

# Sensitivity analysis for principal ignorability violation in estimating complier and noncomplier average causal effects

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joint work with Liz Stuart, Dan Scharfstein, Betsy Ogburn  
(but all problems mine)

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# Outline

Principal stratification

Identification and Principal ignorability

Organizing themes for this work

Mean-based sens analysis: three ratio-type and one difference-type sens params

Distribution-based sens analysis: a quantile mapping method

Conclusion

## Problem: Noncompliance/post-treatment events

The study of treatment effects often complicated by noncompliance or other significant post-treatment events, eg

- ▶ JOBS II study<sup>[1]</sup>: nonattendance of training
- ▶ Head Start<sup>[2]</sup>: families in either arm may enroll kid or not
- ▶ Substance use treatment modalities<sup>[3]</sup>: institutionalization
- ▶ Treatment effect on quality of life<sup>[4]</sup>: death

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[1] Amiram D. Vinokur, Richard H. Price, and Yaacov Schul. "Impact of the JOBS intervention on unemployed workers varying in risk for depression". In: *American Journal of Community Psychology* 23.1 (1995), pp. 39–74. DOI: 10.1007/BF02506922.

[2] Avi Feller, Fabrizia Mealli, and Luke Miratrix. "Principal Score Methods: Assumptions, Extensions, and Practical Considerations". In: *Journal of Educational and Behavioral Statistics* 42.6 (2017), pp. 726–758. DOI: 10.3102/1076998617719726.

[3] Beth Ann Griffin, Daniel F. McCaffrey, and Andrew R. Morral. "An application of principal stratification to control for institutionalization at follow-up in studies of substance abuse treatment programs". In: *The Annals of Applied Statistics* 2.3 (2008), pp. 1034–1055. DOI: 10.1214/08-A0AS179.

[4] Donald B. Rubin. "Causal inference through potential outcomes and principal stratification: Application to studies with "censoring" due to death". In: *Statistical Science* 21.3 (2006), pp. 299–309. DOI: 10.1214/088342306000000114.

## Problem: Noncompliance/post-treatment events

The study of treatment effects often complicated by noncompliance or other significant post-treatment events

In some of these cases, the ATE may no longer be of interest (or defined)

Researchers might be interested in the effect of receiving treatment, or effect of treatment given a post-treatment event

but would break randomization, compare apples to oranges

# Principal stratification

Define groups, termed *principal strata*, based on potential values of the post-treatment variable<sup>[1]</sup> (treatment received)

## Notation

- ▶  $Z$  treatment assigned (binary)
- ▶  $Y$  outcome;  $Y_1, Y_0$  potential outcomes
- ▶  $S$  treatment received;  $S_1, S_0$  potential treatment received
- ▶  $X$  baseline covariates
- ▶  $C$  principal stratum, defined based on  $(S_1, S_0)$ , is a pre-treatment variable

Principal causal effects:  $E[Y_1 - Y_0 \mid C]$

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[1] Constantine E. Frangakis and Donald B. Rubin. "Principal Stratification in Causal Inference". In: *Biometrics* 58.1 (2002), pp. 21–29.  
DOI: 10.1111/j.0006-341X.2002.00021.x.

## The setting we focus on

There are different settings, depending on

- ▶ the type of variable  $S$  is: binary or other
- ▶ using  $S_1$  only or both  $S_1, S_0$  (one-sided or two-sided noncompliance)
- ▶  $Y$  is well-defined generally or conditional on  $S$

Our focus: binary  $S$  + one-sided noncompliance +  $Y$  well-defined generally

interested in complier and noncomplier average causal effects (CACE, NACE)

$$\Delta_c := E[Y_1 - Y_0 \mid C = c] \text{ for } c = 1, 0$$

illustrative example: JOBS II

- ▶ unemployed workers are randomized to either a one-week training aiming to improve job searching skills and mental health (*intervention*) or to receive a booklet with job search tips (*control*)
- ▶ about half of those assigned to intervention didn't attend
- ▶ outcomes: work, earnings, depressive symptoms

