Conditional logistic regression and propensity score analysis

CMED6020 – Session 6

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Session 6 learning objectives

After this session, students should be able to

- Fit conditional logistic regression model to data from case control study
- Understand the assumptions of the propensity score method
- Interpret results from propensity score method

Conditional logistic regression

Case control study

- Comparison between case and controls who are at risk and have the same exposure distribution as the case
- Types of case control study
  - Matched case-control study
  - Nested case-control study
  - Risk set sampling
- Matching: balancing certain characteristics between groups to increase efficiency
- Types of matching
  - Individually matched (paired)
  - Frequency matched

Analysis of matched data

- More coherent in the same stratum
  - Correlated in the same stratum / match set
- Unconditional analysis
  - Estimate the parameter β of primary interest
  - Need to specify the stratum-specific parameters α
  - Suitable for frequency matching and multiple controls
- Conditional analysis
  - Group matched individuals into strata and perform comparison within strata
  - Analogy: paired t-test
  - Needed for individual matching

Conditional logistic regression

- Model incorporating the stratum-specific effect:
- $\text{logit}(p_{ij}) = \alpha_i + \beta_1 x_{1ij} + \ldots$
  - for the j^{th} individual in match set i
- α_i are nuisance parameters
- Conditional likelihood is used to 'remove' the nuisance parameters

$$\prod_{i=1}^{I} \frac{\exp(\cancel{\alpha_i} + \beta_1 x_{ij1} + \cdots)}{\sum_{j=1}^{J_i} \exp(\cancel{\alpha_i} + \beta_1 x_{ij1} + \cdots)}$$

- analogy: risk set in survival analysis

The life table (using 4-year time periods)

Period (years)	n ♯ at risk	d ♯ deaths	c ♯ censor	n' ♯ at risk	p Prob of death in period	q Prob to survive period	S Cumulative survival at end of period
0 – 4	45	14	0	45	0.31	0.69	0.69
4 – 8	31	8	2	30	0.27	0.73	0.51
8 – 12	21	4	5	18.5	0.22	0.78	0.40
12 – 16	12	2	3	10.5	0.19	0.81	0.32
16 – 20	7	0	7	3.5	0.00	1.00	0.32

(extracted from CMED6100)

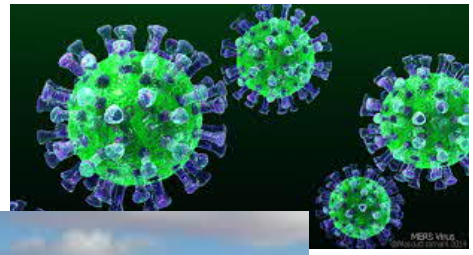
Conditional logistic regression in R

clogit(*formula, data, subset, …*) (in package: survival)

- syntax similar to glm
- formula: need to specify the strata
  - case.status ~ exposure + strata(matched.set)
- data: specifies the data frame
- subset: specifies subset of the data

Dataset - MERS and dromedary camel exposure

- saved in ‘examplemers.csv’
- population: 100 persons from the general population at risk of MERS
- 1:1 case-control study matched by age, sex and residence
- outcome variable – MERS infection
- exposure of interest: dromedary camel exposure
- other associating factors
  - currently smoking
  - exposure to sheep



Dataset - MERS and dromedary camel exposure

```
> mers <- read.csv("examplemers.csv")
> head(mers)
  id strata case age male loc dromedary sheep smoking
1  1      1    1  69    1   4         0     0       0
2  2      1    0  69    1   4         0     0       0
3  3      2    1  54    0   2         0     0       0
4  4      2    0  54    0   2         0     0       0
5  5      3    1  36    0   2         1     1       0
6  6      3    0  36    0   2         0     0       1
```

Fitting a conditional logistic regression model

```
> clr.mers <- clogit(case ~ dromedary + sheep + smoking +
   strata(strata), data=mers)
> summary(clr.mers)
Call:
coxph(formula = Surv(rep(1, 100L), case) ~ dromedary + sheep +
   smoking + strata(strata), data = mers, method = "exact")

  n= 100, number of events= 50

             coef exp(coef) se(coef)      z Pr(>|z|)
dromedary  2.2966    9.9403   0.8711  2.637  0.00838 **
sheep     -0.4022    0.6688   0.6075 -0.662  0.50791
smoking    2.7015   14.9027   0.9007  2.999  0.00271 **
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

Fitting a conditional logistic regression model (cont'd)

```
           exp(coef) exp(-coef) lower .95 upper .95
dromedary     9.9403     0.1006    1.8028     54.81
sheep         0.6688     1.4952    0.2033      2.20
smoking      14.9027     0.0671    2.5501     87.09

