to assess success of step 2: PS estimation
  - better balance
  - better overlap [no extrapolation!]
  - PS $= 0$ or PS $= 1$ needs close inspection

```
boxplot(PS ~ RHC=='RHC', data = analytic.data,
        lwd = 2, ylab = 'PS')
stripchart(PS ~ RHC=='RHC', vertical = TRUE,
           data = analytic.data, method = "jitter",
           add = TRUE, pch = 20, col = 'blue')
```

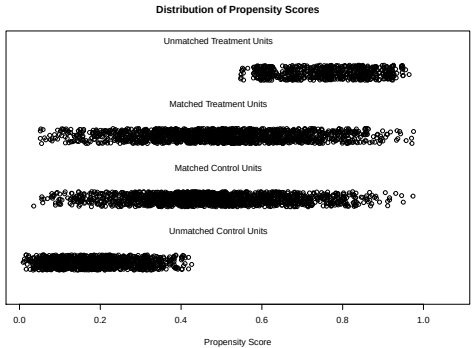


[3] Propensity Score Matching

Step 3

Vizualization

```
plot(match.obj, type = "jitter")
```



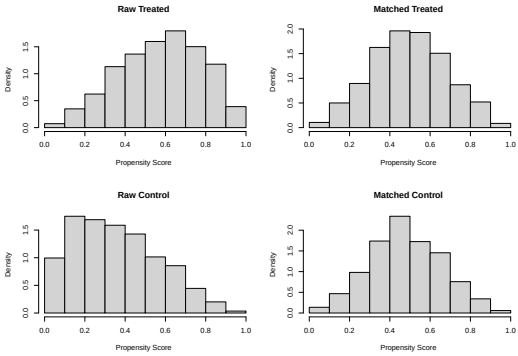

```
## [1] "To identify the units, use first mouse button; to stop, use second
```

[3] Propensity Score Matching

Step 3

Vizualization for assessing overlap issues

```
plot(match.obj, type = "hist")
```



[3] Propensity Score Matching

Step 3

Assessment of Balance: Better than regression diagnostics!

```
matched.data <- match.data(match.obj)
tab1m <- CreateTableOne(vars = baselinevars,
                        data = matched.data, strata = "RHC",
                        includeNA = TRUE,
                        test = TRUE, smd = TRUE)
```

Compare the similarity of baseline characteristics between treated and untreated subjects in a the propensity score-matched sample.

- In this case, we will compare SMD < 0.1 or not.
- In some literature, other generous values (0.25) are proposed.

An introduction to **propensity score** methods for reducing the effects of confounding in observational studies

PC **Austin** - Multivariate behavioral research, **2011** - Taylor & Francis

The propensity score is the probability of treatment assignment conditional on observed baseline characteristics. The propensity score allows one to design and analyze an observational (nonrandomized) study so that it mimics some of the particular characteristics …

☆ 99 Cited by 5235 Related articles All 15 versions Import into BibTeX

[3] Propensity Score Matching

Step 3

```
print(tab1m, showAllLevels = FALSE, smd = TRUE, test = FALSE)
```

```
##                                Stratified by RHC
##                                 No RHC          RHC             SMD
##    n                              1519            1519
##    age (%)                                                       0.042
##       [-Inf,50)                    367 (24.2)      365 (24.0)
##       [50,60)                      255 (16.8)      272 (17.9)
##       [60,70)                      385 (25.3)      395 (26.0)
##       [70,80)                      368 (24.2)      351 (23.1)
##       [80, Inf)                    144 ( 9.5)      136 ( 9.0)
##    sex = Female (%)                560 (36.9)      572 (37.7)    0.016
##    race (%)                                                      0.017
##       white                        1212 (79.8)     1212 (79.8)
##       black                         229 (15.1)      234 (15.4)
```

