Realistic policies on influenza vaccination and risk of subsequent influenza among university students: application of targeted maximum likelihood with interference

Paul Zivich

Department of Epidemiology

UNC | GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH

Acknowledgements[1]

- Supported by T32-HD091058, T32-AI007001

- Special thanks to my dissertation committee: Allison Aiello (chair), M. Alan Brookhart, Michael Hudgens, James Moody, David Weber

pzivich@unc.edu

pzivich

[1] Footnotes are reserved for asides or references

Defining Vaccine Effectiveness (VE)

Potential outcomes

$$Y_i(\boldsymbol{v}) = Y_i(v_i, v_{-i})$$

where $\boldsymbol{v} = (v_1, v_2, \dots, v_i, \dots, v_n)$

Under no interference

$$Y_i(v_i, v_{-i}) = Y_i(v_i)$$

Vaccine effectiveness (VE)

- Direct or unit-specific VE
  - Common in both randomized and observational studies[2]

$$\frac{1}{n}\sum_{i}^{n} Y_i(1, v_{-i}) - Y_i(0, v_{-i})$$

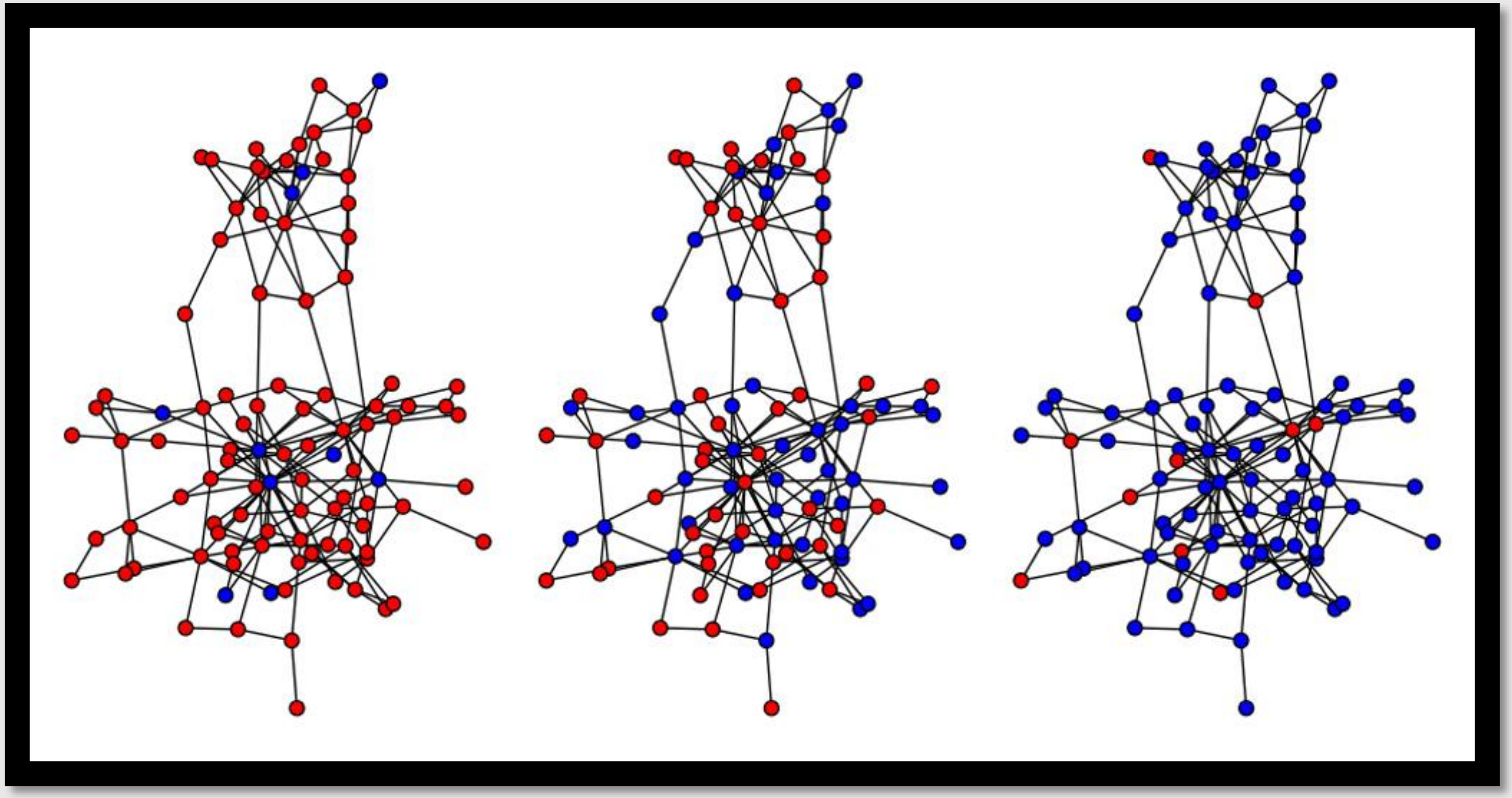
- “What is the expected risk of changing a single person’s vaccination status, holding the vaccination status of the remainder of the population as constant?”