Rsquare= 0.216   (max possible= 0.5 )
Likelihood ratio test= 24.34  on 3 df,   p=2.118e-05
Wald test            = 11.28  on 3 df,   p=0.01029
Score (logrank) test = 19.15  on 3 df,   p=0.0002542
```

- exposure to dromedary is significantly associated with MERS infection (OR=9.9, 95%CI = 1.8-54.8)
- also for smoking

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

Cao-Lormeau et al, Lancet, 2016

Summary

Background Between October, 2013, and April, 2014, French Polynesia experienced the largest Zika virus outbreak ever described at that time. During the same period, an increase in Guillain-Barré syndrome was reported, suggesting a possible association between Zika virus and Guillain-Barré syndrome. We aimed to assess the role of Zika virus and dengue virus infection in developing Guillain-Barré syndrome.

Methods In this case-control study, cases were patients with Guillain-Barré syndrome diagnosed at the Centre Hospitalier de Polynésie Française (Papeete, Tahiti, French Polynesia) during the outbreak period. Controls were age-matched, sex-matched, and residence-matched patients who presented at the hospital with a non-febrile illness (control group 1; n=98) and age-matched patients with acute Zika virus disease and no neurological symptoms (control group 2; n=70). Virological investigations included RT-PCR for Zika
immunofluorescent and seroneutralisation assays for Zika virus and dengue virus.
studied in patients with Guillain-Barré syndrome using both ELISA and combinatoria
2012 census). The association between Zika virus positive serology, dengue positive serology, and Guillain-Barré syndrome was analysed with exact conditional logistic regression. Because the humoral response elicited by acute Zika virus infection might trigger production of anti-dengue virus IgG related to past dengue infections, we adjusted the odds ratio (OR) describing the association between anti-dengue IgG and Guillain-Barré syndrome for the presence of anti-Zika virus IgG. All ORs are given with 95% CIs.

	Guillain-Barré syndrome*(n=42)	Control group 1 (n=98)	OR (95% CI)	OR† (95% CI)	Control group 2 (n=70)	OR (95% CI)	OR† (95% CI)
Zika virus IgM and/or IgG positivity	41 (98%)	35 (36%)	59·7 (10·4–+∞)	..	..	..	..
Positive Zika virus seroneutralisation	42 (100%)	54 (56%)	34·1 (5·8–+∞)	..	..	..	..
Dengue virus IgG positivity	40 (95%)	87 (89%)	2·0 (0·4–19·9)	1·0 (0·2–11·5)	58 (83%)	6·0 (0·8–269·5)	4·0 (0·5–184·7)

Data are n (%), unless otherwise shown. *Tested samples for patients with Guillain-Barré syndrome are late samples (around 3 months after admission). †Adjusted for Zika virus IgG positivity. OR=odds ratio.

Table 4: Zika virus and dengue virus serological patterns associated with Guillain-Barré syndrome

Propensity score analysis

Propensity score analysis

- to analyze data from ‘quasi experiment’
  - quasi experiment: little control on the allocation of treatment and associating factors
  - selection bias / group nonequivalence
    - treatment may tend to select patients with certain characteristics
    - patients with certain characteristics may select treatment

    $\Rightarrow$ patients across different treatments may not be comparable
- to balance observed characteristics across treatment
  - so that more accurate estimates of the treatment effect can be estimated
- allow analysis on factors associated with treatment assignment

Propensity score analysis (cont'd)

- adjustment of confounders by regression analysis
  - a rule of thumb – observed 10 events per level of the predictors
  - otherwise under-powered
  - propensity score method has higher power and more robust especially when the number of observed events is small
  - estimate the conditional effect: $E(Y_1-Y_0|X)$
- can estimate the population marginal effect
  - marginal effect: $E(Y_1-Y_0)$
  - marginal effect may differ from conditional effect with uneven distribution of X

Propensity score analysis – MI example

- saved in ‘examplemi.csv’
- population: 400 men aged 40-70 admitted to hospital with suspected myocardial infarction
- outcome variable – 30-day mortality
- treatment: newer clot-busting drug vs standard therapy
- main confounding factors
  - age
  - pre-existing risk factor level (0-5, 5: highest risk)
  - admission severity score (0-10, 10: most severe)

Dataset - MI example

```
> mi <- read.csv("examplemi.csv")
> mi[1:10,]
   age male risk severity trt death
1   48    1    3        8   0     0
2   59    1    4        6   1     0
3   67    1    3        6   0     1
4   51    1    0        6   0     0
5   56    1    1        6   1     0
6   60    1    1        6   0     0
7   53    1    0        3   1     0
8   54    1    1        2   0     0
9   54    1    2        7   0     0
10  62    1    0        4   0     0
```

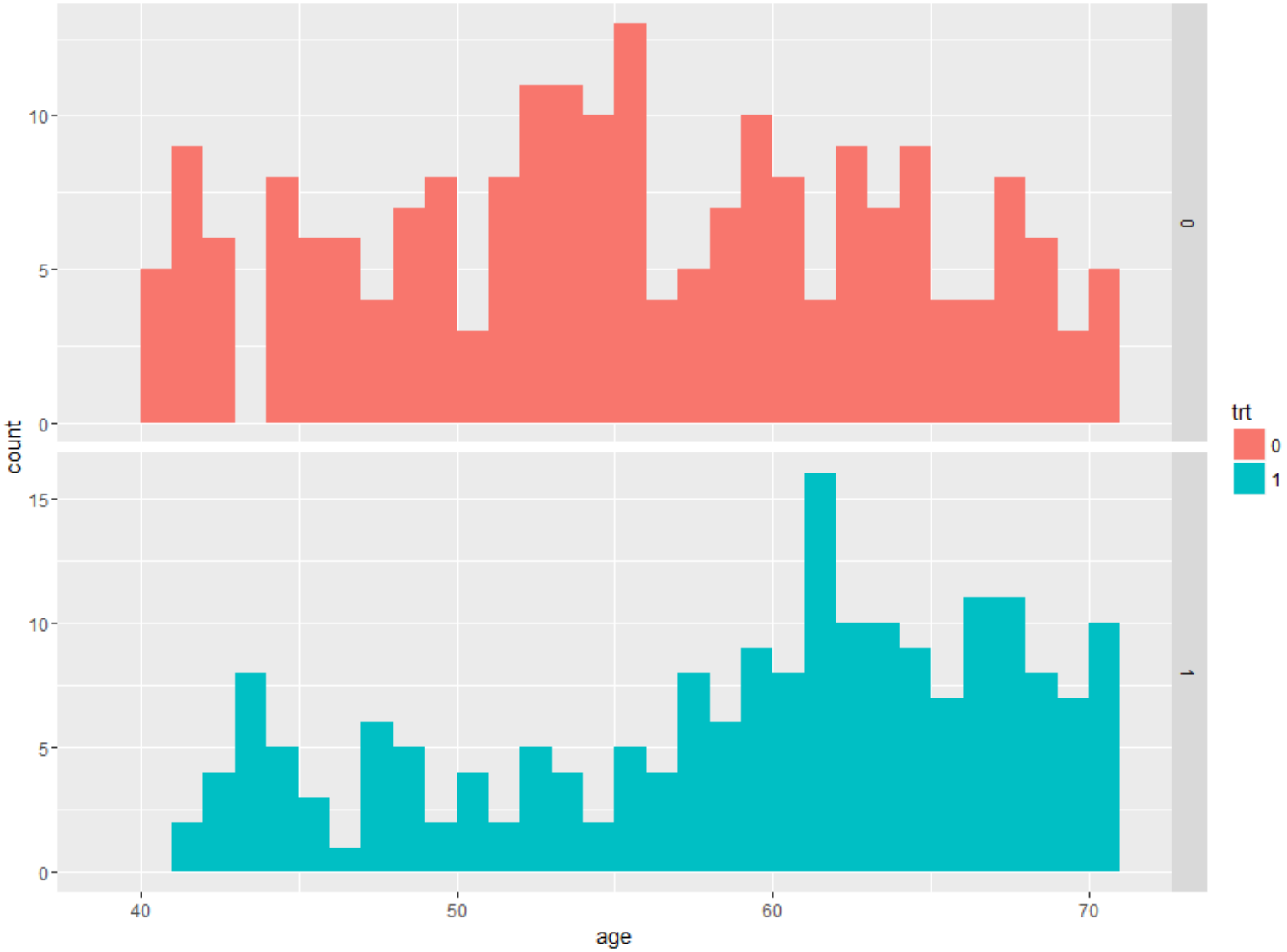
Crude mortality - MI example