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## The identification challenge: $C$ is only partially observed

$$\Delta_c = E[Y_1 | C = c] - E[Y_0 | C = c]$$

$E[Y_1 | C = c]$  is identified under the standard causal inference assumptions

- A0 (consistency):  $Y = ZY_1 + (1 - Z)Y_0, S = ZC$   
A1 (treatment assignment ignorability):  $Z \perp\!\!\!\perp (Y_1, Y_0, C) | X$   
A2 (treatment assignment positivity):  $0 < P(Z = 1 | X) < 1$

but  $E[Y_0 | C = c]$  is not identified under these assumptions alone



## Several identification strategies

- ▶ Instrumental variable strategy<sup>[2]</sup>
  - ▶ rely on the *exclusion restriction* (ER) assumption, which implies  $\tau_{00} = \tau_{10}$  and NACE = 0
  - ▶ not appropriate if treatment receipt not strictly binary<sup>[3]</sup>
    - ▶ compliance is defined using one important component of the intervention
    - ▶ dichotomizing a continuous participation variable
  - ▶ does not allow psychological effects, effects of compensating behaviors, etc.

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[2] Joshua D. Angrist and Guido W. Imbens. "Two-stage least squares estimation of average causal effects in models with variable treatment intensity". In: *Journal of the American Statistical Association* 90.430 (1995), pp. 431–442. DOI: 10.1080/01621459.1995.10476535.

[3] John Marshall. "Coarsening Bias: How Coarse Treatment Measurement Upwardly Biases Instrumental Variable Estimates". en. In: *Political Analysis* 24.2 (2016), pp. 157–171. DOI: 10.1093/pan/mpw007. (Visited on 02/05/2023), Martin E Andresen and Martin Huber. "Instrument-based estimation with binarised treatments: issues and tests for the exclusion restriction". In: *The Econometrics Journal* 24.3 (Sept. 2021), pp. 536–558. DOI: 10.1093/ectj/utab002. (Visited on 02/05/2023).

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- ▶ Principal ignorability (PI) strategy<sup>[2]</sup>
  - ▶ PI assumption:  $C \perp\!\!\!\perp Y_0 \mid X$ , or  $E[Y_0 \mid X, C = 1] = E[Y_0 \mid X, C = 0]$
  - ▶ appealing if have reach covariate data
  - ▶ justifies the *principal score weighting* method
  - ▶ does not assume NACE = 0, thus may be useful where ER is not justified

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[2] Elizabeth A. Stuart and Booil Jo. "Assessing the sensitivity of methods for estimating principal causal effects". In: *Statistical Methods in Medical Research* 24.6 (2015), pp. 657–674. DOI: 10.1177/0962280211421840, Avi Feller, Fabrizia Mealli, and Luke Miratrix. "Principal Score Methods: Assumptions, Extensions, and Practical Considerations". In: *Journal of Educational and Behavioral Statistics* 42.6 (2017), pp. 726–758. DOI: 10.3102/1076998617719726, Peng Ding and Jiannan Lu. "Principal stratification analysis using principal scores". In: *Journal of the Royal Statistical Society. Series B: Statistical Methodology* 79.3 (2017), pp. 757–777. DOI: 10.1111/rssb.12191. arXiv: 1602.01196, Zhichao Jiang, Shu Yang, and Peng Ding. "Multiply robust estimation of causal effects under principal ignorability". en. In: *Journal of the Royal Statistical Society. Series B: Statistical Methodology* 84.4 (2022), pp. 1423–1445. DOI: 10.1111/rssb.12538.

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- ▶ Other strategies
  - ▶ Auxiliary independence:  $W \perp\!\!\!\perp Y_0 \mid C, X$  for auxiliary variable  $W$ <sup>[2]</sup>
    - ▶ requires that such a special auxiliary variable exists

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[2] Zhichao Jiang and Peng Ding. "Identification of Causal Effects Within Principal Strata Using Auxiliary Variables". In: *Statistical Science* 36.4 (2021), pp. 1–49. doi: 10.1214/20-STS810.