[3] Propensity Score Matching

Step 3

Possible to get p-values to check balance: but strongly discouraged

- P-value based balance assessment can be influenced by sample size

A tutorial and case study in **propensity score** analysis: an application to estimating the effect of in-hospital smoking cessation counseling on mortality
PC **Austin** - Multivariate behavioral research, **2011** - Taylor & Francis
Propensity score methods allow investigators to estimate causal treatment effects using observational or nonrandomized data. In this article we provide a practical illustration of the appropriate steps in conducting propensity score analyses. For illustrative purposes, we use ...
☆ 99 Cited by 304 Related articles All 13 versions Import into BibTeX

```
print(tab1m, showAllLevels = FALSE, smd = FALSE, test = TRUE)
```

```
##                                  Stratified by RHC
##                                   No RHC          RHC             p
##    n                                1519            1519
##    age (%)                                                       0.859
##       [-Inf,50)                      367 (24.2)      365 (24.0)
##       [50,60)                        255 (16.8)      272 (17.9)
##       [60,70)                        385 (25.3)      395 (26.0)
```

[3] Propensity Score Matching

Step 3

Assessment of balance in the matched data

```
smd.res <- ExtractSmd(tab1m)
t(round(smd.res,2))
```

```
##          age  sex race Disease.category DNR.status APACHE.III.score
## 1 vs 2 0.04 0.02 0.02              0.04       0.01              0.07
##        Pr.2mo.survival No.of.comorbidity DASI.2wk.prior Temperature Hea
## 1 vs 2            0.06               0.01             0        0.01
##        Blood.pressure Respiratory.rate WBC.count PaO2.by.FIO2 PaCO2   pH
## 1 vs 2           0.05              0.04      0.01         0.04  0.01 0.03
##        Creatinine Albumin GComa.Score
## 1 vs 2       0.02    0.03        0.01
```

[3] Propensity Score Matching

Step 3: Variance ratio

- Variance ratios ~ 1 means:
- equal variances in groups
- group balance
- could vary from $1/2$ to 2
- other cut-points are suggested as well (0.8 to 1.2)

Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples

PC Austin - Statistics in medicine, 2009 - Wiley Online Library

The propensity score is a subject's probability of treatment, conditional on observed baseline covariates. Conditional on the true propensity score, treated and untreated subjects have similar distributions of observed baseline covariates. Propensity-score matching is a popular method of using the propensity score in the medical literature. Using this approach, matched sets of treated and untreated subjects with similar values of the propensity score are formed. Inferences about treatment effect made using propensity-score matching are …

☆ 99 Cited by 2214 Related articles All 11 versions Import into BibTeX

[HTML] Matching methods for causal inference: A review and a look forward

EA Stuart - Statistical science: a review journal of the Institute of …, 2010 - ncbi.nlm.nih.gov

When estimating causal effects using observational data, it is desirable to replicate a randomized experiment as closely as possible by obtaining treated and control groups with similar covariate distributions. This goal can often be achieved by choosing well-matched samples of the original treated and control groups, thereby reducing bias due to the covariates. Since the 1970's, work on matching methods has examined how to best choose treated and control subjects for comparison. Matching methods are gaining popularity in …

☆ 99 Cited by 3066 Related articles All 22 versions Import into BibTeX »

[3] Propensity Score Matching

Step 3: Variance ratio

```
require(cobalt)
baltab.res <- bal.tab(x = match.obj, data = analytic.data,
                      treat = analytic.data$RHC,
                      disp.v.ratio = TRUE)
```

```
## Note: 's.d.denom' not specified; assuming pooled.
```

```
baltab.res$Balance$V.Ratio.Adj
```

```
##  [1] 1.0990553        NA        NA        NA        NA        NA
##  [8]        NA        NA        NA        NA        NA        NA
## [15]        NA 1.0867497 0.9714495 0.9605864 0.8305596 0.8395535 0.94089
## [22] 0.9841995 1.0655834 1.0262382 0.9733399 1.0919443 1.0916685 0.61008
## [29] 2.0325397 0.9847091
```

[3] Propensity Score Matching

Step 4: Outcome modelling

- Some flexibility in choosing outcome model
  - considered independent of exposure modelling
  - some propose double robust approach
  - adjusting imbalanced covariates only?