```
> with(mi, table(trt, death),1)
   death
trt   0   1
  0 168  40
  1 162  30
> round(with(mi, prop.table(table(trt, death),1)),3)
   death
trt     0     1
  0 0.808 0.192
  1 0.844 0.156
```

- treatment: 15.6%, control (standard therapy): 19.2%
  - estimated treatment effect = 3.6%, 95% CI (-3.9%, 11.1%)
- confounders not adjusted

with(mi, t.test(death~trt))

Patient characteristics - MI example

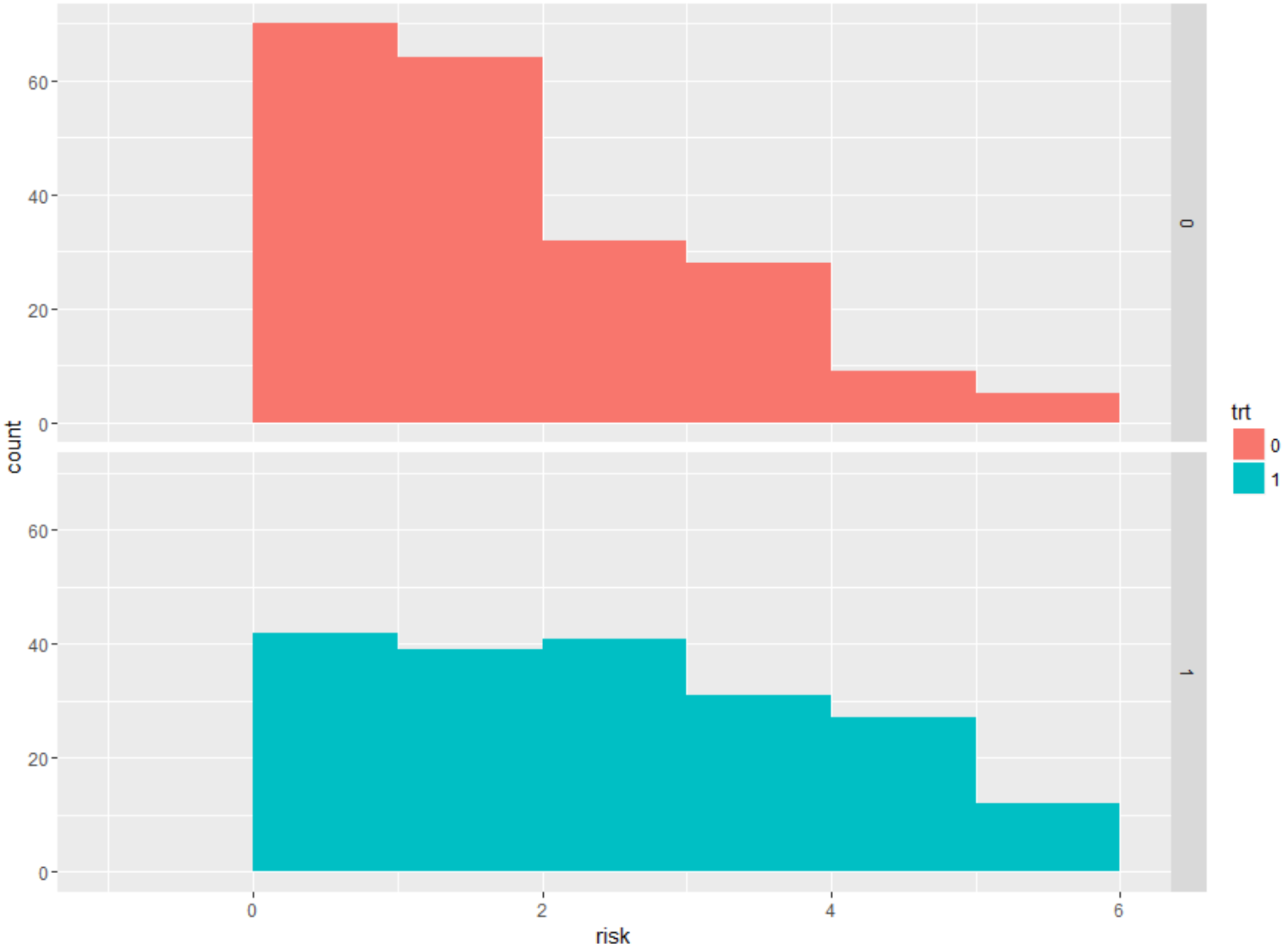



```
mi$trt <- as.factor(mi$trt)

ggplot(mi, aes(x=age, fill=trt)) +
geom_histogram(binwidth=1) +
facet_grid(trt ~ .)
```

- patients receiving the newer treatment tends to be older

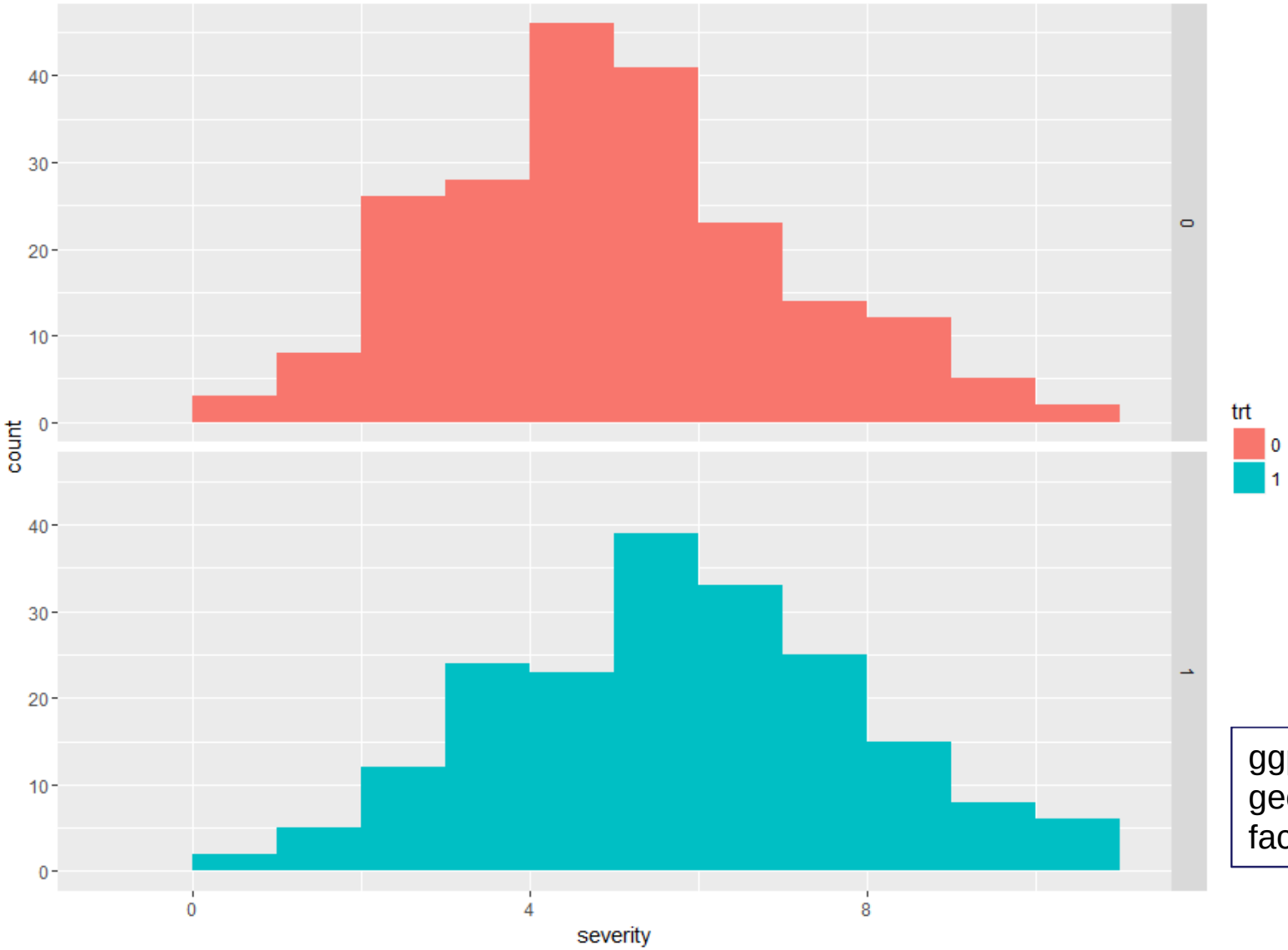
Patient characteristics - MI example




