Causal Inference for Infectious Disease Prevention

Brian Richardson

Department of Biostatistics,
University of North Carolina at Chapel Hill

November 17, 2025

Scan for slides

Outline

- About Me

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- About Me
- Intro to Biostatistics

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- Intro to Biostatistics
- Intro to Causal Inference

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- About Me
- Intro to Biostatistics
- Intro to Causal Inference
- Research Project: Social Distancing to Reduce Transmission of the Flu on College Campuses

About Me

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Richmond, VA
Greensboro
Chapel Hill
Durham
Raleigh
CARRBORO
Asheville
Charlotte
Greenville
New Bern
Greenville, SC
Wilmington

About Me

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UNIVERSITY OF NORTH CAROLINA CHAPEL HILL LVX LIBERTAS

UNC CFAR Center for AIDS Research

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Bicycle Route
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STOP

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Why Biostatistics?

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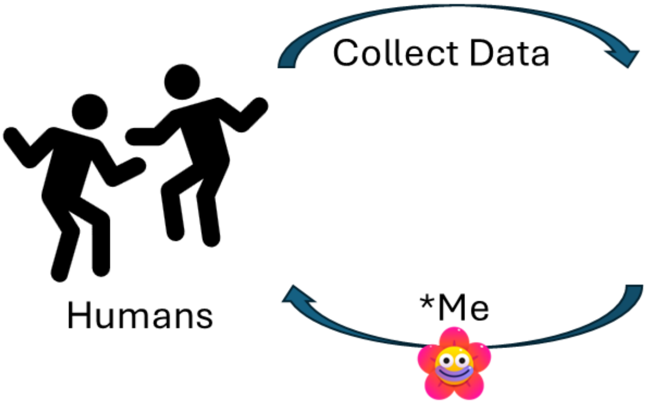
Humans

Data

X	Y	Z
0	100	H
0	50	L
1	100	H
1	120	H

Why Biostatistics?



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0	100	H
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1	100	H
1	120	H

Why Biostatistics?

Humans
(complicated)

Data

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NA	>100	L or H
NA	100	L or H
1	>100	H

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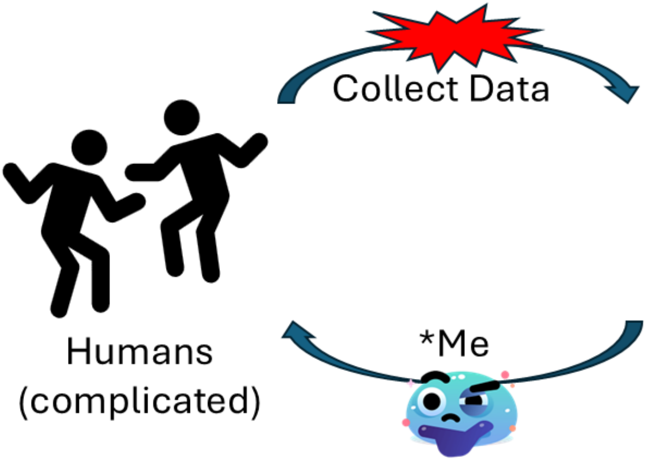

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0	100	H
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NA	100	L or H
1	>100	H

Why Biostatistics?

Collect Data

Humans
(complicated)
(and precious)

Data

X	Y	Z
0	100	H
NA	>100	L or H
NA	100	L or H
1	>100	H

*Me

Causal Inference

We are often interested in **causation**, as opposed to **association**

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- **Associational question**: Do people who get the COVID-19 vaccine get sick?

Causal Inference

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- **Associational question**: Do people who get the COVID-19 vaccine get sick?
- **Causal question**: If someone *were* to get the COVID-19 vaccine, *would* they get sick?

Associational Question

Do people who get the COVID-19 vaccine get sick?

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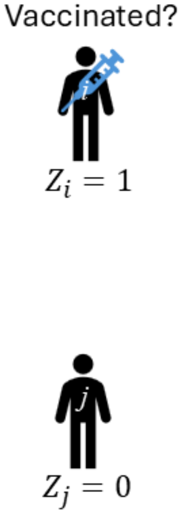

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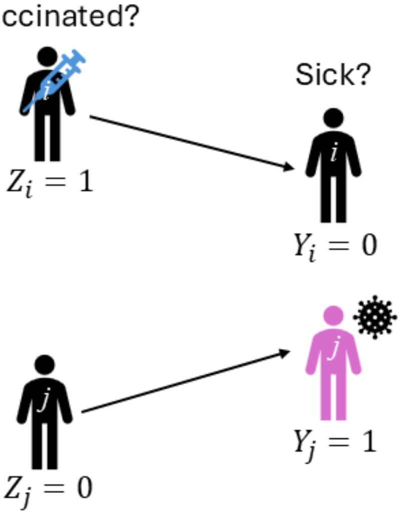

