# Marginal Structural Models
## for Estimating the Effects of Chronic Community Violence Exposure on Aggression & Depression


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*Carnegie Mellon University, Department of Statistics*


Modern Modeling Methods Conference

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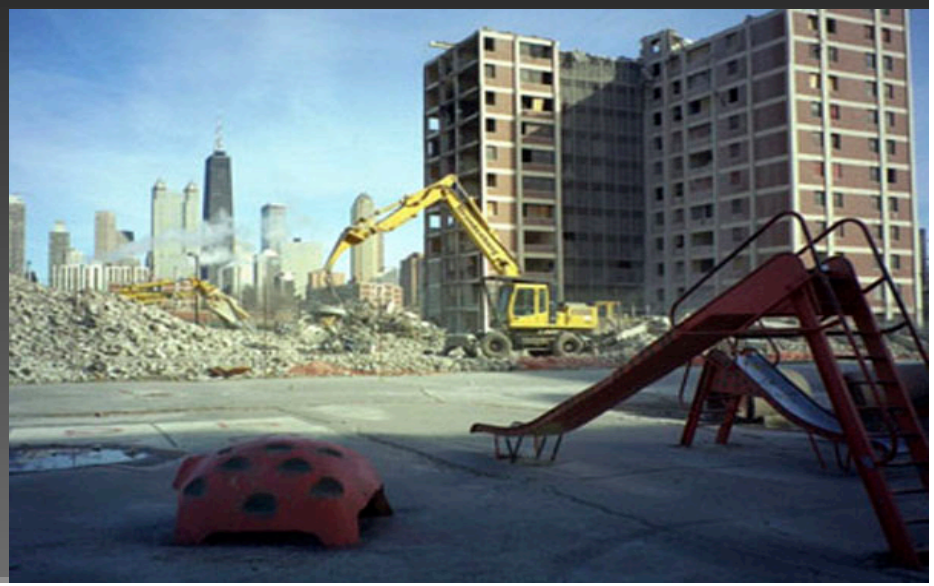
# Today's Talk

1. Community violence exposure
2. Causal inference & marginal structural models (MSM)
3. Application
4. Results
5. Discussion
6. Resources

# Community Violence Exposure & Youth Mental Health

- High prevalence of youth CVE in U.S. cities
- Range of outcomes
  - Internalizing symptoms
    - Depression, anxiety, PTSD
  - Externalizing symptoms
    - Aggression, delinquency



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  - Linear
  - Supported in literature
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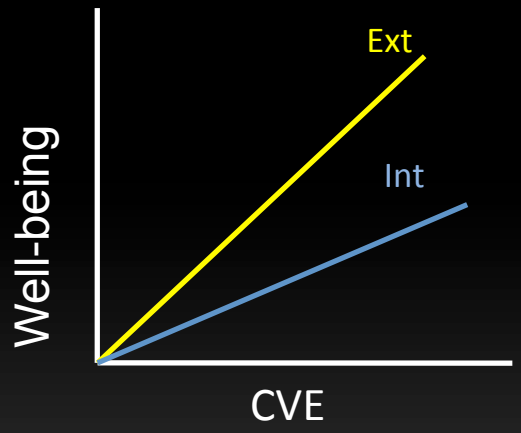

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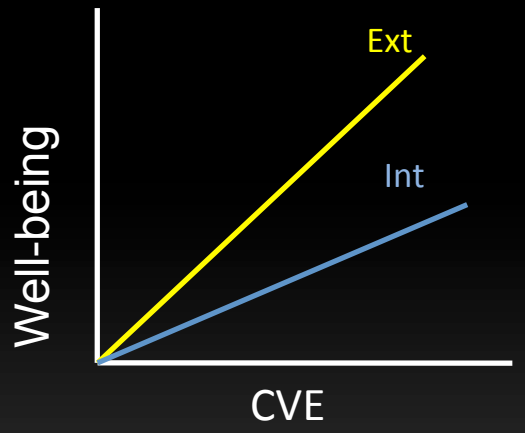


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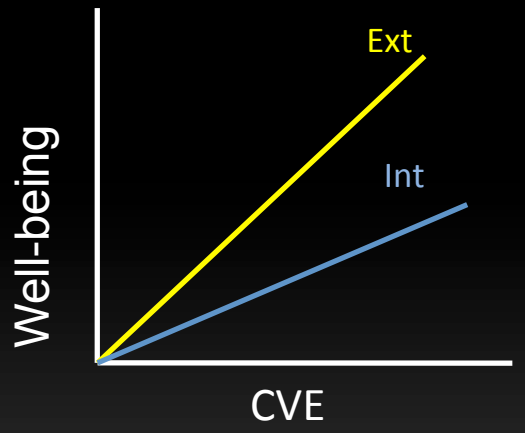


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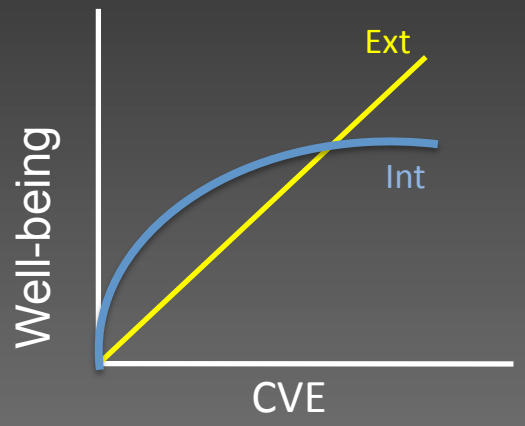

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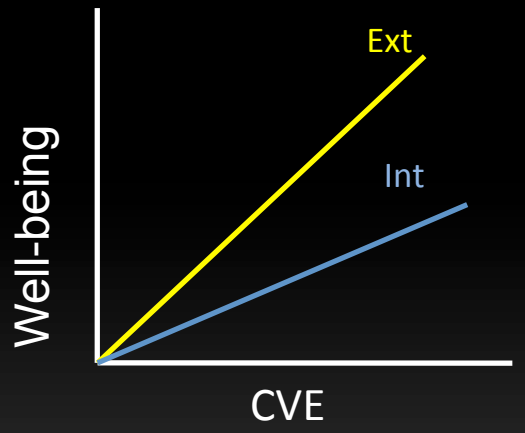