```
ggplot(mi, aes(x=risk, fill=trt)) +
geom_histogram(binwidth=1) +
facet_grid(trt ~ .)
```

- patients receiving the newer treatment tend to have higher risk

Patient characteristics - MI example




```
ggplot(mi, aes(x=severity, fill=trt)) +
geom_histogram(binwidth=1) +
facet_grid(trt ~ .)
```

- patients receiving the newer treatment slightly more severe

Summary of patient characteristics

- those received the newer clot-busting drug are in general:
  - older
  - more pre-existing risk factors
  - slightly more severe
- these factors are highly associated with mortality

Propensity score

- derive a “propensity score” for each case
- propensity score p_i
  - the probability (propensity) of assigning to treatment for individual *i*
  - depends on the covariates / factors
  - does not depend on the outcome
- rationale:
  - to compare individuals with similar propensity scores (treatment vs no treatment)
  - any difference in the outcome should then be due to the treatment effect only

Propensity score analysis – key assumptions

- conditional independence / unconfoundedness
  - given the observable predictors X, potential outcomes Y are independent of treatment assignment T

  $\Rightarrow$ treatment assignment only depends on observed characteristics
- common support / overlap condition
  - P(T=1|X) < 1 for some observed predictors X
    - If P(T=1|X) = 1, all individuals with observed predictors X are treated and no ‘similar’ control can be found for comparison
  - to ensure sufficient sample size between treatment groups for comparison

Deriving the propensity score

- estimate propensity score p_i
  - logistic regression (predict treatment vs control)
    - $\text{logit}(p_i) = X_i\beta$
  - multinomial regression (several treatment groups)
  - other models can also be considered
    - e.g. classification trees, probit regression
  - predictors
    - excluding the outcome of the treatment
    - may include interaction terms to increase accuracy to predict treatment assignment
    - important to check if balance of characteristics across treatment groups is achieved
  - balancing patient characteristics more important than parsimony

Deriving the propensity score – MI example

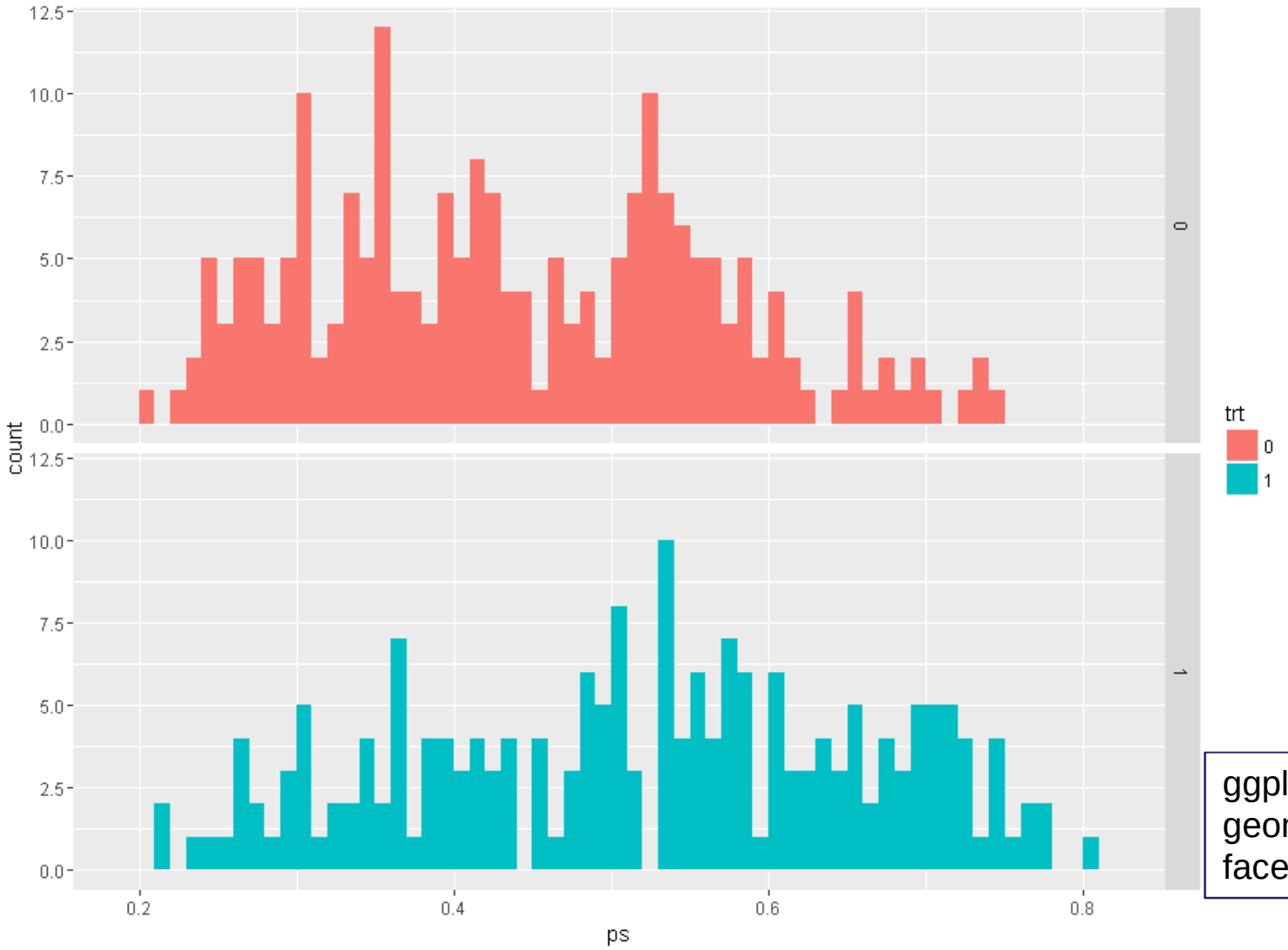
- fit a logistic regression to predict treatment assignment
  - propensity score: predicted probability of receiving clot-busting drug
  - predictors: age, risk factor score, admission severity score
  - interactions may also be considered if it improves accuracy or improve balance of characteristics across groups
  - outcome of the treatment should not be included as predictors

Deriving the propensity score – MI example

– fit logistics regression model to predict treatment, without the final outcome of interest (death)