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- ▶ Other strategies
  - ▶ Auxiliary independence:  $W \perp\!\!\!\perp Y_0 \mid C, X$  for auxiliary variable  $W$ 
    - ▶ requires that such a special auxiliary variable exists
  - ▶ Principal strata sufficiently prognostic:  $X \perp\!\!\!\perp Y_0 \mid C$ 
    - ▶ underlies methods that impute unobserved  $C$  based only on  $X$  or use the principal score in place of  $X$  in modeling  $Y_0$
    - ▶ highly unrealistic

## Our focus on PI

PI is an important identification assumption

But we need sensitivity analyses – just like with any other untestable assumptions

## Zooming in: the identification problem and the PI solution

$$E[Y_z | C = c] = \frac{\overbrace{E\{P(C = c | X)\}}^{=: \pi_c(X)} \overbrace{E[Y_z | X, C = c]\}}^{=: \mu_{zc}(X)}}{E[P(C = c | X)]}$$

Under A0, A1, A2

$E[Y_1 | C = c]$  is identified because  $\pi_c(X)$  and  $\mu_{1c}(X)$  are identified

$$\pi_c(X) = P(C = c | X, Z = 1)$$

$$\mu_{1c}(X) = E[Y | X, Z = 1, C = c]$$

but  $\mu_{0c}(X)$  is not identified so  $E[Y_0 | C = c]$  is not

## Zooming in: the identification problem and the PI solution

The problem: one equation with two unknowns

$$\pi_1(X)\mu_{01}(X) + \pi_0(X)\mu_{00}(X) = \mu_0(X)$$

where  $\mu_0(X) := E[Y_0 | X]$ , which under A0, A1, A2 is identified by  $E[Y | X, Z = 0]$

The solution given by the PI assumption:

$$\mu_{01}(X) = \mu_{00}(X) = \mu_0(X)$$

## Existing sensitivity analyses for PI violation

Ding & Lu<sup>[2]</sup> use a mean ratio sens param  $\frac{\mu_{01}(X)}{\mu_{00}(X)}$ , and propose an estimator that under/over-weights the principal score – for the setting with randomized treatment

- ▶ when used with a binary (or bounded) outcome, this sens param may predict out of range
- ▶ this motivates us to develop methods that use a range of sens params

Wang et al.<sup>[3]</sup>, when handling a survival outcome, uses a hazard ratio sens param in a Weibull (or Weibull mixture) model for  $Y_0 | X, C$ , and impute unobserved  $C$  and  $Y_0$  as part of the fitting of a Bayesian joint model

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[2] Peng Ding and Jiannan Lu. "Principal stratification analysis using principal scores". In: *Journal of the Royal Statistical Society. Series B: Statistical Methodology* 79.3 (2017), pp. 757–777. DOI: 10.1111/rssb.12191. arXiv: 1602.01196.

[3] Craig Wang et al. "Sensitivity analyses for the principal ignorability assumption using multiple imputation". en. In: *Pharmaceutical Statistics* 22.1 (2023), pp. 64–78. DOI: 10.1002/pst.2260. (Visited on 02/05/2023).



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## Organizing themes

2 sens analysis approaches

3 estimator types

## Two sensitivity analysis approaches

anchoring on and deviating from  
the mean and distribution versions of PI

$$\text{A3m: } \mu_{01}(X) = \mu_{00}(X)$$

$$\text{A3d: } C \perp\!\!\!\perp Y_0 \mid X$$

## Three estimator types

A sensitivity analysis often follows and is secondary to a main analysis, so consider sens analysis as modification of main analysis of different types

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- ▶ Type A estimators ( $\approx$  outcome regression estimators)
  - ▶ estimates  $\mu_0(X)$  to first estimate (non)complier effects conditional on covariates and then aggregates them to estimate CACE/NACE, eg

$$\frac{\sum_{i=1}^n \hat{\pi}_c(X_i) [\hat{\mu}_{1c}(X_i) - \hat{\mu}_0(X_i)]}{\sum_{i=1}^n \hat{\pi}_c(X_i)}, \quad \frac{\sum_{i=1}^n \frac{Z_i}{\hat{e}(X_i, Z_i)} I(C_i = c) [Y_i - \hat{\mu}_0(X_i)]}{\sum_{i=1}^n \frac{Z_i}{\hat{e}(X_i, Z_i)} I(C_i = c)}$$

- ▶ sensitivity analysis technique: replace  $\mu_0(X)$  by the identification result of  $\mu_{0c}(X)$  under the sensitivity assumption

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- ▶ Type B estimators ( $\approx$  influence function based estimators)