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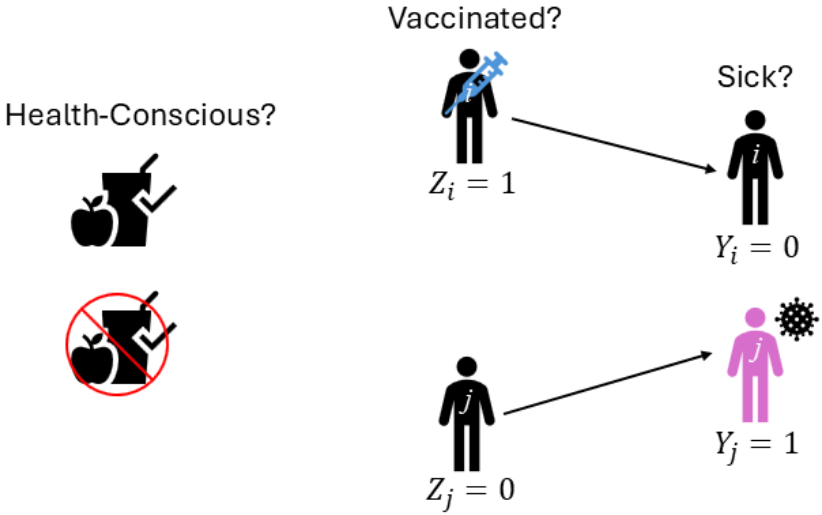

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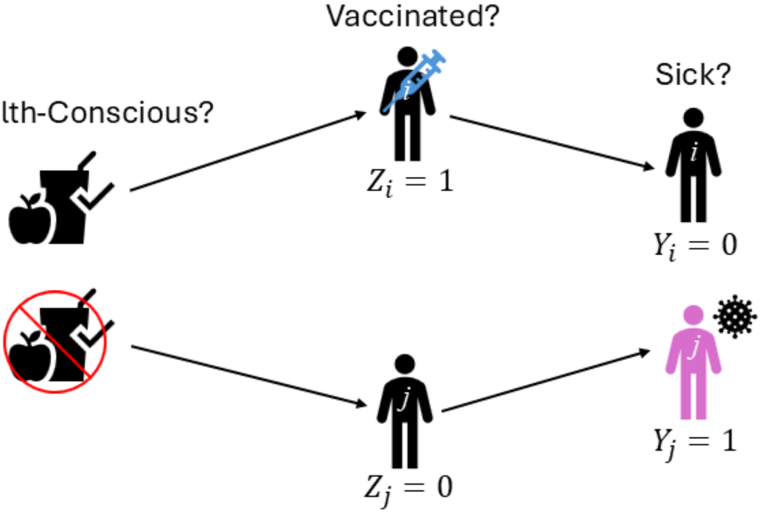

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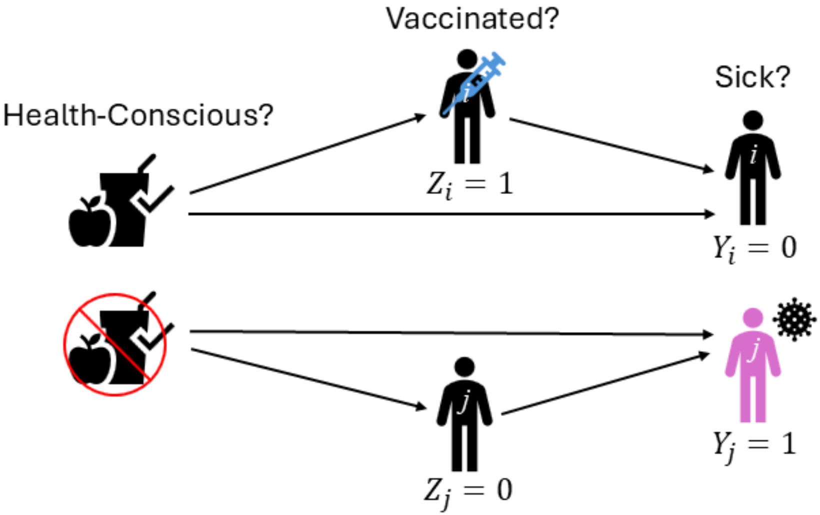