```
ps.model <- glm(trt ~ age + risk + severity, data=mi,
   family=binomial)
mi$ps <- predict(ps.model, type='response')
> head(mi)
  age male risk severity trt death        ps
1  48    1    3        8   0     0 0.5773106
2  59    1    4        6   1     0 0.6362960
3  67    1    3        6   0     1 0.6506088
4  51    1    0        6   0     0 0.4009893
5  56    1    1        6   1     0 0.4824049
6  60    1    1        6   0     0 0.5126509
```

propensity score distribution by treatment




```
ggplot(mi, aes(x=ps, fill=trt)) +
geom_histogram(binwidth=0.01) +
facet_grid(trt ~ .)
```

– common support in the range 0.2 – 0.8

Propensity score methods

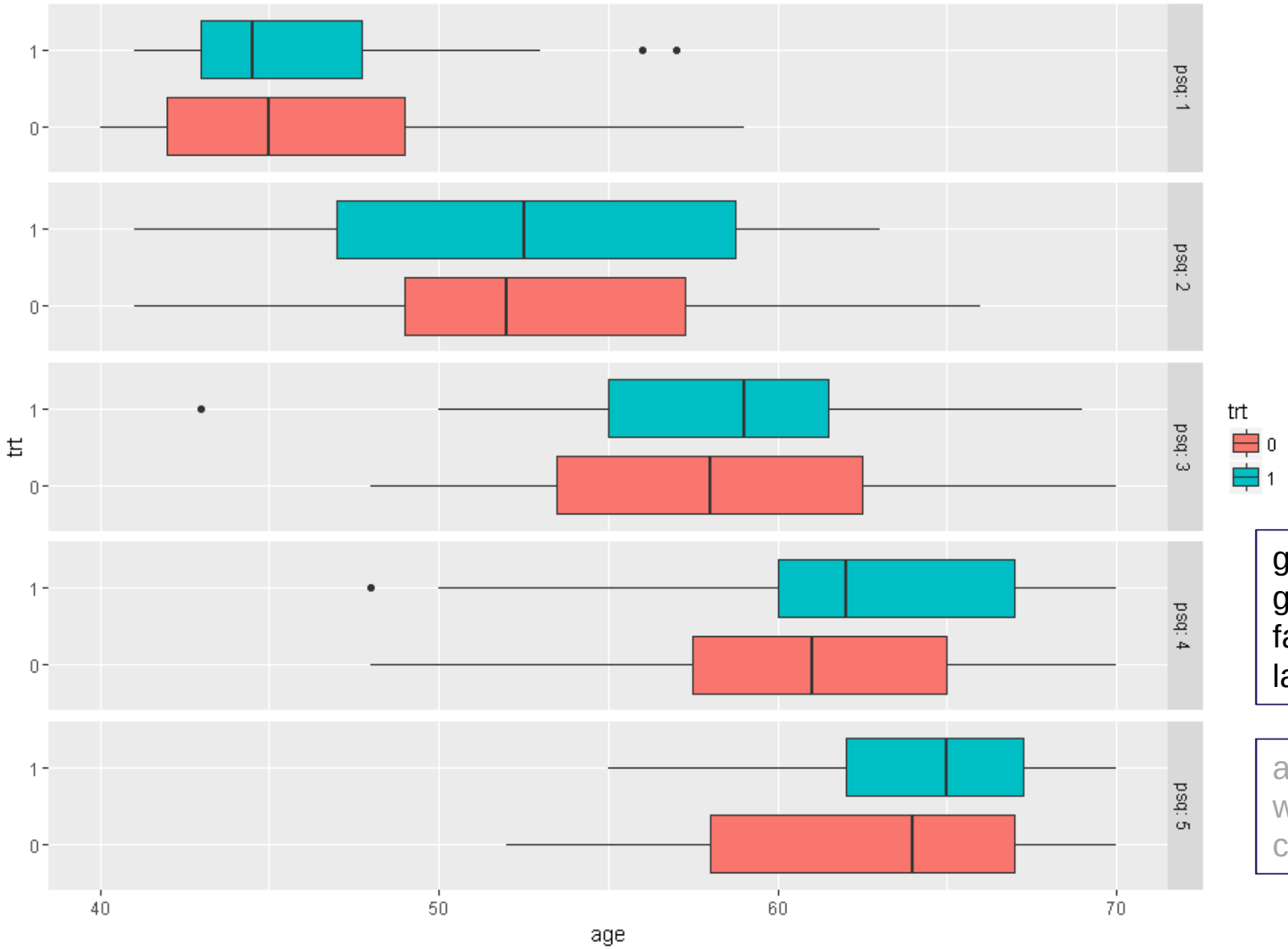
- Stratification by propensity score
  - e.g. stratified by quintiles of the propensity score
  - to remove most of the selection bias
  - treatment effect is estimated within each stratum
  - overall treatment effect can be estimated by (weighted) mean of the stratum-specific treatment effect

Stratification by propensity score quintiles