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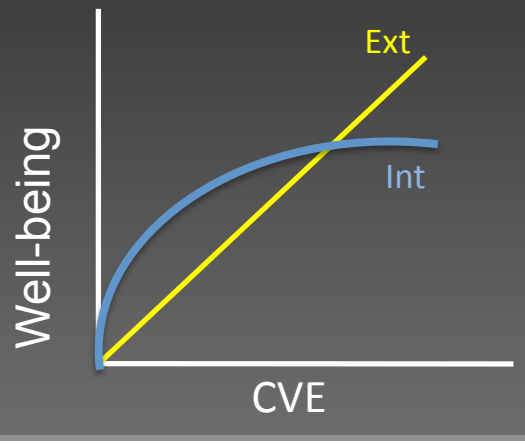
  - "pathologic adaptation"



# Community Violence Exposure & Causal Inference

- Associations
  - CVE → symptoms
  - Observational
  - Correlation ≠ Causation

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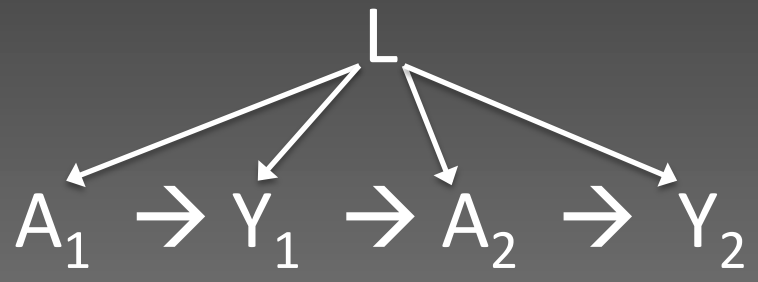

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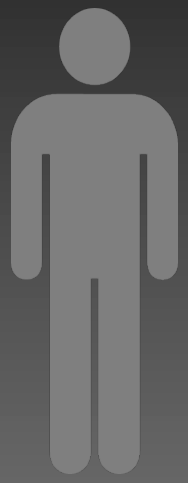

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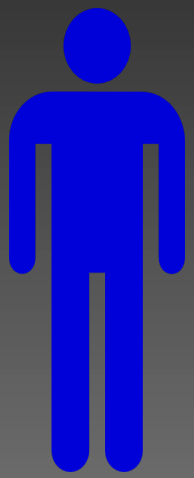

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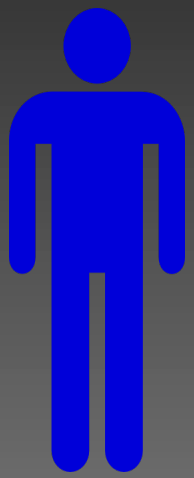

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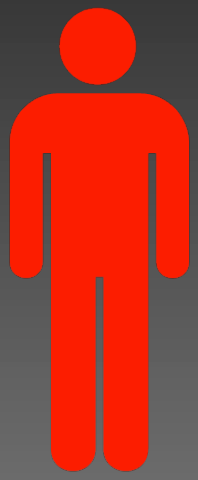

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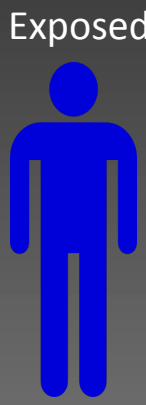


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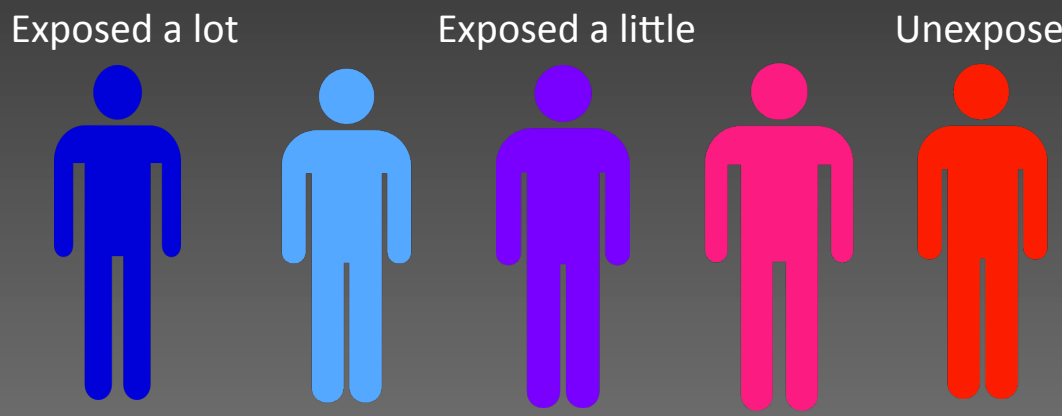

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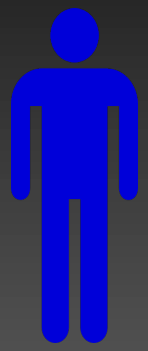
Exposed a lot



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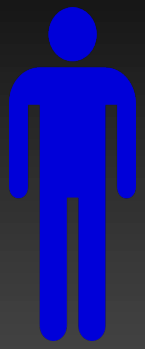
  - But  may be different from  in many ways…

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- Potential outcomes ($Y^a$)
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  - … which may instead/also explain why they differ on the outcome (e.g., mental health)

# Community Violence Exposure & Causal Inference

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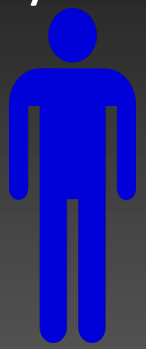
    - e.g., exposed to a specific level of violence
  - We only know what an individual's mental health looks like under  which may be the same or different under 

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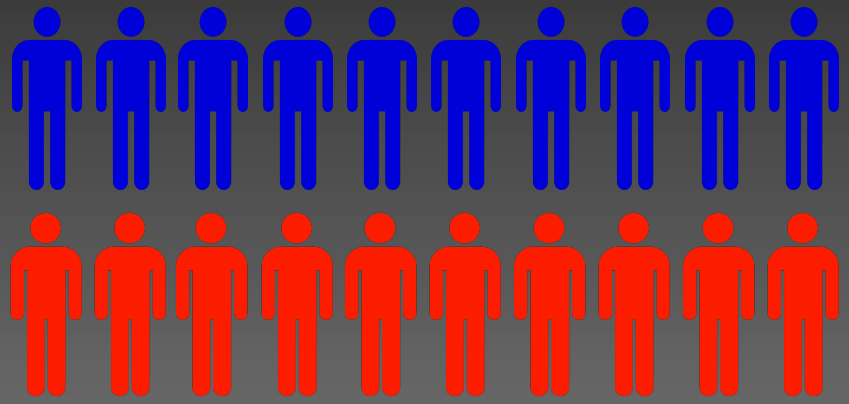
  - On average, everyone identical except exposure