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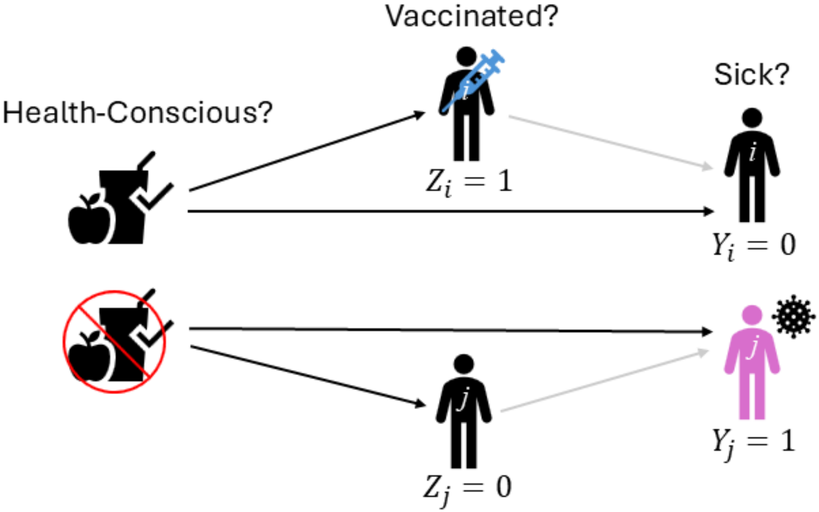

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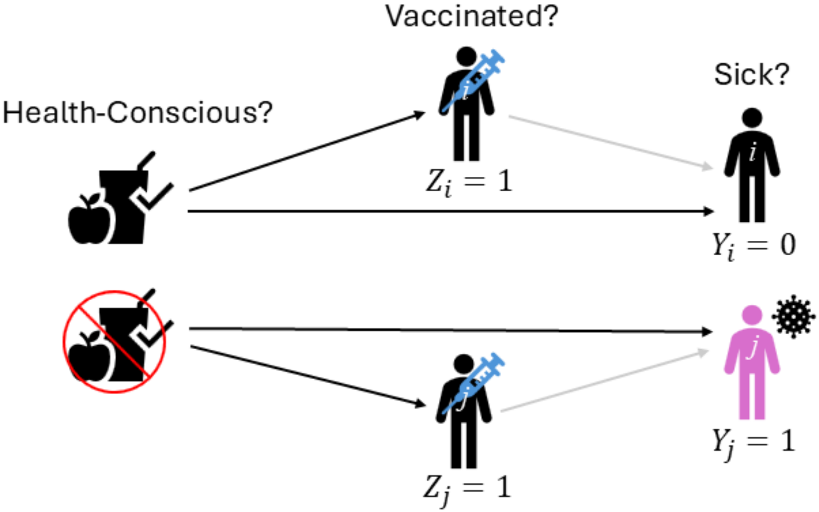

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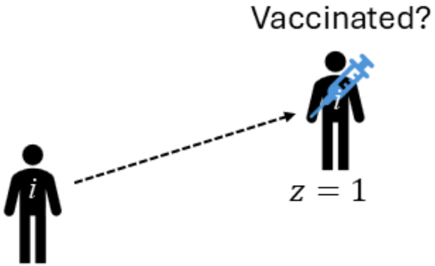

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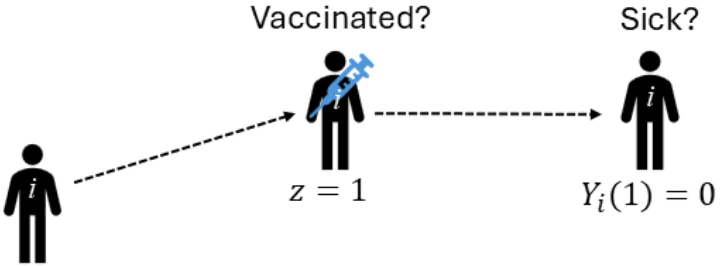

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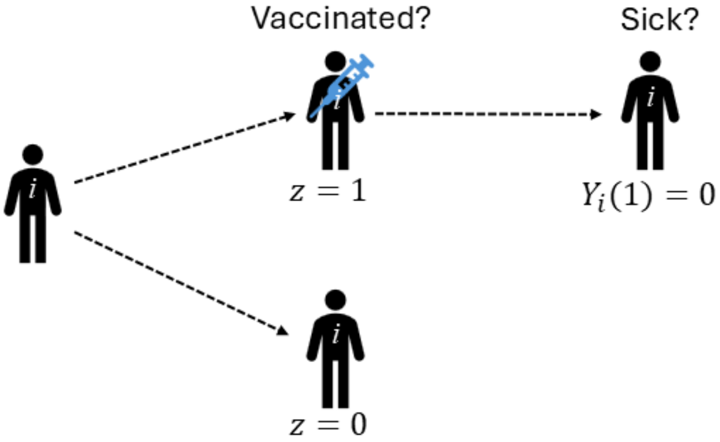