```
ps.boundary <- quantile(mi$ps, 0:5/5)
> ps.boundary
       0%       20%       40%       60%       80%      100%
0.2014026 0.3458898 0.4271172 0.5255349 0.6054821 0.8082802
mi$psq <- cut(mi$ps, ps.boundary, right=F,
   include.lowest=T, label=1:5)
```

- the cut off points for the quintiles are 0.346, 0.427, 0.526, 0.605
- define the stratification according to the quintiles
- next step: is balance of characteristics across treatment groups achieved?

Boxplot – age by PS strata



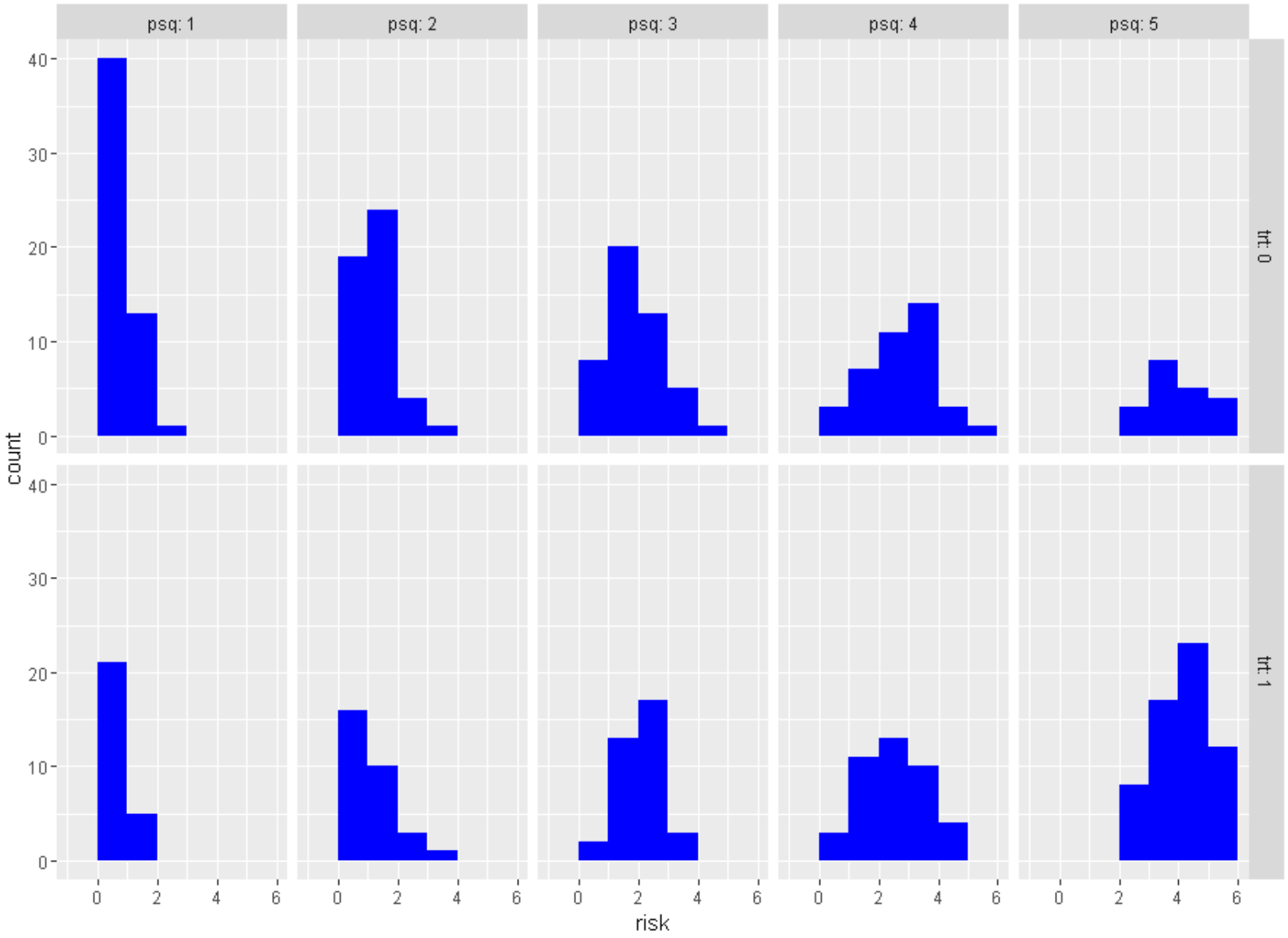
Age is more balanced across treatment type in each propensity score strata

```
ggplot(mi, aes(x=trt, y=age)) +
geom_boxplot(aes(fill=trt)) +
facet_grid(psq ~ .,
labeller=label_both) + coord_flip()
```

alternatively:

```
with(mi, boxplot(age ~ trt*psq,
col=c("red", "yellow")))
```

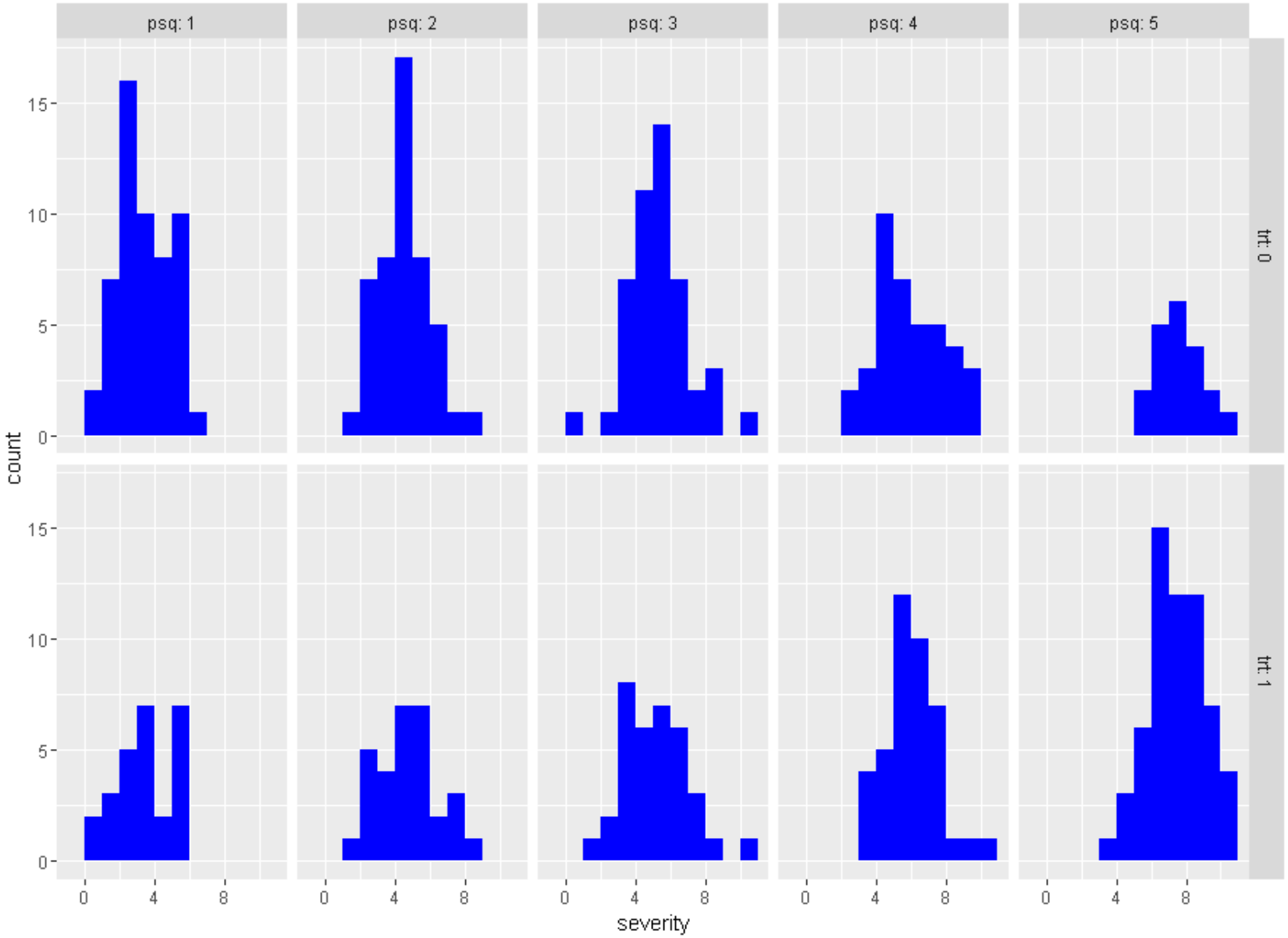
Boxplot – risk by PS strata



may also be used to evaluate factors of treatment assignment

