Causal Inference in Case-Control Studies: Vignette

Overview

This vignette describes how to use package "ciccr" that is based on the paper entitled "Causal Inference in Case-Control Studies" (Jun and Lee, 2020).

Tutorials

We first load the ciccr and MASS packages.

```
library(ciccr)
library(MASS)
```

To illustrate the usefulness of the package, we use the dataset ACS that is included the package. This dataset is a extract from American Community Survey (ACS) 2018, restricted to white males residing in California with at least a bachelor's degree. The ACS is an ongoing annual survey by the US Census Bureau that provides key information about US population. We use the following variables:

```
  y = ACS$topincome
  t = ACS$baplus
  x = ACS$age
```

- The binary outcome 'Top Income' (Y) is defined to be one if a respondent's annual total pre-tax wage and salary income is top-coded. In our sample extract, the top-coded income bracket has median income \$565,000 and the next highest income that is not top-coded is \$327,000.
- The binary treatment (T) is defined to be one if a respondent has a master's degree, a professional degree, or a doctoral degree.
- The covariate (X) is age in years and is restricted to be between 25 and 70.

The original ACS sample is not a case-control sample but we construct one by the following procedure.

1. The case sample ($Y = 1$) is composed of 921 individuals whose income is top-coded.
2. The control sample ($Y = 0$) of equal size is randomly drawn without replacement from the pool of individuals whose income is not top-coded.

We now construct cubic b-spline terms with three inner knots using the age variable.

```
  x = splines::bs(x, df = 6)
```

Define $\beta(y) = E[\log \mathrm{OR}(X)|Y = y]$ for $y = 0, 1$, where $\mathrm{OR}(x)$ is the odds ratio conditional on $X = x$:

$$\mathrm{OR}(x) = \frac{P(T = 1|Y = 1, X = x)}{P(T = 0|Y = 1, X = x)} \frac{P(T = 0|Y = 0, X = x)}{P(T = 1|Y = 0, X = x)}.$$

Using the retrospective sieve logistic regression model, we estimate $\beta(1)$ by

```
  results_case = avg_retro_logit(y, t, x, 'case')
  results_case$est
#>         y
#> 0.7286012
```

```
  results_case$se
#>         y
#> 0.1013445
```

Here, option `'case'` refers to conditioning on $Y = 1$.

Similarly, we estimate $\beta(0)$ by

```
  results_control = avg_retro_logit(y, t, x, 'control')
  results_control$est
#>         y
#> 0.5469094
  results_control$se
#>         y
#> 0.1518441
```

Here, option `'control'` refers to conditioning on $Y = 1$.

We carry out causal inference by

```
results = cicc(y, t, x, 0.2, 0.95)
```

Here, 0.2 is the specified upper bound for unknown $p = \Pr(Y = 1)$. If it is not specified, the default choice for the upper bound for p is p_upper = 1. Here, 0.95 refers to the level of the confidence interval (0.95 is the default choice).

The S3 object `results` contains a grid of estimates `est`, standard errors `se`, and one-sided confidence intervals `ci` ranging from `p = 0` to `p = p_upper`. In addition, the grid `pseq` from 0 to `p_upper` is saved as part of the S3 object `results`.

```
 # point estimates
 results$est
#>  [1] 0.5469094 0.5488219 0.5507345 0.5526470 0.5545596 0.5564721 0.5583847
#>  [8] 0.5602972 0.5622097 0.5641223 0.5660348 0.5679474 0.5698599 0.5717725
#> [15] 0.5736850 0.5755976 0.5775101 0.5794227 0.5813352 0.5832477
 # standard errors
 results$se
#>  [1] 0.1518441 0.1502495 0.1486627 0.1470838 0.1455132 0.1439511 0.1423978
#>  [8] 0.1408536 0.1393188 0.1377937 0.1362787 0.1347740 0.1332800 0.1317971
#> [15] 0.1303256 0.1288660 0.1274187 0.1259841 0.1245626 0.1231546
 # confidence intervals
 results$ci
#>  [1] 0.7966706 0.7959604 0.7952628 0.7945784 0.7939075 0.7932506 0.7926083
#>  [8] 0.7919808 0.7913688 0.7907728 0.7901933 0.7896308 0.7890860 0.7885594
#> [15] 0.7880516 0.7875633 0.7870953 0.7866480 0.7862224 0.7858191
 # grid points from 0 to p_upper
 results$pseq
#>  [1] 0.00000000 0.01052632 0.02105263 0.03157895 0.04210526 0.05263158
#>  [7] 0.06315789 0.07368421 0.08421053 0.09473684 0.10526316 0.11578947
#> [13] 0.12631579 0.13684211 0.14736842 0.15789474 0.16842105 0.17894737
#> [19] 0.18947368 0.20000000
```