Estimate the effect of treatment on outcomes using propensity score-matched sample

```
fit3 <- glm(I(Death=="Yes")~RHC,
            family=binomial, data = matched.data)
publish(fit3)
```

```
##  Variable  Units OddsRatio       CI.95 p-value
##       RHC No RHC       Ref
##              RHC      2.08 [1.80;2.41]  <1e-04
```

[3] Propensity Score Matching

Step 4: Outcome modelling

```
out.formula
```

```
## I(Death == "Yes") ~ RHC + age + sex + race + Disease.category +
##     DNR.status + APACHE.III.score + Pr.2mo.survival + No.of.comorbidity
##     DASI.2wk.prior + Temperature + Heart.rate + Blood.pressure +
##     Respiratory.rate + WBC.count + PaO2.by.FIO2 + PaCO2 + pH +
##     Creatinine + Albumin + GComa.Score
```

```
fit3b <- glm(out.formula,
             family=binomial, data = matched.data)
publish(fit3b)
```

```
##           Variable     Units OddsRatio       CI.95    p-value
##                RHC    No RHC       Ref
##                           RHC      2.55 [2.14;3.03]    < 1e-04
```

[3] Propensity Score Matching

Step 4: Other cosiderations for outcome model

The above analysis do not take matched pair into consideration while regressing.
Literature proposes different strategies:

- do not control for pairs / clusters
  - use `glm` as is
- control for pairs / clusters
  - use `cluster` option or GEE or conditional logistic
- Bootstrap for matched pairfor WOR
  - may not be appropriate for WR

The use of bootstrapping when using propensity-score matching without replacement: a simulation study
PC Austin, DS Small - Statistics in medicine, 2014 - Wiley Online Library
Propensity-score matching is frequently used to estimate the effect of treatments, exposures, and interventions when using observational data. An important issue when using propensity-score matching is how to estimate the standard error of the estimated treatment effect. Accurate variance estimation permits construction of confidence intervals that have the advertised coverage rates and tests of statistical significance that have the correct type I error rates. There is disagreement in the literature as to how standard errors should be …
☆ 99 Cited by 139 Related articles All 11 versions Import into BibTeX

[3] Propensity Score Matching

Step 4

- The example compared `RHC` (a treated group; target) vs `No RHC` (untreated).
- Thc corresponding treatment effect estimate is known as
  - Average Treatment Effects on the Treated (ATT)
- Other estimates from PS analysis are possible that compared the whole population
  - what if everyone treated vs. what if nobody was treated (ATE)

[3] Propensity Score Matching

Other matching algorithms

- Optimal
- genetic matching
- CEM
- variable ratio NN

[3] Propensity Score Matching

- MatchIt
- Matching

Other useful packages

- cobalt
- twang

Outdated package

- nonrandom

[4] Discipline-specific PS Systematic Reviews

- Propensity score matching most popular
  - Cardiovascular / Infective endocarditis / Intensive care
  - Critical care / anesthesiology / Sepsis / Psychology
  - Cancer / Multiple sclerosis
- Not meta-analysis; but reviews of usage of PS methods in different disciplines

[HTML] Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement
PC Austin - The Journal of thoracic and cardiovascular surgery, 2007 - Elsevier
Objective I conducted a systematic review of the use of propensity score matching in the cardiovascular surgery literature. I examined the adequacy of reporting and whether appropriate statistical methods were used. Methods I examined 60 articles published in the Annals of Thoracic Surgery, European Journal of Cardio-thoracic Surgery, Journal of Cardiovascular Surgery, and the Journal of Thoracic and Cardiovascular Surgery between January 1, 2004, and December 31, 2006. Results Thirty-one of the 60 studies did not ...
☆ 99 Cited by 482 Related articles All 9 versions Import into BibTeX