# Community Violence Exposure & Causal Inference

- Randomization
  - Not feasible/ethical

# Community Violence Exposure & Causal Inference

- How we usually try to approximate causal effects in observational studies
  - Longitudinal data
    - Measure "baseline" levels of outcomes
      - E.g., aggression
    - Adjust for covariates in regression
      - E.g., baseline aggression, SES, age, neighborhood
    - **Problem:** Exposure and outcome vary over time
      - Adjusting for baseline aggression may "adjust away" true effect of violence exposure along the causal pathway

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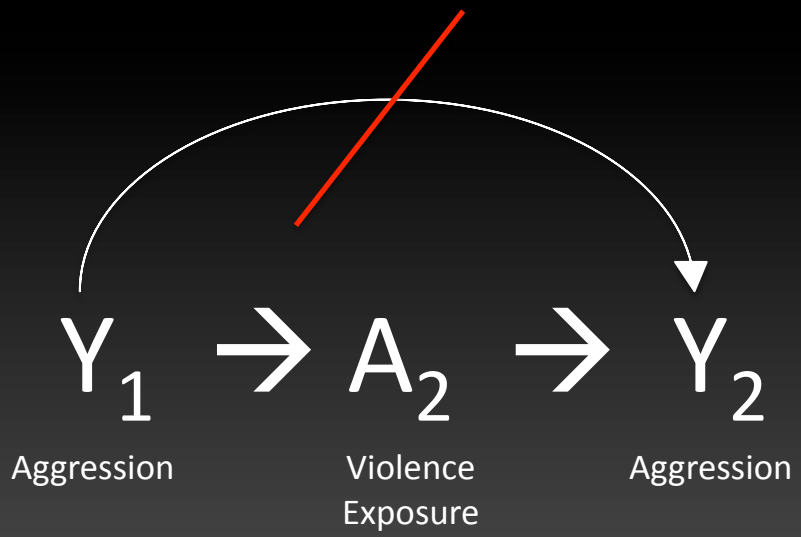

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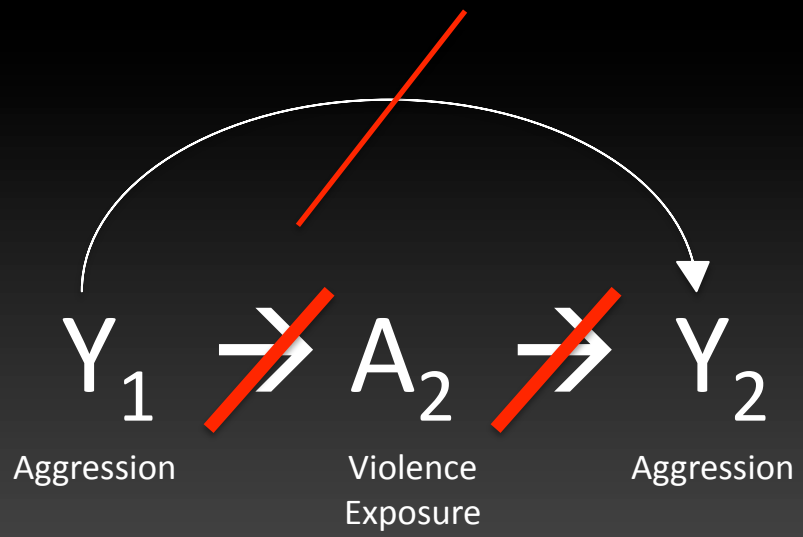

# Marginal Structural Models (MSM)

- Simulate the actual *and* potential outcomes (counterfactural) using observational data

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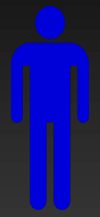
  -  kids have 25% chance of being nonaggressive if exposed to violence, & 50% if unexposed

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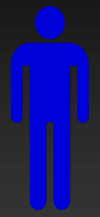
  -  kids have 25% chance of being nonaggressive if exposed to violence, & 50% if unexposed
  - (binary exposure for now, for simplicity)

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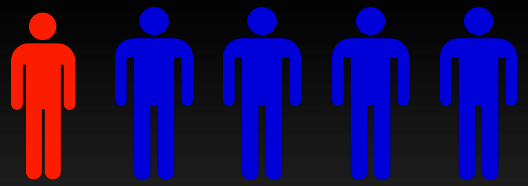

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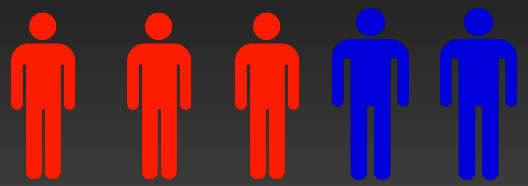

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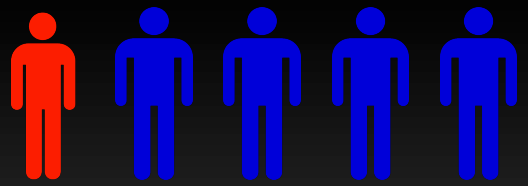

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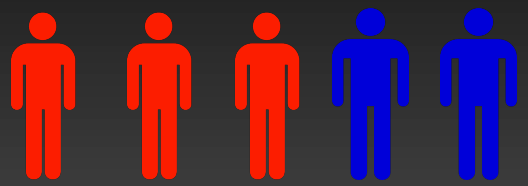

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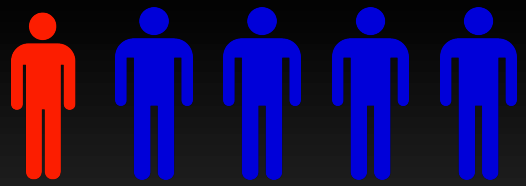

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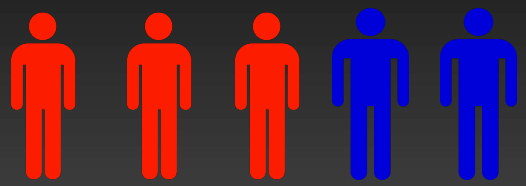

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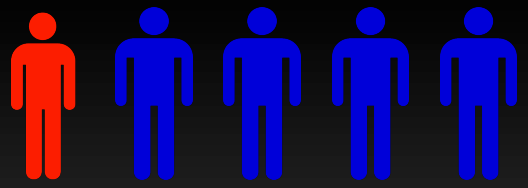
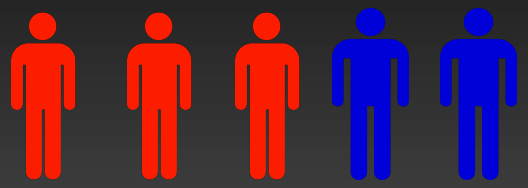
**Exposed**: 