▶ recall  $E[Y_1 | C=c] = \frac{\overbrace{E[\pi_c(X)\mu_{1c}(X)]}^{\nu_{1c}}}{\underbrace{E[\pi_c(X)]}_{\delta_c}}$ , and  $E[Y_0 | C=c] \stackrel{\text{PI}}{=} \frac{\overbrace{E[\pi_c(X)\mu_0(X)]}^{\nu_{0c}^{\text{PI}}}}{\underbrace{E[\pi_c(X)]}_{\delta_c}}$

- ▶ a type B estimator can be expressed as combination of IF-based estimators of  $\delta_c$ ,  $\nu_{1c}$  and  $\nu_{0c}^{\text{PI}}$

$$\frac{\hat{\nu}_{1c, \text{IF}} - \hat{\nu}_{0c, \text{IF}}^{\text{PI}}}{\hat{\delta}_{c, \text{IF}}}$$

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  - ▶ sensitivity analysis technique: replace  $\hat{\nu}_{0c,IF}^{PI}$  with an IF-based estimator of  $\nu_{0c}$  under the sensitivity assumption
- ▶ Type C estimators ( $\approx$  other/weighting estimators)
  - ▶ do not estimate  $\mu_0(X)$
  - ▶ an example is the pure weighting estimator

$$\frac{\sum_{i=1}^n \frac{Z_i}{\hat{e}(X_i, Z_i)} I(C_i = c) Y_i}{\sum_{i=1}^n \frac{Z_i}{\hat{e}(X_i, Z_i)} I(C_i = c)} - \frac{\sum_{i=1}^n \frac{1-Z_i}{\hat{e}(X_i, Z_i)} \hat{\pi}_c(X_i) Y_i}{\sum_{i=1}^n \frac{1-Z_i}{\hat{e}(X_i, Z_i)} \hat{\pi}_c(X_i)}$$

- ▶ no specific sens analysis technique; consider case by case

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## Three ratio-type sens params

A3m (PI, mean version):

$$\mu_{01}(X) = \mu_{00}(X).$$

A4-OR (sens odds ratio):

$$\frac{\mu_{01}(X)/[1 - \mu_{01}(X)]}{\mu_{00}(X)/[1 - \mu_{00}(X)]} = \rho,$$

A4-GOR (sens generalized odds ratio):

$$\frac{[\mu_{01}(X) - l]/[h - \mu_{01}(X)]}{[\mu_{00}(X) - l]/[h - \mu_{00}(X)]} = \rho$$

where  $l$  and  $h$  are the lower and upper bounds of  $Y_0$ ,

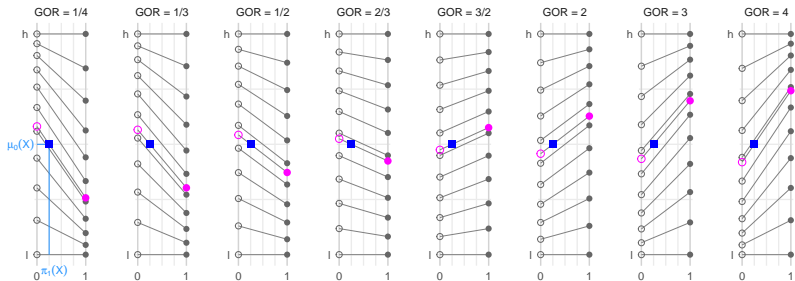
A4-MR (sens mean ratio):

$$\frac{\mu_{01}(X)}{\mu_{00}(X)} = \rho,$$

for some range of  $\rho$  that is considered plausible.

for binary outcomes (OR), outcomes bounded on both ends (GOR), and single-signed and otherwise unbounded outcomes (MR)

## Connection between $\mu_{00}(X)$ and $\mu_{01}(X)$ under A4-GOR for different GOR values



lines show GOR-implied connection between: ●  $\mu_{01}(X)$  ○  $\mu_{00}(X)$

example: ■ a pair of  $\mu_{00}(X)$  and  $\pi_1(X)$  values    ● implied  $\mu_{01}(X)$     ○ implied  $\mu_{00}(X)$

## Identification

Let  $\rho_1 = \rho$ ,  $\rho_0 = 1/\rho$

Under A4-OR combined with A0-A2,

$$\mu_{0c}(X) = \begin{cases} \frac{\overbrace{[\pi_c(X) + \mu_0(X)](\rho_c - 1) + 1}^* - \sqrt{*\^2 - 4\pi_c(X)\mu_0(X)\rho_c(\rho_c - 1)}}{2(\rho_c - 1)\pi_c(X)} & \text{if } \rho_c \neq 1 \\ \mu_0(X) & \text{if } \rho_c = 1 \end{cases}$$