[2] Patterns of vaccination in observational data can lead to a form of confounding, see Zivich et al. (2021) *Am J Epidemiol* for details and simulations

Alternative definition of VE

- Instead, estimate the risk under varying vaccination distributions

$$\frac{1}{n}\sum_{i}^{n} Y_i(\boldsymbol{v}')$$



Application

Motivating question

Importance of university students

1. Elevated risk of influenza
2. Low vaccination rates
3. Negative impacts on well-being
4. Importance for subsequent transmission

What is the 10-week risk of influenza under different distributions of influenza vaccination (policies)?

- Policies shift the log-odds of vaccination

eX-FLU[3]

- Cluster randomized trial
  - Effect of 3-day self-isolation to mitigate transmission
  - Jan – Apr 2013
  - Midwestern university

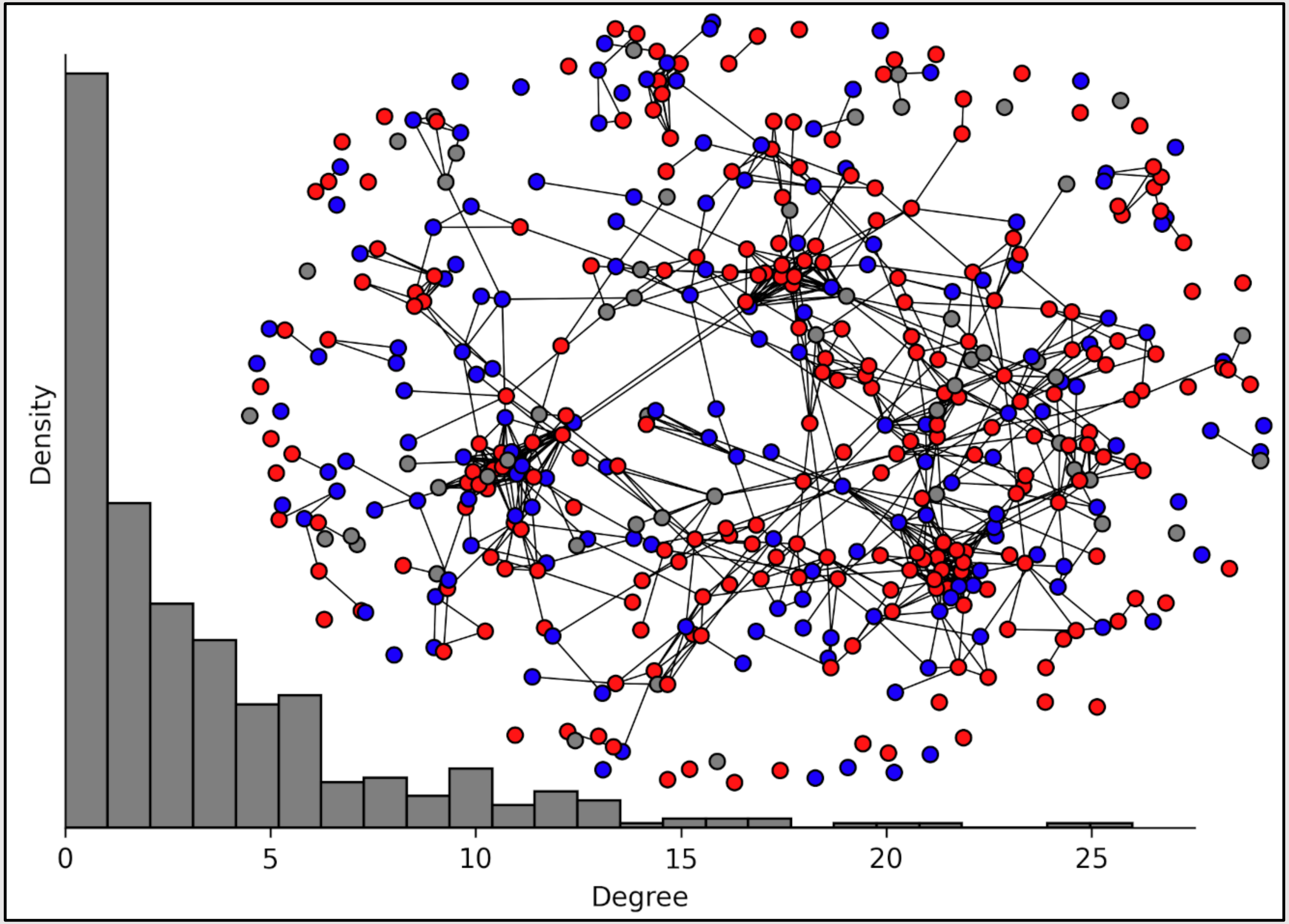
[3] Aiello et al. (2016) *Epidemics*

Covariates

- Exposure
  - Self-reported vaccination

- Outcome
  - Influenza-like illness (coughing + fever, body aches, or chills)
  - Laboratory-confirmed influenza (PCR)

- Confounders
  - Gender, race, stress, hand hygiene, high-risk conditions, sleep quality, alcohol use, assigned intervention



Density
0
5
10
15
20
25
Degree

Measurement error

Self-reported weekly contacts prone to measurement errors

Bayesian network measurement error correction[4]