**Unexposed**: 

- Exposure is clearly harmful
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  - If NONE were exposed, (6/10)0.5 = 30% would be nonaggressive

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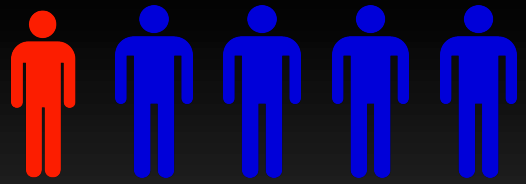

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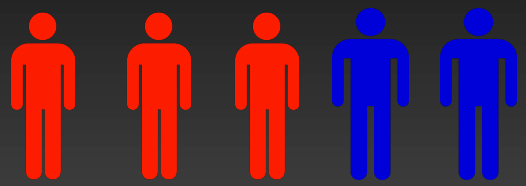

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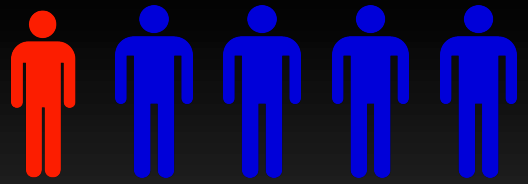

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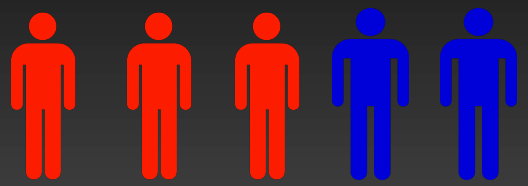

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  - Looks like exposure has **no effect** !

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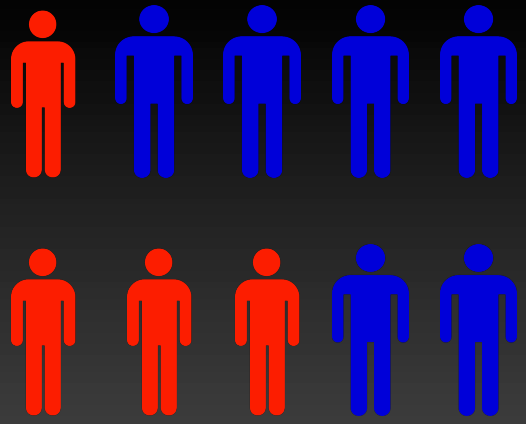

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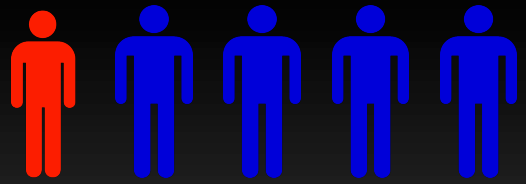

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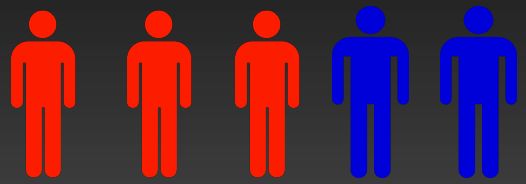

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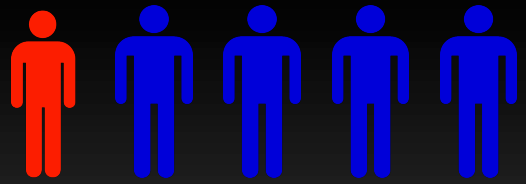

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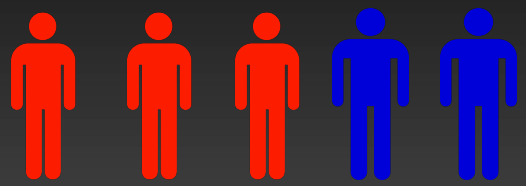


*pr*(exposed |  = 4/6

*pr*(exposed |  = 1/4

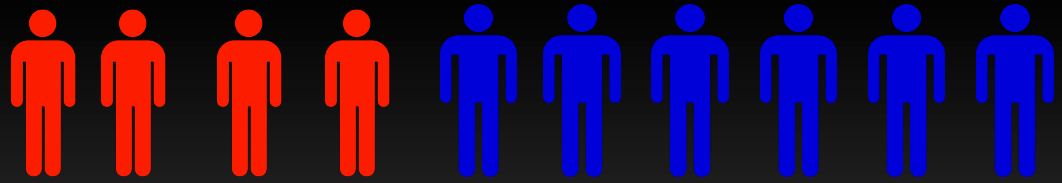
*pr*(unexposed |  = 2/6

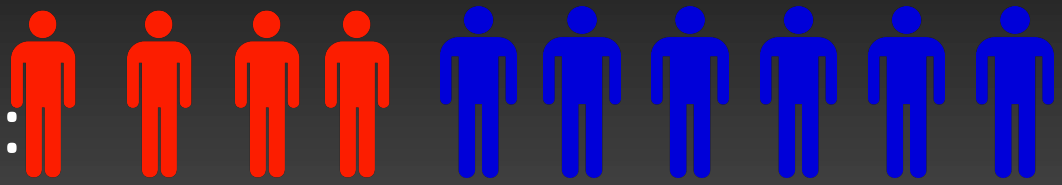
*pr*(unexposed |  = 3/4

Now we can create a **pseudo-population** by weighting each kid by the *inverse probability* of receiving their observed treatment (Robins et al., 2000)

# Marginal Structural Models (MSM)

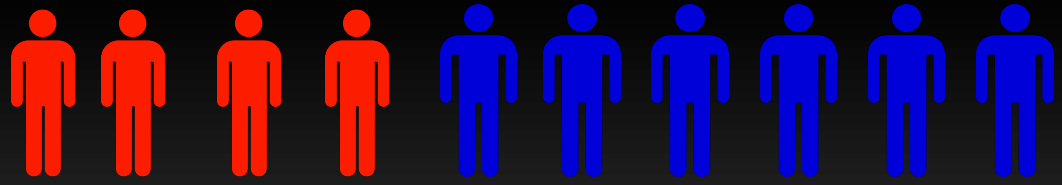
- **Pseudo**-population:

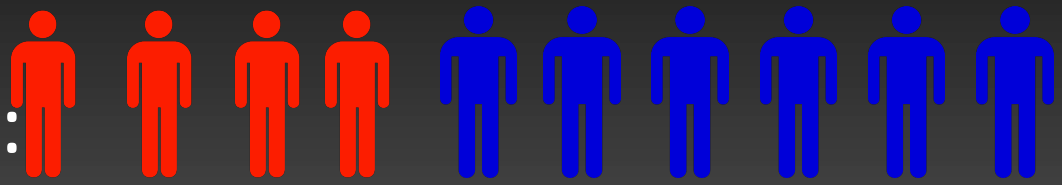
Exposed*: 

Unexposed*: 

# Marginal Structural Models (MSM)

- **Pseudo**-population:

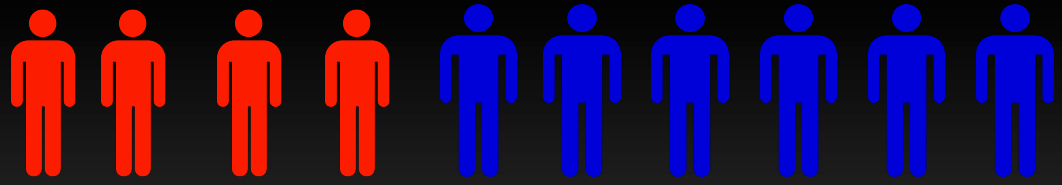
Exposed*: 

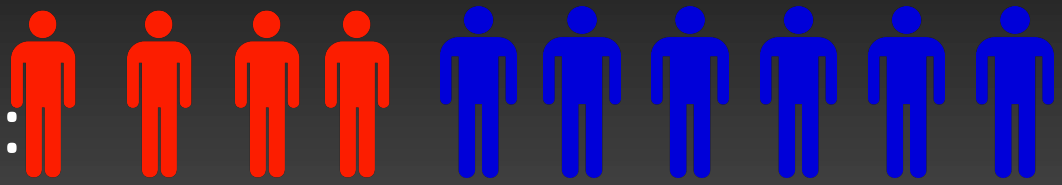
Unexposed*: 

*Down* weight those who are *over*-represented in population, & *up* weight the *under*-represented

# Marginal Structural Models (MSM)

- **Pseudo**-population:

Exposed*: 

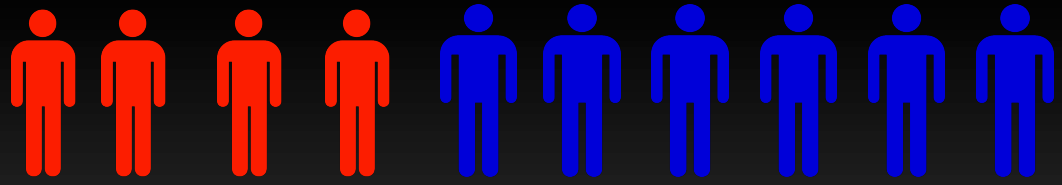
Unexposed*: 

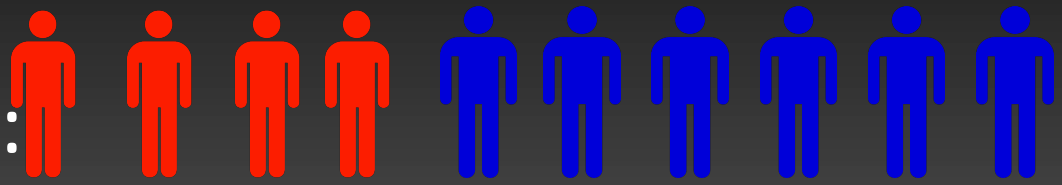
In the pseudo-population:

- 6/10(.25) = 15% of exposed were nonaggressive
- 6/10(.5) = 30% of unexposed were nonaggressive

# Marginal Structural Models (MSM)

- **Pseudo**-population:

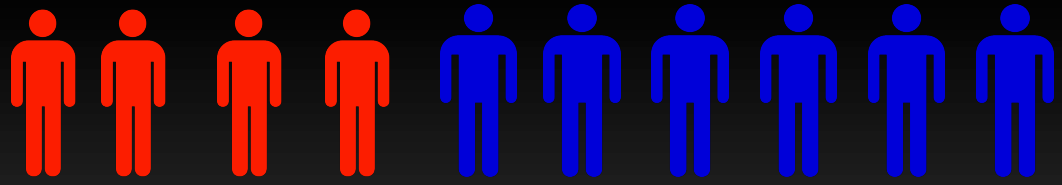
Exposed*: 

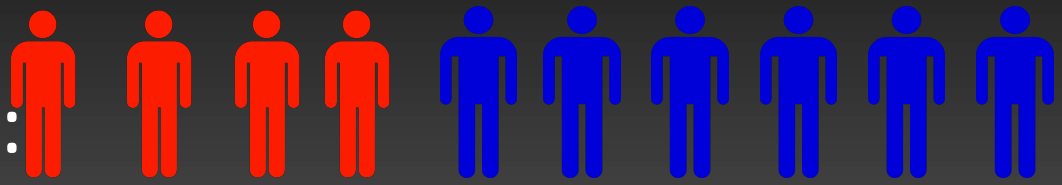
Unexposed*: 

- Matches the counterfactual numbers!

# Marginal Structural Models (MSM)

- **Pseudo**-population:

Exposed*: 

Unexposed*: 

- Matches the counterfactual numbers!
- Same as randomization

# Marginal Structural Models (MSM)

- Weighting = creating a pseudo-population where:

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$$A_2 \rightarrow Y_2$$

Violence Exposure

Aggression

# Marginal Structural Models (MSM)

- Weighting = creating a pseudo-population where:
  - The covariate distribution is the same as in the population
  - There is no association between treatment & covariates
  - Thus, no confounding
    - **Causal** effects can be estimated without additional adjustment

$$A_2 \rightarrow Y_2$$

Violence Exposure — Aggression

# Marginal Structural Models (MSM)

- Time-varying extension of propensity score weighting

# How to Apply MSM

1. Fit propensity score model of probability of exposure
2. Do a weighted regression (using the IPWs)

# Assumptions

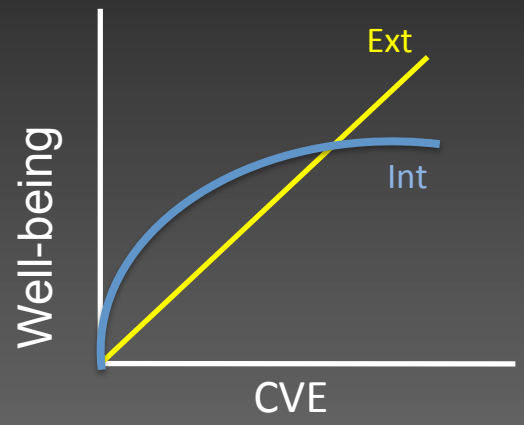
1. Consistency: $Y = Y^a$ when $A = a$
   - We observe the outcome that a given level of exposure causes when we observe that exposure
2. Positivity: $pr(A = a \mid L = l) > 0$
   - There must exist a positive probability of all exposure levels for all strata of covariates
   - No one may have 0 probability of exposure
3. Ignorability: No unmeasured confounding

# Results

- Does community violence exposure differentially affect youths' mental health?