Under A4-GOR combined with A0-A2,

$$\mu_{0c}(X) = \begin{cases} \frac{\overbrace{[\pi_c(X) + \mu_0^\diamond(X)](\rho_c - 1) + 1}^* - \sqrt{*\^2 - 4\pi_c(X)\mu_0^\diamond(X)\rho_c(\rho_c - 1)}}{2(\rho_c - 1)\pi_c(X)} (h - l) + l & \text{if } \rho_c \neq 1 \\ \mu_0(X) & \text{if } \rho_c = 1 \end{cases}$$

where  $\mu_0^\diamond(X) := [\mu_0(X) - l] / (h - l)$

Under A4-MR combined with A0-A2,

$$\mu_{0c}(X) = \frac{\rho_c \mu_0(X)}{(\rho_c - 1)\pi_c(X) + 1}$$

## Sensitivity analysis for the three estimator types

All three assumptions allow using the techniques of replacing  $\mu_0(X)$  and  $\nu_{0c}^{\text{PI}}$  for types A ( $\approx$  outcome regression) and type B ( $\approx$  IF-based) estimators

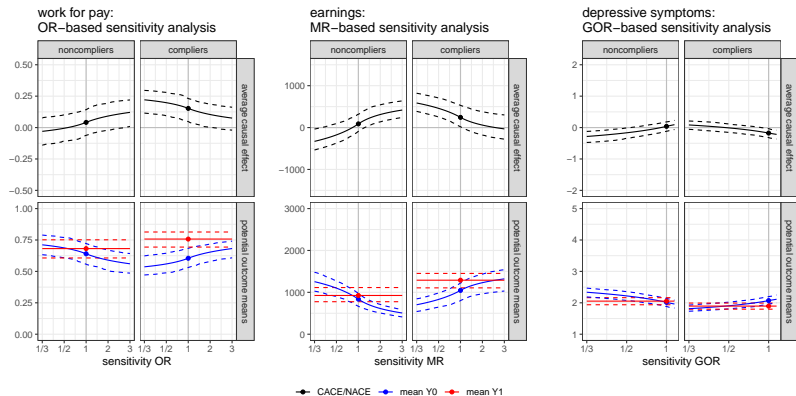
Only A4-MR provides for a simple modification of type C estimators: scale  $Y$  in control units by a factor of  $\frac{\rho_c}{(\rho_c - 1)\pi_c(X) + 1}$

## PI-based analysis results: point estimates (95% BCa confidence intervals)

outcome	variable type	compliers			noncompliers		
		mean $Y_1$ ( $\tau_{11}$ )	mean $Y_0$ ( $\tau_{01}^{PI}$ )	CACE ( $\Delta_1^{PI}$ )	mean $Y_1$ ( $\tau_{10}$ )	mean $Y_0$ ( $\tau_{00}^{PI}$ )	NACE ( $\Delta_0^{PI}$ )
work	binary	75.4% (69.4, 81.4)	61.1% (53.1, 68.4)	14.3 percentage points (4.7, 23.1)	68.5% (60.7, 75.2)	64.2% (55.7, 72.2)	4.3 percentage points (-6.2, 14.2)
earnings	actual range \$0-5,667	\$1,279 (1,107, 1,452)	\$1,014 (802, 1,221)	\$266 (18, 530)	\$928 (776, 1,115)	\$835 (666, 972)	\$92 (-90, 318)
depressive symptoms	scale range 1 to 5	1.90 (1.80, 1.99)	2.07 (1.96, 2.20)	-0.18 (-0.32, -0.04)	2.05 (1.94, 2.16)	2.02 (1.88, 2.14)	0.02 (-0.12, 0.18)

- ▶ for compliers, the intervention increased work and earnings, and decreased depressive symptoms
- ▶ for noncompliers, effects are close to null and non-sig

# JOBS II illustration



caution about using the MR sens param (if time permits)

## One difference-type sens param

Let  $\sigma_{0c}^2(X) := \text{var}(Y_0 | X, C = c)$  and  $\sigma_0^2(X) := \text{var}(Y_0 | X)$

