### STATISTICS 536B, Lecture #9

March 26, 2015

Have  $(Y, X, C_1, \ldots, C_p)$  data, interested in the association between Y and X given C.

Direct route: study this via regression of Y on X and C.

Indirect route: consider  $Z = Pr(X = 1|C) = \pi(C)$  (in theory), or  $\hat{Z} = \hat{\pi}(C)$  (in practice). Then focus on the association between Y and X given Z.

The underlying mathematics validates this approach.

# Mongelluzzo et. al. - corticosteroids and mortality from bacterial meningitis

Outcome Y is time-to-event (time from hospitalization for bacterial meningitis to death, or time from hospitalization to discharge)

Binary exposure X is *adjuvant* use of corticosteroids

Potential confounders (C) include sex, race, vancomycin use within 24 hours, etc,...

Traditional analysis might involve proportional hazards regression model for Y using X and  $C_1, \ldots, C_p$  as explanatory variables. Instead, these authors use X and  $\hat{Z} = \hat{\pi}(C)$  as the explanatory variables. Fitted propensity model for (X|C) model gives AUC=0.74 ... "better than chance, but "little concern about nonoverlapping propensity score distributions" ??? But then: "The propensity scores were not equally distributed. When the propensity scores were stratified by quintiles, a greater proportion of X=1 patients were in the highest quintile and a greater proportion of X = 0 patients were in the lowest quintile. To address this imbalance..."

PUZZLING!!!

'Residual confounding by indication' concern.

Often plausible that sicker patients more likely to get the intervention (X = 1) being studied. (So a crude two group comparison would be 'unfair' on X = 1).

Not a problem if 'sicker' is completely captured by C.

Otherwise, can make an intervention appear less efficacious than it really is. E.g., say that  $(C, C^*)$  completely capture 'sicker', but  $C^*$  is unmeasured.

- Table 3: no evidence for a (Y, X) association given C for either Y.
- Table 4: no evidence for a (Cost, X) association given *C*. Suggestive of (or at least consistent with) *C* being 'good enough.' Plausible that if *C* wasn't fully capturing disease severity and X = 1 was being preferentially offered to those with more severe disease, then we would see a positive association between *X* and Cost given *C*.

## Back to simpler framework of continuous outcome Y. Where are we at?

Trying to estimate

$$\Delta = E\{E(Y|X=1,C) - E(Y|X=0,C)\}.$$

If we are confident in our ability to model Y given X and C: Could fit a (Y|X, C) outcome model, to estimate  $m_x(C) = E(Y|X = x, C)$ , then

$$\hat{\Delta}_R = \frac{1}{n} \sum_{i=1}^n \hat{m}_1(c_i) - \hat{m}_0(c_i)$$

is a consistent estimator, if the form of the outcome model is right.

If we are confident in our ability to model X given C: Recall (last time) we can rewrite the target parameter as

$$\Delta = E\left\{Y\left(\frac{X}{\pi(C)} - \frac{1-X}{1-\pi(C)}\right)\right\}$$

Could fit a (X|C) propensity model, to estimate  $\pi(C) = Pr(X = 1|C)$ , then

$$\hat{\Delta}_{IPW} = \frac{1}{n} \sum_{i=1}^{n} y_i \left( \frac{x_i}{\hat{\pi}(c_i)} - \frac{1-x_i}{1-\hat{\pi}(c_i)} \right).$$

is a consistent estimator if form of propensity model is right.

```
### outcome model and fitted values
outmod <- lm(y~x+cnf)
m0 <- cbind(1,0,cnf)%*%coef(outmod)
m1 <- cbind(1,1,cnf)%*%coef(outmod)</pre>
```

```
### propensity model and fitted values
promod <- glm(x<sup>cnf</sup>, family=binomial)
prpns <- fitted(promod, response=T)</pre>
```

```
### regression estimate
mean(m1-m0)
[1] 1.23
```

```
### IPW estimate
mean(y*(x/prpns - (1-x)/(1-prpns)))
[1] 1.14
```

```
### Double-robust estimate
  mean((y*x - (x-prpns)*m1)/prpns) - mean((y*(1-x) + (x-prpns)*m0)/(1-prpns))
[1] 1.16
```

#### Standard errors for these estimates?

All three estimates are means of n values, but ...

#### So bootstrap...

```
ests.bb <- matrix(NA,200,3)</pre>
for (i in 1:200) {
  smp <- sample(1:n, replace=T)</pre>
  ### outcome model
  outmod <- lm(y[smp]~x[smp]+cnf[smp,])</pre>
  . . .
  ### propensity model
  promod <- glm(x[smp]~cnf[smp,], family=binomial)</pre>
  . . .
  ests.bb[i,] <- c(mean(m1-m0), ...)</pre>
}
sqrt(apply(ests.bb,2,var))
[1] 0.12 0.12 0.12
```