# Results

- Does community violence exposure differentially affect youths' mental health?
  - Desensitization hypothesis:
    - Quadratic effect on *internalizing* symptoms
    - Linear effect on *externalizing* symptoms



# Results

- **Data**
  - Project on Human Development in Chicago Neighborhoods (PHDCN)

(Earls, Brooks-Gunn, Raudenbush, & Sampson, 1994-2002)

  - Longitudinal Cohort Study
  - Youth & primary caregiver
  - Stratified probability sample: N = 4,149
  - Waves 2 & 3
  - Cohort ages at Wave 2: 6, 9, 12, 15, 18
  - Representative sample

# Results

- **Measures**
  - Baseline demographic covariates
    - Age, sex, race, income, SES
  - Community violence exposure (CVE)
    - My Exposure to Violence
    - Past year CVE frequency on 20 items
    - Witnessing & victimization
  - Mental health
    - CBCL Internalizing & Externalizing
      - Controlled for prior levels in GEE models

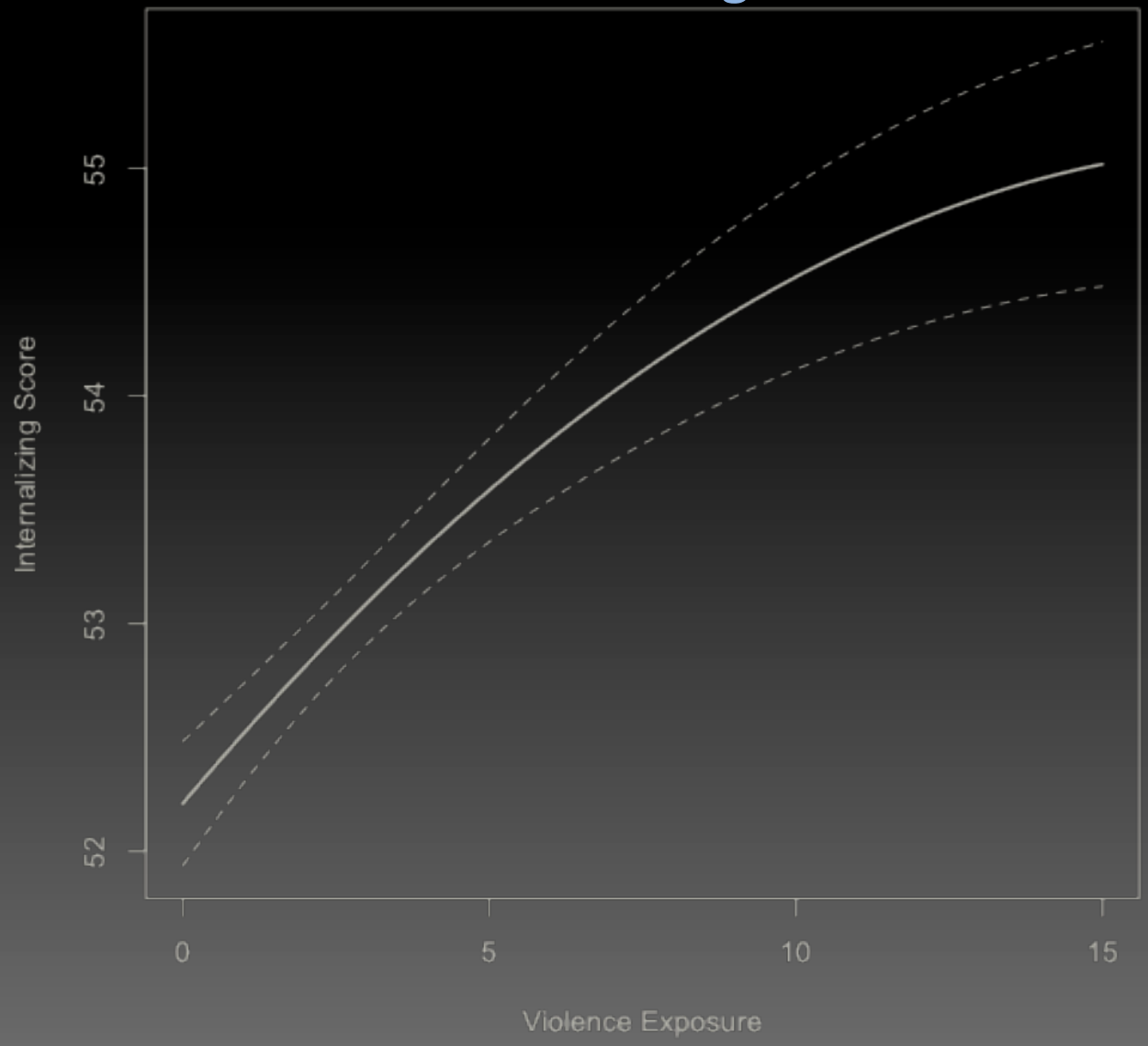
# Results

- GEE & MSM
- $CVE_2 \rightarrow agg_2$ & $CVE_3 \rightarrow agg_3$
- Baseline covariates & prior aggression
- Conditional *densities* instead of probabilities for continuous exposure (CVE)