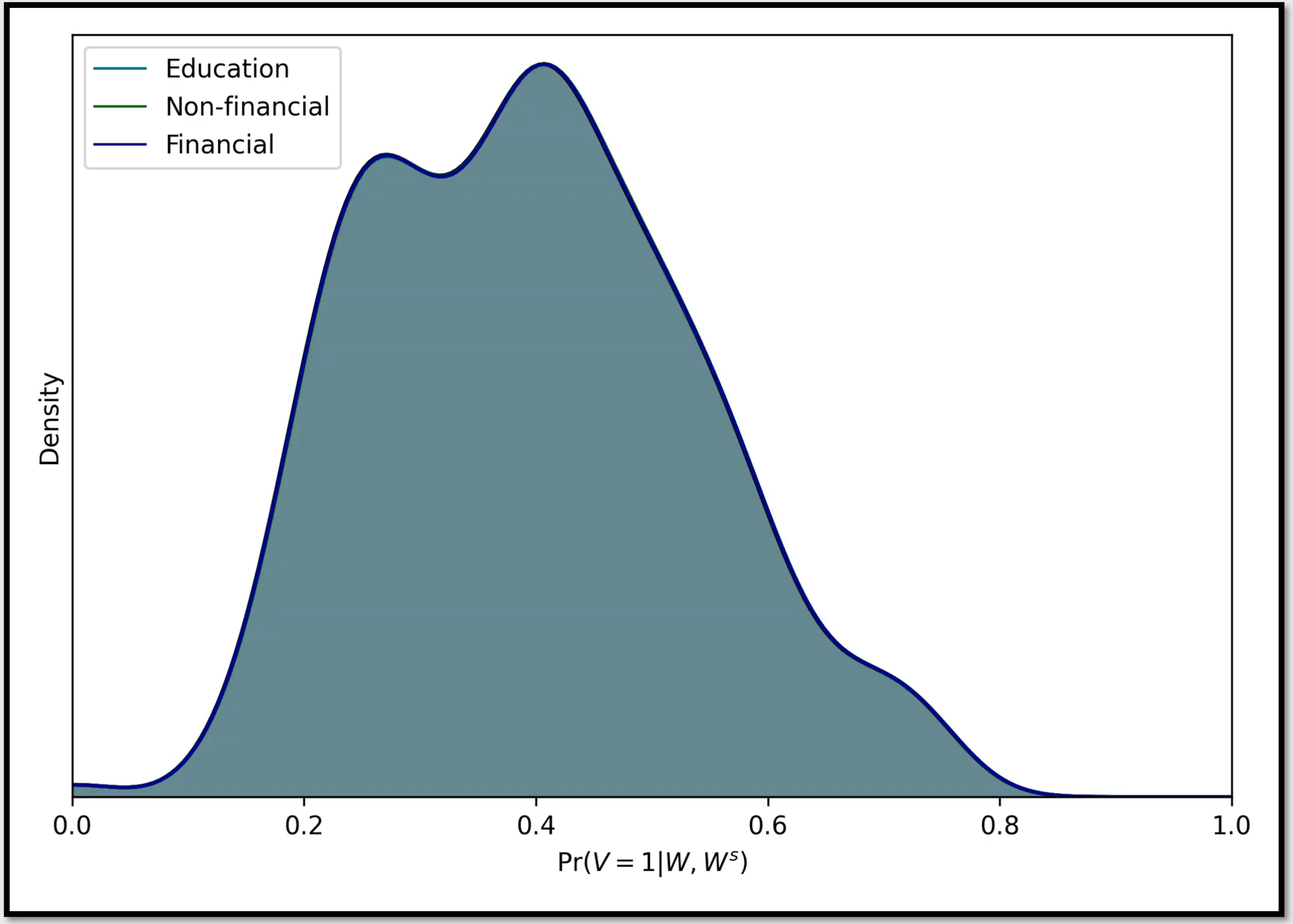
- Sensitivity and specificity
  - Subsample (n=103) had Bluetooth-collected contacts
- Estimate probability of edges between all pairs
- Multiple imputation for measurement error correction
  - Generated 100 networks

[4] Young et al. (2020) *Journal of Complex Networks*

Policies

- Three categories of policies
  - Based on self-reported reasons for unvaccinated
  1. **Educational** (dispel myths and highlight benefits)
  2. **Non-financial barriers** (ease access and availability)
  3. **Financial barriers** (reduce cost)
- Shift in log-odds of vaccination
  - Shift by ω if targeted, $\omega/3$ otherwise
  - $\omega = (0, 0.25,\ 0.50, \dots, 3)$

	Unvaccinated (n=241, 53%)
Educational	50 (21%)
Non-financial	93 (39%)
Financial	18 (8%)
Allergy	2 (1%)


Education
Non-financial
Financial
Density
0.0
0.2
0.4
0.6
0.8
1.0
Pr(V = 1|W, W^s)