```
ggplot(mi, aes(x=risk)) +
geom_histogram(binwidth=1,
fill='blue') + facet_grid(trt ~
psq, labeller=label_both)
```

Boxplot – severity by PS strata




```
ggplot(mi, aes(x=severity)) +
geom_histogram(binwidth=1,
fill='blue') + facet_grid(trt ~
psq, labeller=label_both)
```

Assessment of balance across treatment groups

- assuming continuous outcome for risk and severity
- t-statistics unadjusted and adjusted for PS strata (by linear regression)

	unadjusted	**adjusted**
Age	4.41	0.73
Risk	4.75	-0.16
Severity	3.84	0.15

For age:
summary(lm(age~trt, data=mi))
summary(lm(age~trt+psq, data=mi))

- all three factors are much more balanced in the PS strata
- may also assess balance by mean standardized difference

MI mortality by PS strata - result

```
> mean.tp <- aggregate(death~trt+psq, data=mi, FUN=mean)
> count.tp <- aggregate(death~trt+psq, data=mi, FUN=length)
> cbind(mean.tp, count.tp$death)
   trt psq      death count.tp$death
1    0   1 0.11111111            54
2    1   1 0.03846154            26
3    0   2 0.20833333            48
4    1   2 0.16666667            30
5    0   3 0.14893617            47
6    1   3 0.17142857            35
7    0   4 0.30769231            39
8    1   4 0.14634146            41
9    0   5 0.25000000            20
10   1   5 0.20000000            60
```

in general, mortality rates were lower for patients receiving clot-busting drug

MI mortality by PS strata - result

```
> n.psq <- as.numeric(table(mi$psq))
> n.psq
[1] 80 78 82 80 80
> cbind(mean.tp, count.tp$death)
   trt psq      death count.tp$death
1    0   1 0.11111111             54
2    1   1 0.03846154             26
3    0   2 0.20833333             48
4    1   2 0.16666667             30
5    0   3 0.14893617             47
6    1   3 0.17142857             35
7    0   4 0.30769231             39
8    1   4 0.14634146             41
9    0   5 0.25000000             20
10   1   5 0.20000000             60
```

overall treatment effect = [80*(0.04-0.11) + 78*(0.17-0.20) + 82*(0.17-0.15) + 80*(0.15-0.31) + 80*(0.20-0.25)] / 400 = -0.0603

```
sum((mean.tp$death[mean.tp$trt==1]-mean.tp$death[mean.tp$trt==0])*n.psq)/sum(n.psq)
```

MI mortality by PS strata - result

```
> var.tp <- aggregate(death~trt+psq, data=mi, FUN=var)
> cbind(var.tp, count.tp$death)
   trt psq      death count.tp$death
1    0   1 0.10062893             54
2    1   1 0.03846154             26
3    0   2 0.16843972             48
4    1   2 0.14367816             30
5    0   3 0.12950971             47
6    1   3 0.14621849             35
7    0   4 0.21862348             39
8    1   4 0.12804878             41
9    0   5 0.19736842             20
10   1   5 0.16271186             60
```

variance of estimated treatment effect

$= [\ 80^2(0.10/54 + 0.04/26) +$

$\quad 78^2(0.17/48+0.14/30) + \ldots\ ] / 400^2$

$= 0.00159$

```
sum((var.tp$death/count.tp$death)*rep(n.psq, each=2)^2)/sum(n.psq)^2
```

95% CI = (-0.14, 0.02)

Propensity score methods

- Propensity score matching
  - match each treated individual to 1 or n individuals from the control group
  - matching methods
    - nearest-neighbor matching
    - caliper matching
      - matched controls to cases with propensity score within a preset distance
    - Mahalanobis metric matching
      - standardized squared distance relative to variation
    - stratification is also a kind of matching (by range)
  - compare outcome in the ‘case’ vs ‘control’
    - e.g. paired t-test, McNemar’s test
    - unconditional or conditional analysis (on matched pairs/sets)

Propensity score matching

matchit(*formula, data, method = “nearest”, distance = “logit”,…*) (in package: MatchIt)

- ***formula*** syntax similar to glm
- ***data***: indicates the data frame to be used
- ***method***: specifies a matching method: "exact", "nearest" (nearest neighbor matching), "optimal", and "subclass“ (subclassification)
- ***distance***: specifies the method used to estimate the distance measure. The default is logistic regression, "logit"

MI example – propensity score matching

```
> m.out <- matchit(trt ~ age + risk + severity, data = mi,
   method = "subclass", subclass=20)
> summary(m.out)
```

```
Summary of Balance for All Data:
         Means Treated Means Control Std. Mean Diff. Var. Ratio eCDF Mean eCDF Max
distance        0.5215        0.4417          0.5506     1.3136    0.1616   0.2616
age            58.6354       54.9615          0.4449     0.9959    0.1185   0.2508
risk            1.9896        1.3125          0.4392     1.3872    0.1128   0.2224
severity        5.2760        4.4712          0.3732     1.1276    0.0732   0.1899