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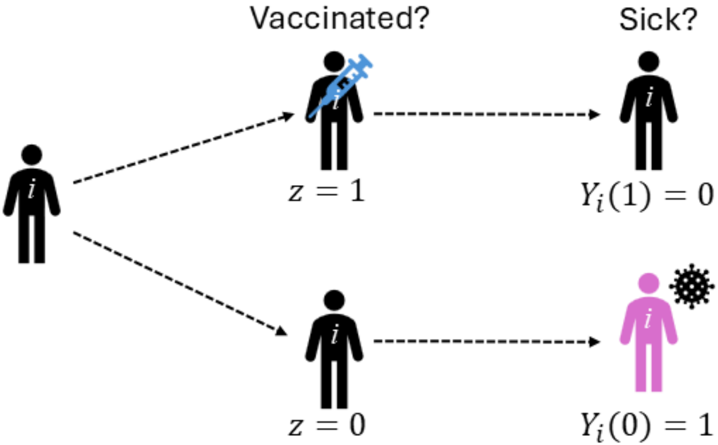

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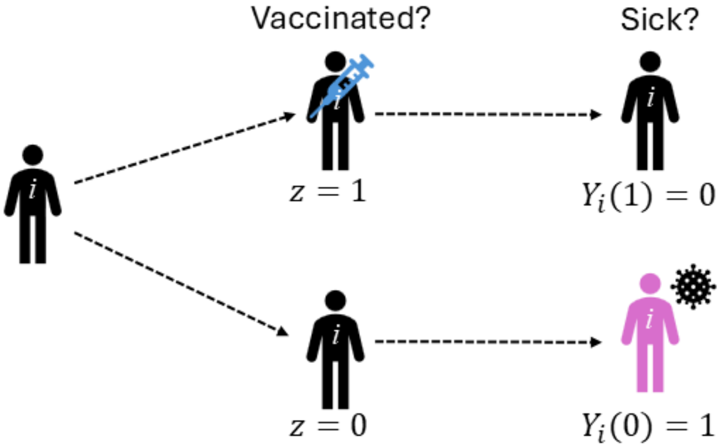

$Y_i(1)$	$Y_i(0)$	Type
0	1	Protected

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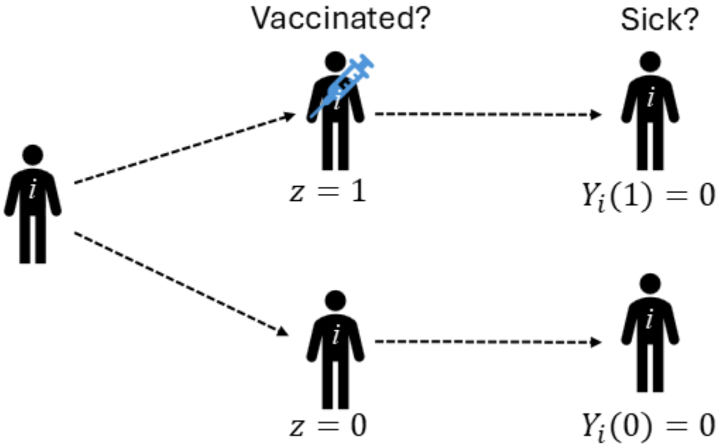

$Y_i(1)$	$Y_i(0)$	Type
0	0	Immune
0	1	Protected

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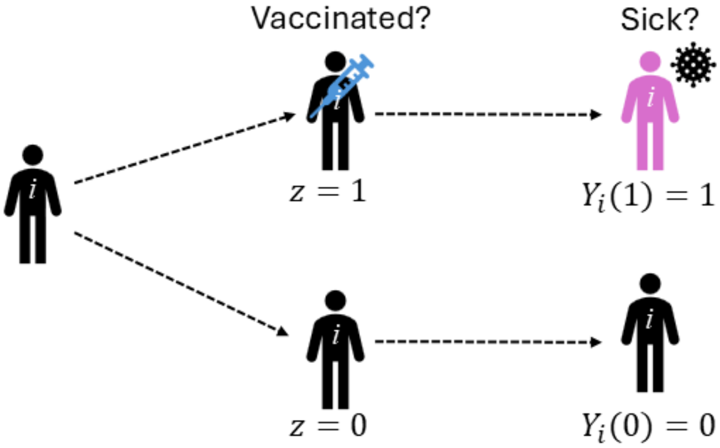