Estimation

Targeted maximum likelihood estimation for network data

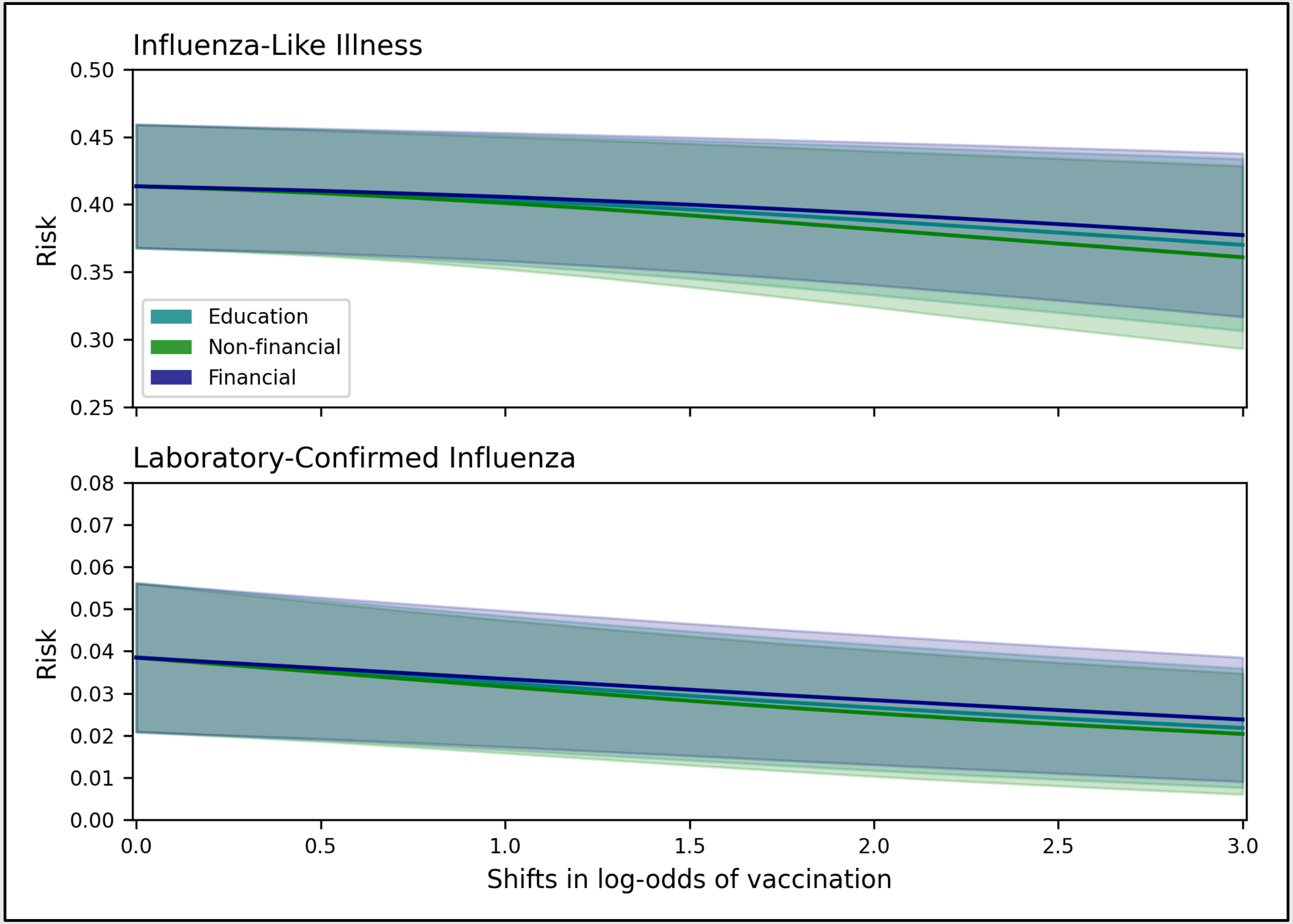
- Allows for dependence due to immediate contacts in network
  - Dependence due to vaccination and other covariates

$$Y_i(v_i, v_{-i}) \quad \rightarrow \quad Y_i(v_i, v_i^s)$$

- Estimation of outcome model and propensity scores
  - Super-learner
    - Generalized linear model, elastic-net penalty, generalized additive model

Descriptive summary

	Overall (n=454)	Vaccinated (n=161)
Influenza-like illness	190 (42%)	65 (40%)
Lab-confirmed influenza	17 (4%)	2 (1%)
Female	269 (60%)	104 (65%)
Class year		
Freshman	256 (57%)	97 (61%)
Sophomore	111 (25%)	35 (22%)
Junior	32 (7%)	12 (8%)
Senior (4+)	50 (12%)	16 (10%)



Influenza-Like Illness
0.50
0.45
0.40
0.35
0.30
0.25
Risk
Education
Non-financial
Financial
Laboratory-Confirmed Influenza
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
Risk
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Shifts in log-odds of vaccination