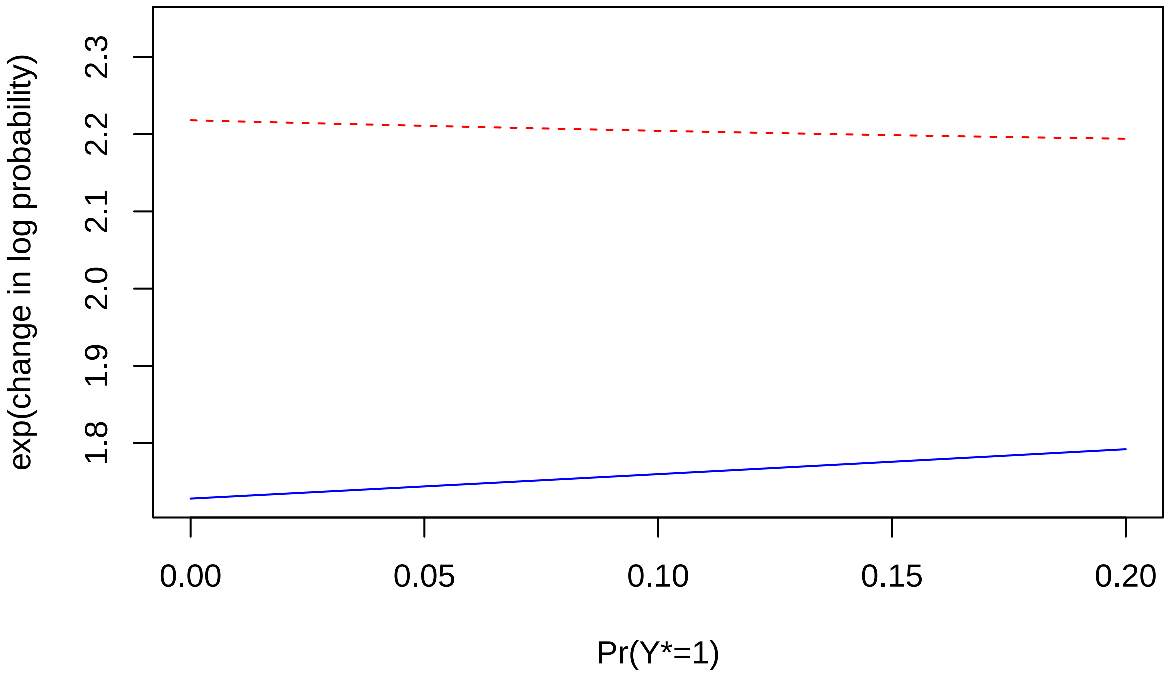
To be more compatible with the odds ratio, it is useful to transform them by the exponential function:

```
 # point estimate
 exp(results$est)
#>  [1] 1.727904 1.731212 1.734527 1.737847 1.741174 1.744507 1.747847
#>  [8] 1.751193 1.754545 1.757904 1.761269 1.764641 1.768019 1.771404
```

```
#> [15] 1.774795 1.778193 1.781597 1.785008 1.788425 1.791848
 # confidence interval estimate
 exp(results$ci)
#>  [1] 2.218144 2.216569 2.215023 2.213507 2.212023 2.210571 2.209151
#>  [8] 2.207765 2.206415 2.205100 2.203822 2.202583 2.201383 2.200224
#> [15] 2.199108 2.198034 2.197005 2.196023 2.195089 2.194203
```

It is handy to examine the results by plotting a graph.

```
  yaxis_limit = c(min(exp(results$est)),(max(exp(results$ci))+0.25*(max(exp(results$ci))-min(exp(result
  plot(results$pseq, exp(results$est), type = "l", lty = "solid", col = "blue", xlab = "Pr(Y*=1)",ylab =
  lines(results$pseq, exp(results$ci), type = "l", lty = "dashed", col = "red")
```



To interpret the results, we assume both marginal treatment response (MTR) and marginal treatment selection (MTS). In this setting, MTR means that everyone will not earn less by obtaining a degree higher than bachelor's degree; MTS indicates that those who selected into higher education have higher potential to earn top incomes. Based on the MTR and MTS assumptions, we can conclude that the treatment effect lies in between 1 and the upper end point of the one-sided confidence interval with high probability. Thus, the estimates in the graph above suggest that the effect of obtaining a degree higher than bachelor's degree is anywhere between [1, 2.2], which roughly implies that the chance of earning top incomes may increase up to by a factor of around 2, but allowing for possibility of no positive effect at all. In other words, it is unlikely that the probability of earning top incomes will more than double by pursuing higher education beyond BA. See Jun and Lee, 2020 for more detailed explanations regarding how to interpret the estimation results.

Comparison with Logistic Regression

We can compare these results with estimates obtained from logistic regression.

```
logit = stats::glm(y~t+x, family=stats::binomial("logit"))
est_logit = stats::coef(logit)
ci_logit = stats::confint(logit, level = 0.9)
#> Waiting for profiling to be done...
# point estimate
```

```r
exp(est_logit)
#> (Intercept)           t          x1          x2          x3          x4
#>  0.05461156  2.06117153  4.42179639 12.99601849 19.03962976 26.83565737
#>          x5          x6
#>  6.42381406 26.14359394
# confidence interval
exp(ci_logit)
#>                     5 %       95 %
#> (Intercept)  0.01960819  0.1304108
#> t            1.75166056  2.4271287
#> x1           1.05679997 21.6604223
#> x2           5.50583091 33.8909622
#> x3           6.79458010 61.3258710
#> x4          10.22943808 78.7353953
#> x5           2.00536450 22.8509008
#> x6           8.66983039 87.6311482
```

Here, the relevant coefficient is 2.06 (`t`) and its two-sided 90% confidence interval is [1.75, 2.43]. If we assume strong ignorability, the treatment effect is about 2 and its two-sided confidence interval is between [1.75, 2.43]. However, it is unlikely that the higher BA treatment satisfies the strong ignorability condition.

Reference

Sung Jae Jun and Sokbae Lee. Causal Inference in Case-Control Studies. https://arxiv.org/abs/2004.08318.