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0	1	Protected
1	0	Harmed

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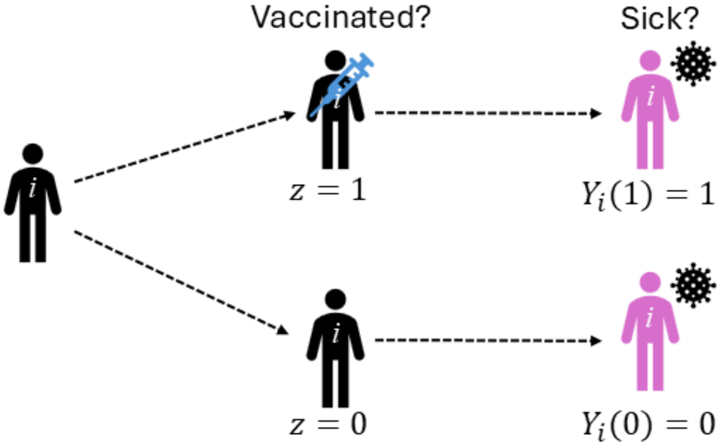

$Y_i(1)$	$Y_i(0)$	Type
0	0	Immune
0	1	Protected
1	0	Harmed
1	1	Doomed

My Causal Questions

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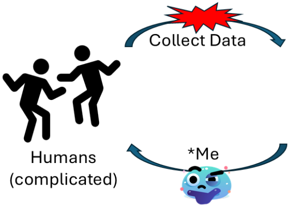

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X	Y	Z
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NA	>100	L or H
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1. If somebody were to have more antibody-dependent cellular phagocytosis (ADCP), would this lower their risk of HIV infection?
   - ADCP is measured with error
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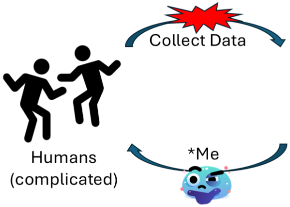

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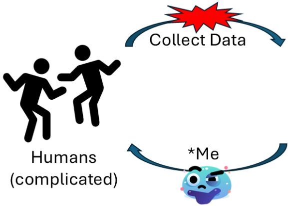

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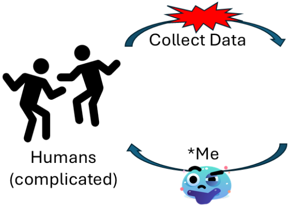
3. If college students were told to social distance when sick with the flu, would this reduce transmission of the flu?
   - Network-dependent data, self-reported network



Data

X	Y	Z
0	100	H
NA	**>100**	**L or H**
NA	100	**L or H**
1	**>100**	H

Social Distancing

If college students were told to social distance when sick with the flu, would this reduce transmission of the flu?

eX-FLU Trial

- **eX-FLU**: trial to evaluate a social distancing intervention on a college campus during flu season (Aiello et al., 2016; Zivich et al., 2020)

Design and methods of a social network isolation study for reducing respiratory infection transmission: The eX-FLU cluster randomized trial

Allison E. Aiello[a,*], Amanda M. Simanek[b,1], Marisa C. Eisenberg[c], Alison R. Walsh[c], Brian Davis[c], Erik Volz[d,1], Caroline Cheng[c], Jeanette J. Rainey[e], Amra Uzicanin[e], Hongjiang Gao[e], Nathaniel Osgood[f], Dylan Knowles[f], Kevin Stanley[f], Kara Tarter[c], Arnold S. Monto[c]

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- **Intervention**: encouragement to isolate in dorm for three days upon developing symptoms of **influenza-like illness** (ILI)
- **Central question**: does the encouragement-to-isolate intervention reduce transmission of ILI?

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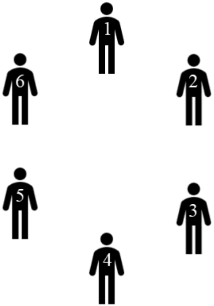
Transmission of Influenza-Like-Illness



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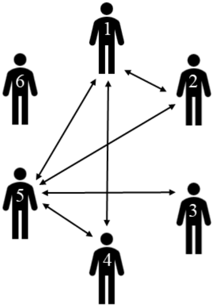

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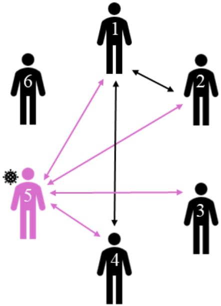