Summary of Balance Across Subclasses
         Means Treated Means Control Std. Mean Diff. Var. Ratio eCDF Mean eCDF Max
distance        0.5215        0.5208          0.0047     1.0082    0.0070   0.0313
age            58.6354       58.0408          0.0720     1.0381    0.0331   0.1061
risk            1.9896        2.0797         -0.0584     0.9182    0.0168   0.0458
severity        5.2760        5.2614          0.0068     1.0380    0.0129   0.0385
```

MI example – matched subclass

```
> matched.mi <- match.data(m.out)
> matched.mi[matched.mi$subclass==1,]
    age male risk severity trt death  distance   weights subclass
27   43    1    0        1   1     0 0.2132211 1.0000000        1
31   42    1    0        2   0     0 0.2308658 0.5416667        1
35   48    1    1        1   0     0 0.2739481 0.5416667        1
45   45    1    0        3   0     0 0.2728490 0.5416667        1
52   46    1    0        1   0     0 0.2288440 0.5416667        1
55   48    1    0        2   1     0 0.2646589 1.0000000        1
64   40    1    0        4   0     0 0.2691281 0.5416667        1
76   47    1    0        2   1     0 0.2588127 1.0000000        1
79   40    1    0        4   0     0 0.2691281 0.5416667        1
81   49    1    0        1   0     0 0.2452549 0.5416667        1
...
```

MI example – propensity score matching

```
> matched.mi <- match.data(m.out)
```

Extract the matched dataset

```
> clr.mi <- clogit(death ~ trt + strata(subclass),
   data=matched.mi)
```

- `summary(clr.mi)`

```
        coef exp(coef) se(coef)      z Pr(>|z|)
trt1 -0.4275    0.6521   0.2857 -1.496    0.135

     exp(coef) exp(-coef) lower .95 upper .95
trt1    0.6521      1.533    0.3725     1.142
```

Propensity score methods (cont'd)

- Propensity score (inverse probability) weighting
  - to estimate $E[Y_1-Y_0]$
  - observed outcome is actually conditioned on assigned treatment
    - ie, observed $E[Y_1|T=1]$ and $E[Y_0|T=0]$
  - estimate $E[Y_i]$ by $E[Y_i\delta(T=i)/P(T=i)]$, i=0, 1
    - δ: indicator function
  - treatment effect = $\frac{1}{N}\left(\sum_{trt=1}\frac{Y_{1i}}{p_{1i}}-\sum_{trt=0}\frac{Y_{0i}}{1-p_{1i}}\right)$
  - approximate variance for binary outcome:

$$\frac{1}{N^2}\left(\sum_{trt=1}\frac{1-p_{1i}}{p_{1i}}+\sum_{trt=0}\frac{p_{1i}}{1-p_{1i}}\right)$$

  - estimated effect for clot-busting therapy = -0.065, 95% CI = (-0.163, 0.033)

Your turn:
Try estimating the treatment effect by PS weighting method

Adjustment by propensity score

- fit linear / logistic regression
- propensity score as the only predictor to predict outcome

```
> lr.ps <- glm(death~trt+ps, data=mi, family=binomial)
> summary(lr.ps)
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)  -2.7162     0.5063  -5.364 8.12e-08 ***
trt1         -0.4932     0.2838  -1.738  0.08220 .
ps            2.8135     1.0116   2.781  0.00541 **
```

Propensity score methods (cont'd)

```
> exp(coef(lr.ps))
(Intercept)         trt1           ps
 0.06612525  0.61067986 16.66896399

> exp(confint(lr.ps))
                  2.5 %      97.5 %
(Intercept) 0.02368166   0.1733016
trt1        0.34705278   1.0591376
ps          2.35437201 125.5768623
```

OR for clot-busting drug = 0.611, 95% CI = (0.35, 1.06)

Example – effectiveness of SARS treatment

- compare SARS fatality rate for patients treated with ribavirin, corticosteroids, or both

	Hong Kong (n = 1743)							
Characteristic	Neither Treatment	(%)	Ribavirin Only	(%)	Corticosteroids Only	(%)	Ribavirin and Corticosteroids	(%)
Men	379	(50.5)	85	(42.1)	23	(45.1)	286	(38.7)
Age ≤ 39 y	297	(39.5)	123	(60.9)	19	(37.3)	403	(54.5)
Age 40-49 y	124	(16.5)	36	(17.8)	6	(11.8)	172	(23.3)
Age 50-59 y	73	(9.7)	15	(7.4)	7	(13.7)	93	(12.6)
Age 60-69 y	70	(9.3)	14	(6.9)	8	(15.7)	30	(4.1)
Age > 69 y	187	(24.9)	14	(6.9)	11	(21.6)	41	(5.5)
Health care worker	120	(16.0)	72	(35.6)	7	(13.7)	205	(27.7)
With preexisting comorbid conditions	220	(29.3)	28	(13.9)	18	(35.3)	90	(12.2)
Data on comorbid conditions missing	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)
Died	175	(23.3)	18	(8.9)	15	(29.4)	93	(12.6)

Lau et al, Am J Med, 2009

  - patient characteristics not balanced across treatment groups
  - patients receiving no treatment seem to have high fatality rate

Example – effectiveness of SARS treatment

- propensity scores were estimated and used as weights for the fatality rate
- patient characteristics were found to be balanced across treatment groups after PS adjustment

	Hong Kong		
Treatment	Case Fatality Ratio[a] (%)	95% CI	*P* Value[b]
Neither ribavirin nor corticosteroids	15.4	(13.2-17.6)	—
Ribavirin	17.0	(6.2-27.8)	.77
Corticosteroids	18.9	(4.6-33.1)	.64
Both	19.2	(14.2-24.3)	.16

  - controlled for patients characteristics, no evidence of lower fatality rate for patients receiving both ribavirin and corticosteroids

Limitations - PS analysis

- assumption of unconfoundedness not testable
- cannot control for unobserved selection to treatment
  - reduce biases but cannot ensure significant biases remain
- need larger samples to achieve balance of patient characteristics (similar to randomized design)
- sufficient overlap of characteristics across treatment groups is needed for accurate estimation of treatment effect

Summary - PS

- estimate treatment effect / group differences, controlled for observed confounders
- estimate propensity score for stratification, matching, weighting or adjustment
- most useful when
  - few events of interest are observed relative to the (confounding) factors needed to be considered
  - interested in factors associated with treatment assignment

Review

- We have discussed how to carry out conditional logistic regression for matched case control study
- We have discussed how to use propensity score method to handle confounding

Further reading

- Khandker SR, Koolwal GB, Samad HA. *Handbook on Impact Evaluation: Quantitative Methods and Practices*. Washington: The World Bank. 2010.

- Vittinghoff, E, et al. *Regression methods in biostatistics.* Springer, 2005