# Results: GEE

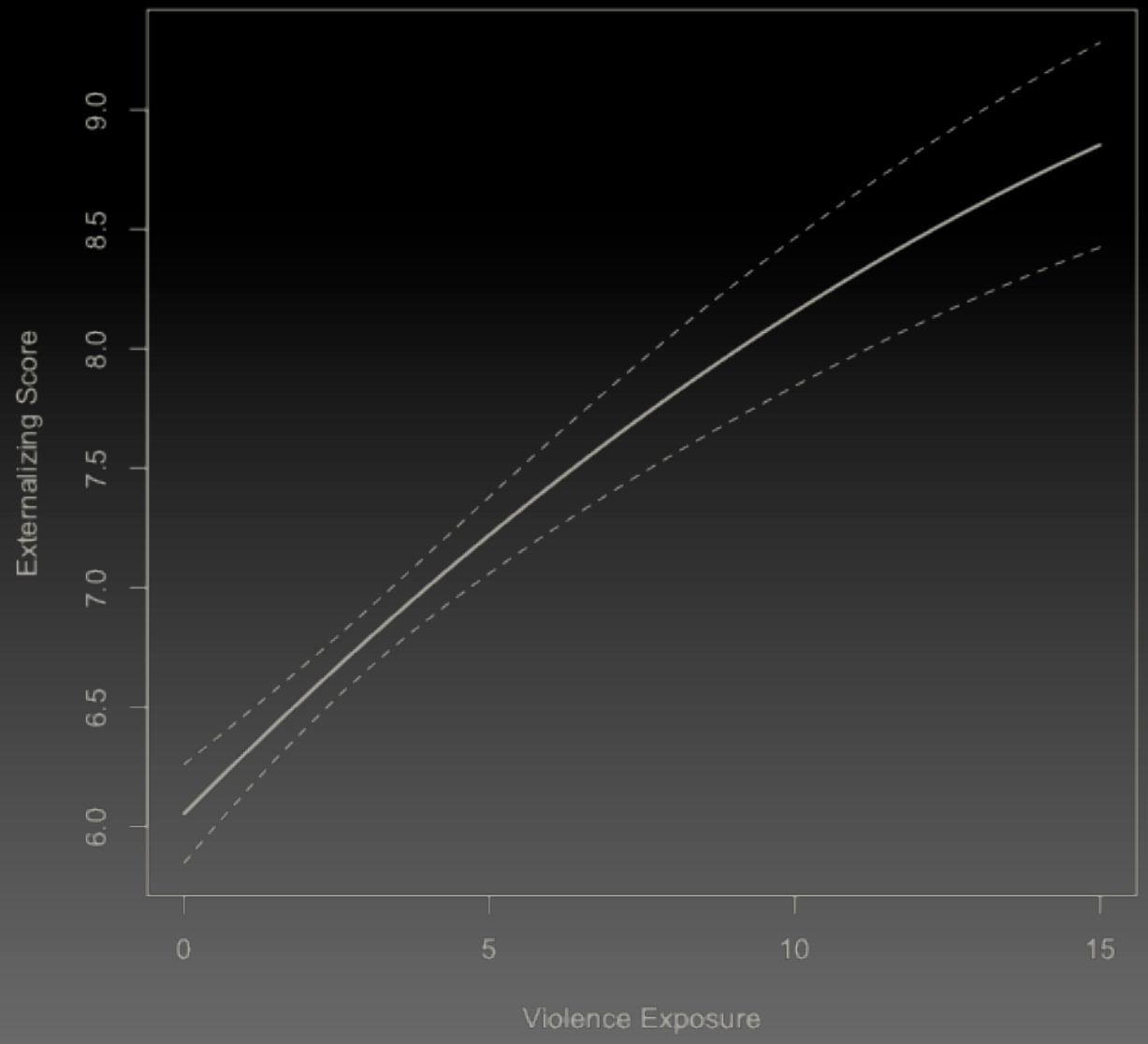
# Results: GEE

## Internalizing



# Results: GEE

## Externalizing



# Results: MSM

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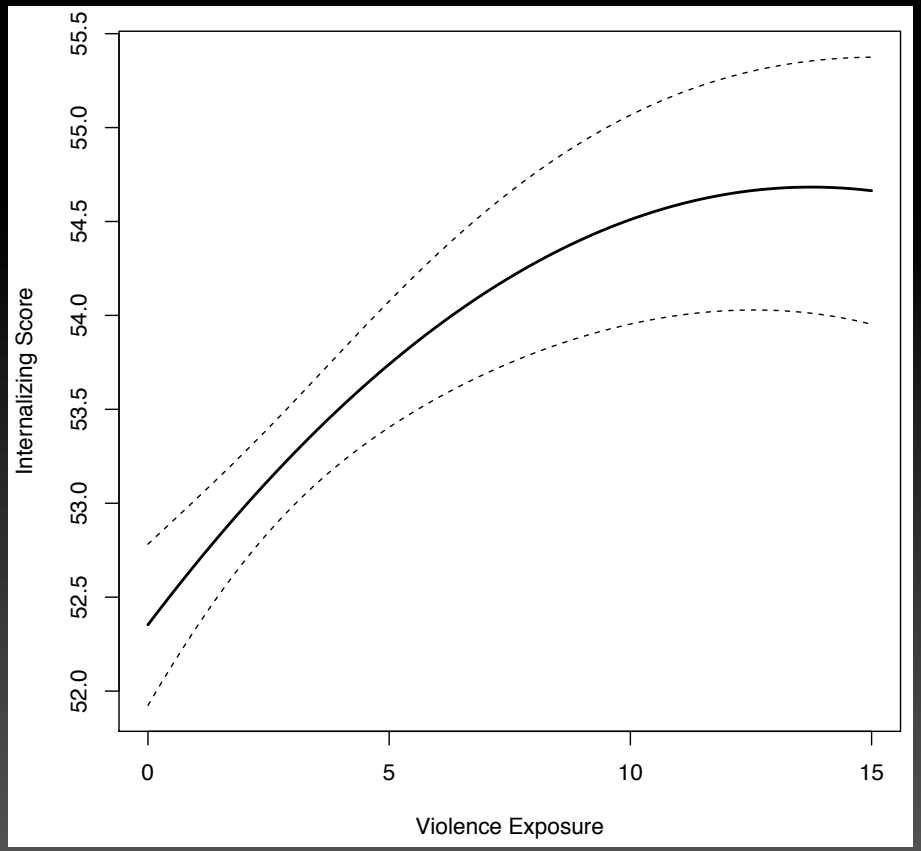
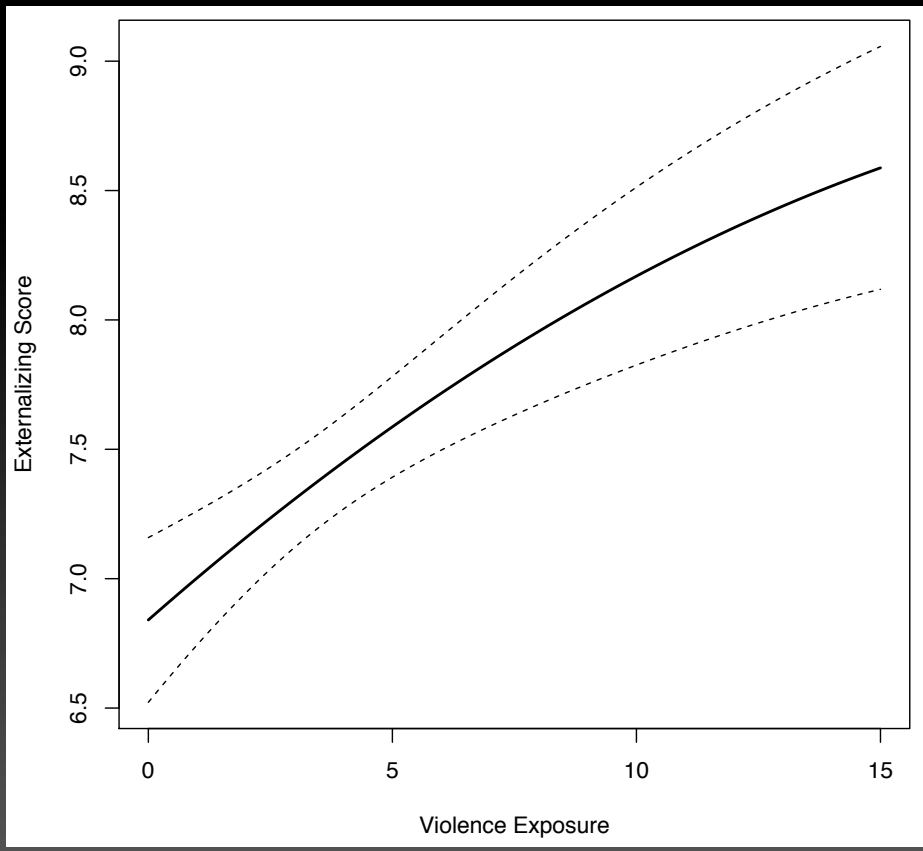
## Internalizing