A4-SMD (sens std mean difference): 
$$\frac{\mu_{01}(X) - \mu_{00}(X)}{\sqrt{(1/2)\sigma_{01}^2(X) + (1/2)\sigma_{00}^2(X)}} = \eta$$
for a range of  $\eta$  considered plausible

This assumption only partially identify  $\mu_{0c}(X)$ , so we consider supplementing it with an equal variance assumption

A4-SMDe (SMD, equal variance): A4-SMD, and  $\sigma_{01}^2(X) = \sigma_{00}^2(X)$



## Identification and estimation

Under A4-SMDe combined with A0-A2,

$$\mu_{0c}(X) = \mu_0(X) + (2c - 1) \frac{\eta \pi_{1-c}(X) \sigma_0(X)}{\sqrt{1 + \eta^2 \pi_1(X) \pi_0(X)}},$$

$$\Delta_c = \Delta_c^{\text{PI}} - (2c - 1) \eta \underbrace{\mathbb{E} \left[ \frac{\pi_1(X) \pi_0(X) \sigma_0(X)}{\sqrt{1 + \eta^2 \pi_1(X) \pi_0(X)}} \right]}_{=: \lambda} / \delta_c =: \Delta_c^{\text{SMDe}}.$$

(If don't assume equal variance, get bounds instead of point identification)

In this case, sens analysis focuses on estimating  $\Delta_c^{\text{PI}} - \Delta_c^{\text{SMDe}}$

use plug-in or IF-based estimation

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The sens assumptions so far are about the conditional means

$$\mu_{0c}(X) := E[Y_0 | X, C = c]$$

For continuous outcomes, there may be values of the sens parameter that conflict with the distribution of  $Y_0 | X$

Now we take an approach that is fully informed by this distribution

Recall the distribution version of PI

A3d:  $C \perp\!\!\!\perp Y_0 \mid X$

Want an assumption that allows  $Y_0$  and  $C$  to be dependent given  $X$  that helps identify  $\mu_{0c}(X)$

The usual exponential tilting technique if applied would relate the probability of  $C$  (given  $X, Y_0$ ) to a simple function of  $Y_0$  and the sens param

but that would not be enough to identify the components of the mixture

## 2-step construction

Let  $\tilde{\pi}_1(X, Y_0) := P(C = 1 \mid X, Y_0)$ . Use shorthand  $\tilde{\pi}_1$

Step 1: Assume a distribution for  $\tilde{\pi}_1$  given  $X$  with mean  $\pi_1(X)$  that allows  $\tilde{\pi}_1$  to vary, indexed by a dispersion param

Step 2: Connect  $Y_0$  to  $\tilde{\pi}_1$  within the confines of that distribution to induce  $Y_0$ - $C$  association

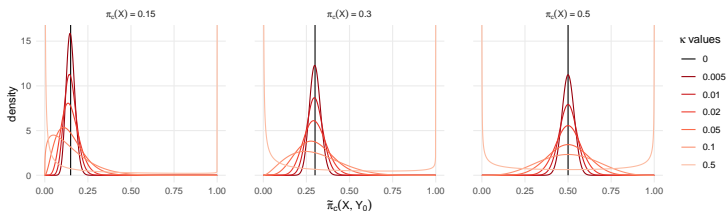
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- ▶ borrow Victor Veitch's idea of using the beta distribution<sup>[4]</sup>

$$\text{Beta} \left( \pi_1(X) \frac{1 - \kappa}{\kappa}, \pi_0(X) \frac{1 - \kappa}{\kappa} \right)$$



[4] Victor Veitch and Anisha Zaveri. "Sense and Sensitivity Analysis: Simple Post-Hoc Analysis of Bias Due to Unobserved Confounding". In: (2020). arxiv: 2003.01747. arXiv: 2003.01747.