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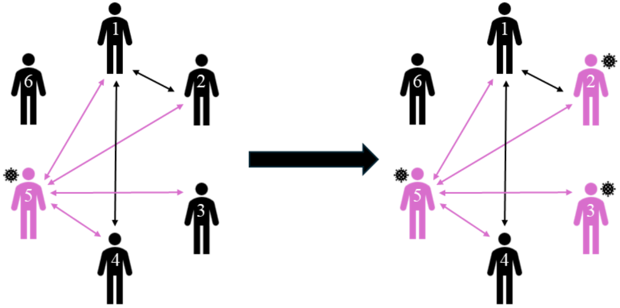
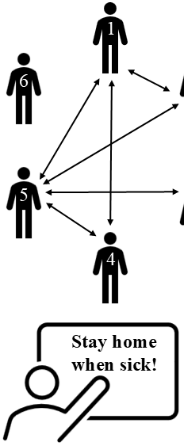


Example I: Intervention Affects Network and Transmission



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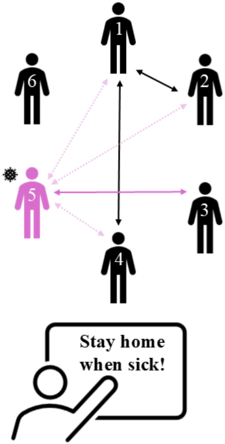

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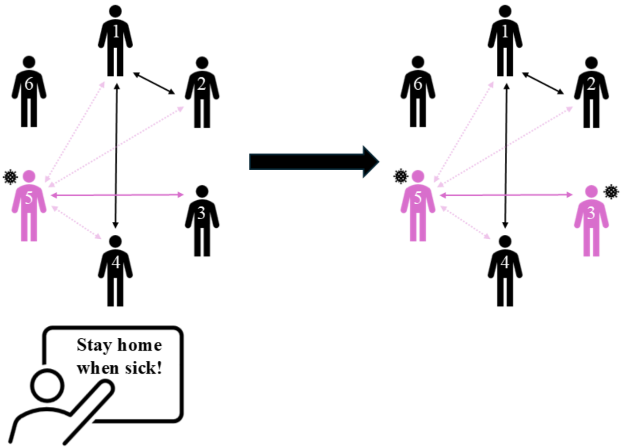
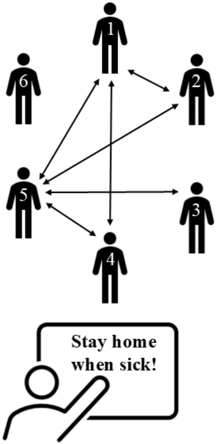


Example II: Intervention Affects Network, Not Transmission



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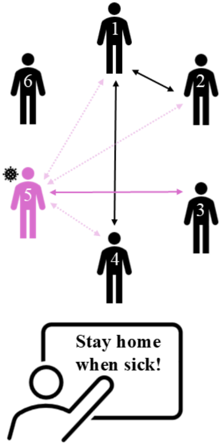

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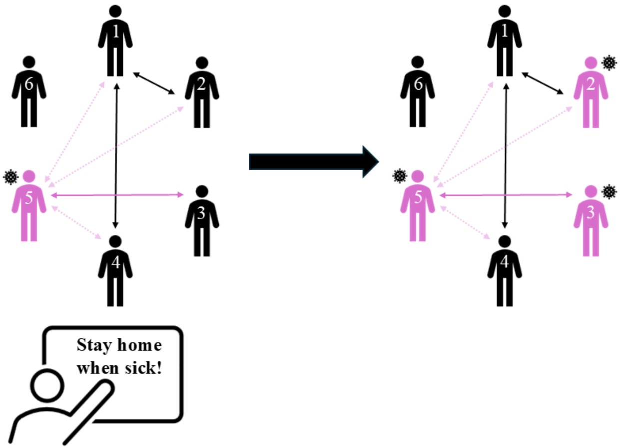
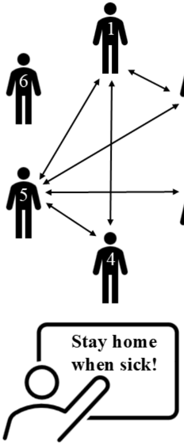


Example III: Intervention Affects Transmission, Not Network



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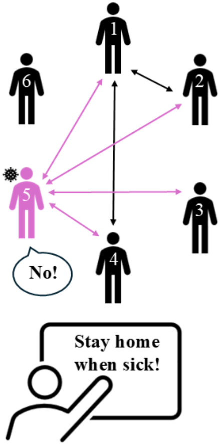