Propensity scores in intensive care and anaesthesiology literature: a systematic review
E Gayat, R Pirracchio, M Resche-Rigon... - Intensive care ..., 2010 - Springer
Introduction Propensity score methods have been increasingly used in the last 10 years. However, the practical use of the propensity score (PS) has been reported as heterogeneous in several papers reviewing the use of propensity scores and giving some advice. No precedent work has focused on the specific application of PS in intensive care and anaesthesiology literature. Objectives After a brief development of the theory of propensity score, to assess the use and the quality of reporting of PS studies in intensive ...
☆ 99 Cited by 107 Related articles All 17 versions Import into BibTeX

[HTML] Observational studies using propensity score analysis underestimated the effect sizes in critical care medicine
Z Zhang, H Ni, X Xu - Journal of clinical epidemiology, 2014 - Elsevier
Abstract Background and Objective Propensity score (PS) analysis has been increasingly used in critical care medicine; however, its validation has not been systematically investigated. The present study aimed to compare effect sizes in PS-based observational studies vs. randomized controlled trials (RCTs)/or meta-analysis of RCTs). Methods Critical care observational studies using PS were systematically searched in PubMed from inception to April 2013. Identified PS-based studies were matched to one or more RCTs in terms of ...
☆ 99 Cited by 49 Related articles All 10 versions Import into BibTeX

[HTML] Propensity scores: methods, considerations, and applications in the Journal of Thoracic and Cardiovascular Surgery
TL McMurry, Y Hu, EH Blackstone... - The Journal of thoracic and ..., 2015 - Elsevier
Objective To review the published literature using propensity scoring, describe shortcomings in the use of this technique, and provide conceptual background for understanding and correctly implementing studies that use propensity matching. Methods We survey the published statistical literature and make recommendations for a set of standard criteria for studies that use propensity matching. We evaluated adherence to these criteria in recent publications in the Journal of Thoracic and Cardiovascular Surgery and determined how ...
☆ 99 Cited by 81 Related articles All 7 versions Import into BibTeX

A systematic review of propensity score methods in the social sciences
PJ Thoemmes, ES Kim - Multivariate behavioral research, 2011 - Taylor & Francis
The use of propensity scores in psychological and educational research has been steadily increasing in the last 2 to 3 years. However, there are some common misconceptions about the use of different estimation techniques and conditioning choices in the context of propensity score analysis. In addition, reporting practices for propensity score analyses often lack important details that allow other researchers to confidently judge the appropriateness of reported analyses and potentially to replicate published findings. In this article we conduct ...
☆ 99 Cited by 401 Related articles All 10 versions Import into BibTeX

Reporting and guidelines in propensity score analysis: a systematic review of cancer and cancer surgical studies
XI Yao, X Wang, PJ Speicher, ES Hwang... - JNCI: Journal of the ..., 2017 - academic.oup.com
Background: Propensity score (PS) analysis is increasingly being used in observational studies, especially in some cancer studies where random assignment is not feasible. This systematic review evaluates the use and reporting quality of PS analysis in oncology studies. Methods: We searched PubMed to identify the use of PS methods in cancer studies (CS) and cancer surgical studies (CSS) in major medical, cancer, and surgical journals over time and critically evaluated 33 CS published in top medical and cancer journals in 2014 ...
☆ 99 Cited by 92 Related articles All 11 versions Import into BibTeX

[HTML] The role of valve surgery in infective endocarditis management: a systematic review of observational studies that included propensity score analysis
IM Tleyjeh, T Kashour, V Zimmerman... - American heart ..., 2008 - Elsevier
Background The potential role of valve surgery in infective endocarditis (IE) management is controversial. No randomized trials have been conducted to date; accordingly, some studies use propensity score analysis (PSA) to minimize selection bias in observational studies. Methods A systematic review of the literature addressing the role of valve surgery in IE was performed. Studies in which PSA was applied to the management of IE were identified using Medline, Web of Science, Zetoc, and Article First from inception to June 2007. Cohort studies ...
☆ 99 Cited by 58 Related articles All 9 versions Import into BibTeX