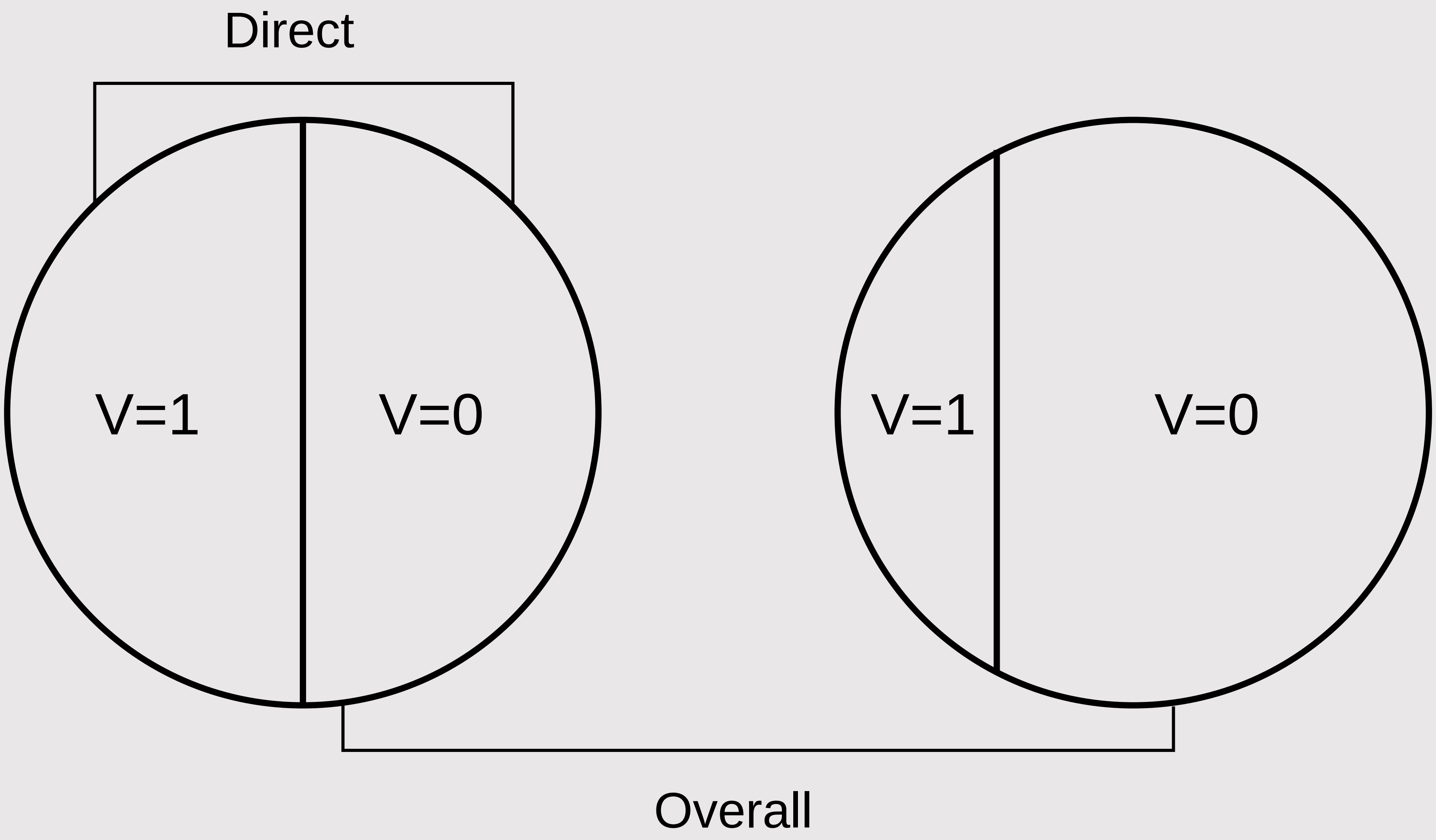
Conclusions

- General challenges to evaluating VE
  - Parameter of public health importance
    - COVID vaccination, masks, etc.
- Limitations
  - Power
  - Interference limited to immediate contacts

Realistic policies on influenza vaccination and risk of subsequent influenza among university students: application of targeted maximum likelihood with interference

Paul Zivich (pzivich@unc.edu)

UNC | GILLINGS SCHOOL OF GLOBAL PUBLIC HEALTH



Adapted from Halloran ME, Longini Jr IM, Struchiner CJ. Design and Analysis of Vaccine Studies. New York, NY: Springer; 2010