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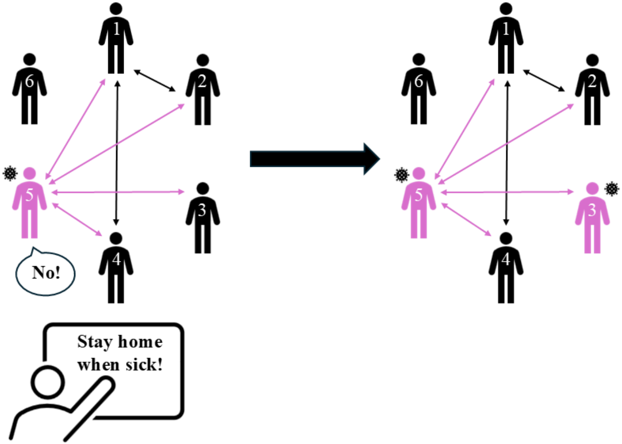
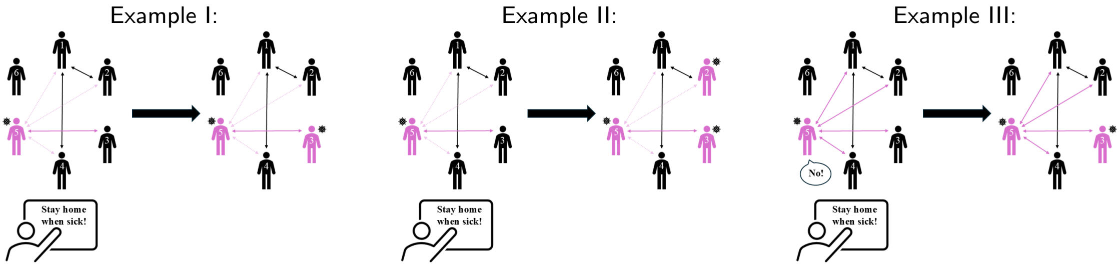


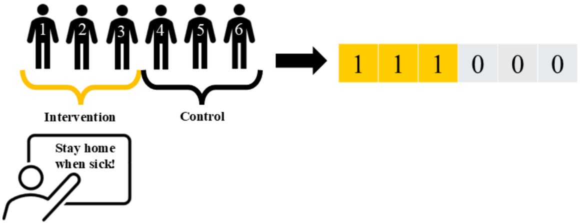
Central Question: Does the Intervention Affect Transmission of ILI?



In Examples I and III, the answer is yes

eX-FLU Observed Data

- Baseline randomization assignments
  $\mathbf{Z} = (Z_1, \ldots, Z_n) \in \mathcal{Z}$, for
  $Z_i = \mathbb{1}(\text{student } i \text{ gets intervention})$



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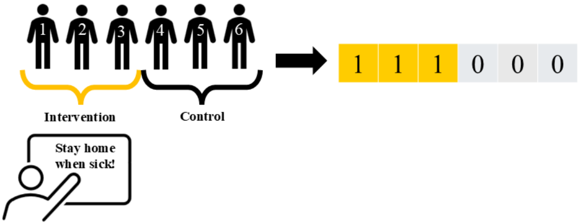
  - randomization distribution $r(\mathbf{z})$



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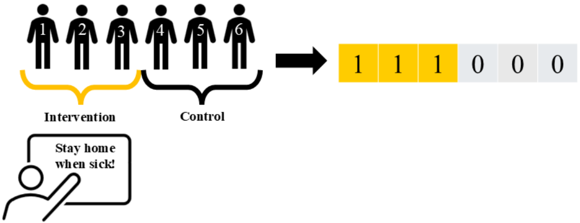
  - randomization distribution $r(\mathbf{z})$
- At weeks $k = 1, \ldots, \tau$, we observe:



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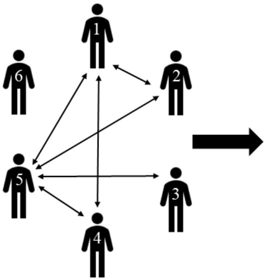
  - networks $\mathbf{A}^k = [A_{ij}^k]$, for $A_{ij}^k = \mathbb{1}(\text{students } i, j \text{ in contact at week } k)$



	1	2	3	4	5	6
1	0	1	0	1	1	0
2	1	0	0	0	1	0
3	0	0	0	0	1	0
4	1	0	0	0	1	0
5	1	1	1	1	0	0
6	0	0	0	0	0	0

eX-FLU Observed Data

- Baseline randomization assignments $\mathbf{Z} = (Z_1, \ldots, Z_n) \in \mathcal{Z}$, for $Z_i = \mathbb{1}(\text{student } i \text{ gets intervention})$
  - randomization distribution $r(\mathbf{z})$
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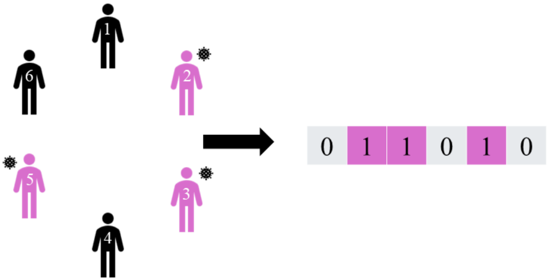
  - networks $\mathbf{A}^k = [A_{ij}^k]$, for $A_{ij}^k = \mathbb{1}(\text{students } i, j \text{ in contact at week } k)$
  - infections $\mathbf{Y}^k = (Y_1^k, \ldots, Y_n^k)$, for $Y_i^k = \mathbb{1}(\text{student } i \text{ infected at week } k)$