[HTML] Do the observational studies using propensity score analysis agree with randomized controlled trials in the area of sepsis?
Z Zhang, H Ni, X Xu - Journal of critical care, 2014 - Elsevier
Background and objectives Sepsis is a leading cause of mortality and morbidity in the intensive care unit, and many studies have been conducted aiming to improve its outcome. Randomized controlled trials (RCTs) and observational studies using propensity score (PS) method are commonly used for this purpose. However, the agreement between these two major methodological designs has never been investigated in this specific area. The present study aimed to compare the effect sizes between RCTs and PS-based studies. Methods ...
☆ 99 Cited by 20 Related articles All 10 versions Import into BibTeX

[HTML] Evaluation of propensity score used in cardiovascular research: a cross-sectional survey and guidance document
M Samuel, B Balomen, J Rivette, J Kim, RW Platt... - BMJ open, 2020 - bmjopen.bmj.com
Background Propensity score (PS) methods are frequently used in cardiovascular clinical research. Previous evaluations revealed poor reporting of PS methods, however a comprehensive and current evaluation of PS use and reporting is lacking. The objectives of the present survey were to (1) evaluate the quality of PS methods in cardiovascular publications,(2) summarise PS methods and (3) propose key reporting elements for PS publications. Methods A PubMed search for cardiovascular PS articles published between ...
☆ 99 All 4 versions Import into BibTeX

[4] Discipline-specific PS Systematic Reviews

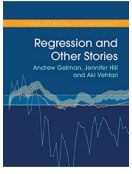
Reporting Guideline

- Be specific about population of interest
  - ATT vs. ATE
  - exclusion criteria
- Be specific about exposure
  - no multiple version of treatment
  - no interference
  - comparator
- Report clearly about missing data
  - how handled
- Why PS matching (or other approach) was selected?
- Software

[4] Discipline-specific PS Systematic Reviews

Reporting Guideline

- How variables selected
- Any important variables not measured
  - proxy
- Model selection
  - interaction or polynomials
  - logistic vs. machine learning
- Overlap vs. balance
  - numeric and visual



[4] Discipline-specific PS Systematic Reviews

Reporting Guideline

- Reduction % of the matched data: main objection against this method!
- Residual imbalance
  - refit PS model
- Subgroup analysis
  - Refit within each group for matching
- Sensitivity analysis
  - unmeasured confounder / hdPS
  - any positivity issue? Deleting extremes has consequences!
    - ad-hoc methods: truncation / trimming: bias-variance trade-off

Propensity score methods in health technology assessment: principles, extended applications, and recent advances

MS Ali, D Prieto-Alhambra, L Lopes... - Frontiers in ..., 2019 - frontiersin.org

Randomized clinical trials (RCTs) are considered the gold-standard approach to estimate effects of treatment on outcomes. They are also the designs of choice for health technology assessment (HTA). Randomization ensures comparability, in both measured and unmeasured pre-treatment characteristics, of patients assigned to treatment and control or comparator. However, even adequately powered RCTs are not always feasible for reasons such as cost, time, ethical, and practical constraints. RCTs rely on data collected on ...

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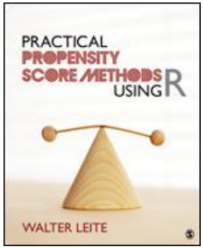
Can we train machine learning methods to outperform the **high-dimensional propensity score** algorithm?

ME **Karim**, M Pang, RW Platt - Epidemiology, 2018 - ingentaconnect.com

The use of retrospective health care claims datasets is frequently criticized for the lack of

Further Reading



[BOOK] **Practical propensity score methods using R**

W Leite - 2016 - books.google.com

Practical Propensity Score Methods Using R by Walter Leite is a practical book that uses a step-by-step analysis of realistic examples to help students understand the theory and code for implementing propensity score analysis with the R statistical language. With a …

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