## Externalizing



# Conclusions

- Desensitization effect of CVE
  - Pathologic adaptation?
- Similar, but slightly *weaker* effects using MSM
  - Sometimes effect disappears, or reverses direction
- More accurate causal effect of CVE
- Intervention implications
  - Everyone exposed vs everyone unexposed

- (Interactions were ns)

# Limitations

- Model specification
  - More flexibility (splines) probably needed
- CVE measurement
  - Retrospective report
  - Ordinal coding
  - Time between assessments

# Limitations

- MSM assumptions
  - Likely unmeasured confounding
    - E.g., parenting, school attendance, etc.
  - Positivity
    - May be youth with zero probability of CVE

# MSM Tips

- Specify question precisely to operationalize & isolate causal effect of interest
  - RCT framework
    - E.g.:
      - Who *exactly* are the subjects?
      - What *exactly* is the treatment?
      - For *exactly* how long are they treated?

# MSM Tips

- Avoid unmeasured confounding
  - Measure all possible confounders
    - Fancy statistics cannot fix bad designs
  - Sensitivity analysis
    - VanderWeele (2010) Bias formulas for sensitivity analysis for direct and indirect effects, *Epidemiology, 21*, 540-551
    - Brumback et al (2004) Sensitivity analyses for unmeasured confounding assuming a marginal structural model for repeated measures, *Statistics in Medicine, 23*(5), 749-767

# MSM Tips

- Use stabilized weights
  - Inverse probabilities become unwieldy
  - Incorporate baseline covariates to stabilize
  - Robins et al (2000) Marginal structural models and causal inference in epidemiology, *Epidemiology, 11*, 550-560

# MSM Extensions

- Although MSMs often use IPW, other approaches to estimate MSM parameters:
  - Regression-based g-computation
  - Doubly robust estimating equations
  - Targeted maximum likelihood (TMLE)

# MSM Extensions

- MLM, growth curve modeling, SEM, etc.
  - Simply apply IPW weights
- Mediation (e.g., Coffman & Zhong, 2012; VanderWeele)
- Additional time points
- Compounded effects over time
  - E.g., effects of $CVE_2$ & $CVE_3$ on agg3
- Effect of *removing* vs adding exposure
- Incremental interventions (Kennedy, under review)
  - More realistic intervention implications

# Applications

- Typically medicine & epidemiology
  - E.g., HIV treatment
- Expand to psychology & social sciences
  - Time-dependent confounding & reciprocal effects
  - E.g.:
    - Mental health treatment
    - Bullying
    - ADHD stimulant medications
    - RCTs with noncompliance

# Concluding Thoughts

- Use MSMs!
- R, SAS, & Stata

# References & Resources

- **Conceptual**
  - Robins & Hernán book draft: https://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/
  - Robins et al (2000) – *Epidemiology*
  - Robins & Hernán (2009) – Chapter 1 in *Longitudinal Data Analysis*
  - Faries & Kadziola chapter: Analysis of longitudinal observational data using marginal structural models
  - VanderWeele (2009) – *Epidemiology*
    - Mediation
  - Kennedy (under review) Nonparametric causal effects based on incremental propensity score interventions

    https://arxiv.org/abs/1704.00211

# References & Resources

- **Applied**
  - Bacak & Kennedy (2015) – *J. of Marriage and Family*
    - Marriage & recidivism
  - Hernán et al (2002) – *Statistics in Medicine*
    - HIV treatment effectiveness
  - Patel et al (2008) – *Clinical Infectious Diseases*
    - Pediatric HIV treatment effectiveness
  - VanderWeele et al (2011) – *JCCP*
    - Loneliness & depression
  - VanderWeele et al (2016) – *Soc Psychiatry & Psychiatr Epidem*
    - Religion & mental health

# References & Resources

- **Software**
  - **R**
    - Bacak & Kennedy (2015) – *J. of Marriage and Family*
    - Coffman & Zhong (2012) – *Psychological Methods*
    - Moerkerke et al (2015) – *Psychological Methods*
      - Mediation
  - **SAS**
    - Faries & Kadziola chapter: Analysis of longitudinal observational data using marginal structural models
    - Crowson et al (2013) The basics of propensity scoring and marginal structural models
  - **SAS, Stata, & R**
    - Robins & Hernán book draft

# Conferences & Workshops

- Penn Causal Inference & Big Data Summer Institute
  July 24-27, 2017 – Edward Kennedy
  http://www.med.upenn.edu/cbd/
- Causal Inference Methods for PCOR using Observational Data (CIMPOD) – NIH
  http://cimpod2017.org/
- Atlantic Causal Inference Conference
  May 2018 – Carnegie Mellon University
  http://causal.unc.edu/acic2017/
- Statistical Horizons – Causal Mediation Analysis
  October 13-14, 2017 – Tyler Vanderweele
  https://statisticalhorizons.com/seminars/public-seminars

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(PI: Brooke S. G. Molina)

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