## 2-step construction

Let  $\tilde{\pi}_1(X, Y_0) := P(C = 1 \mid X, Y_0)$ . Use shorthand  $\tilde{\pi}_1$

Step 1: Assume a distribution for  $\tilde{\pi}_1$  given  $X$  with mean  $\pi_1(X)$  that allows  $\tilde{\pi}_1$  to vary, indexed by a dispersion param

- ▶ borrow Victor Veitch's idea of using the beta distribution

$$\text{Beta} \left( \pi_1(X) \frac{1 - \kappa}{\kappa}, \pi_0(X) \frac{1 - \kappa}{\kappa} \right)$$

Step 2: Connect  $Y_0$  to  $\tilde{\pi}_1$  within the confines of that distribution to induce  $Y_0$ - $C$  association

- ▶ use quantile-to-quantile mapping
  - ▶ either same-quantiles or opposite-quantiles

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A5 (sens beta quantile):

$$B_{X, \kappa}(\tilde{\pi}_1) = \begin{cases} F_{Y_0|X}(Y_0) & \text{if assume positive } Y_0\text{-}C \text{ association} \\ 1 - F_{Y_0|X}(Y_0) & \text{if assume negative } Y_0\text{-}C \text{ association} \end{cases}$$



## Identification and estimation

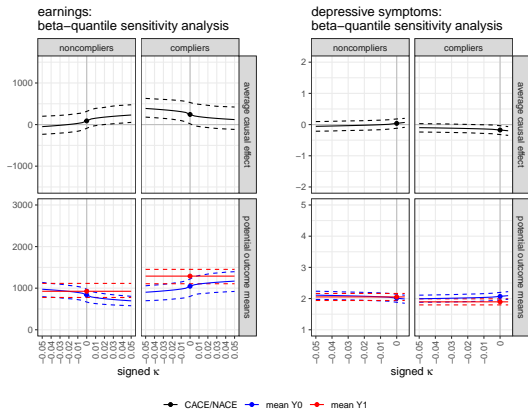
Under A5 combined with A0-A2,

$$\mu_{0c}(X) = \frac{E[\tilde{\pi}_c Y \mid X, Z = 0]}{E[\tilde{\pi}_c \mid X, Z = 0]},$$

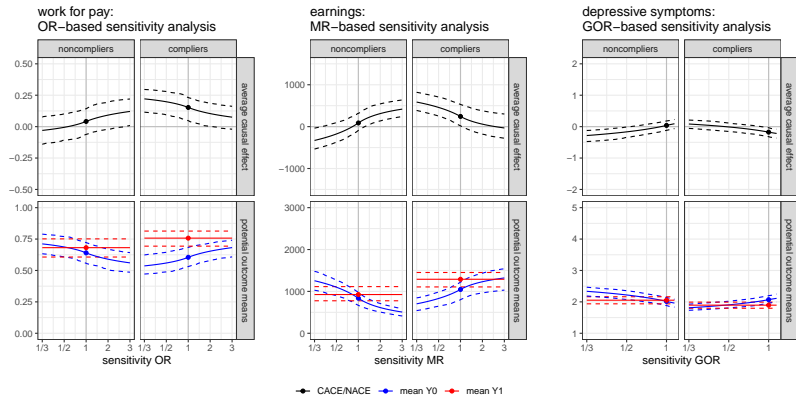
where  $\tilde{\pi}_c$  and  $Y$  are quantile-to-quantile connected

We estimate  $P(Y \mid X, Z = 0)$  and then estimate  $\mu_{0c}(X)$  using numerical integration

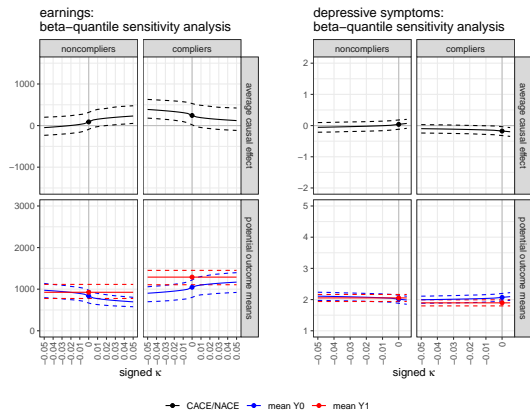
# JOBS II illustration



# JOBS II illustration



# JOBS II illustration



Results are less extreme than mean-based sens analysis

# Outline

Principal stratification

Identification and Principal ignorability

Organizing themes for this work

Mean-based sens analysis: three ratio-type and one difference-type sens params

Distribution-based sens analysis: a quantile mapping method

Conclusion

We have expanded solutions for sensitivity analysis for IV violation in estimating complier and noncomplier average causal effects

THANK YOU!