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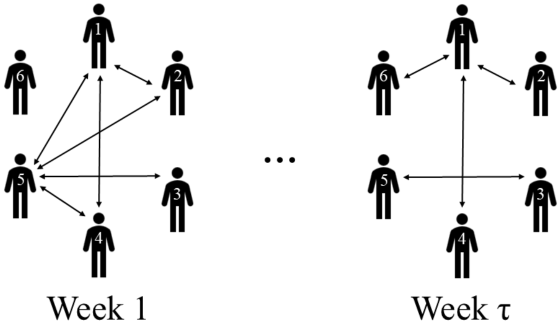
  - randomization distribution $r(\mathbf{z})$
- At weeks $k = 1, \ldots, \tau$, we observe:
  - networks $\mathbf{A}^k = [A_{ij}^k]$, for $A_{ij}^k = \mathbb{1}(\text{students } i, j \text{ in contact at week } k)$
  - infections $\mathbf{Y}^k = (Y_1^k, \ldots, Y_n^k)$, for $Y_i^k = \mathbb{1}(\text{student } i \text{ infected at week } k)$
- network history: $\overline{\mathbf{A}} = \{\mathbf{A}^k\}_{k=1}^{\tau}$



eX-FLU Observed Data

- Baseline randomization assignments $\mathbf{Z} = (Z_1, \ldots, Z_n) \in \mathcal{Z}$, for $Z_i = \mathbb{1}(\text{student } i \text{ gets intervention})$
  - randomization distribution $r(\mathbf{z})$
- At weeks $k = 1, \ldots, \tau$, we observe:
  - networks $\mathbf{A}^k = [A^k_{ij}]$, for $A^k_{ij} = \mathbb{1}(\text{students } i, j \text{ in contact at week } k)$
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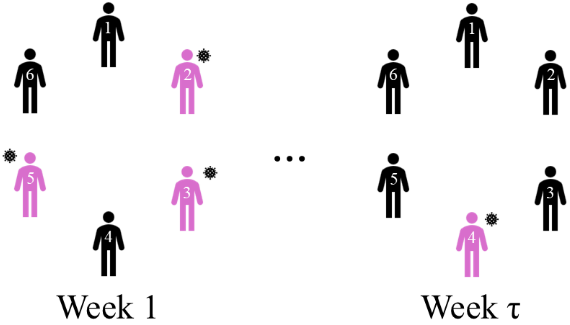

eX-FLU Potential Outcomes

Potential outcomes are defined for the networks and ILI infections:

$$\overline{\mathbf{A}}(\mathbf{z}), \quad \overline{\mathbf{Y}}(\mathbf{z}) \quad \text{for } \mathbf{z} \in \mathcal{Z}$$

- $\overline{\mathbf{A}}(\mathbf{z})$: sequence of networks that **would** occur if students **were** encouraged to isolate according to $\mathbf{z}$
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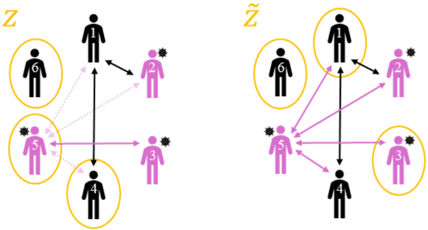
- Both of these depend on the entire vector $\mathbf{z}$
  - potential outcomes for one student depend on intervention assignment of other students (**interference**) (Hudgens and Halloran, 2008)
- Assume **causal consistency**:

$$\overline{\mathbf{A}} = \overline{\mathbf{A}}(\mathbf{Z}) \text{ and } \overline{\mathbf{Y}} = \overline{\mathbf{Y}}(\mathbf{Z})$$

eX-FLU Null Hypotheses

$$H_0^Y : \overline{\mathbf{Y}}(\mathbf{z}) = \overline{\mathbf{Y}}(\widetilde{\mathbf{z}}) \text{ for all } \mathbf{z}, \widetilde{\mathbf{z}} \in \mathcal{Z}$$

("the intervention has no effect on the infections")



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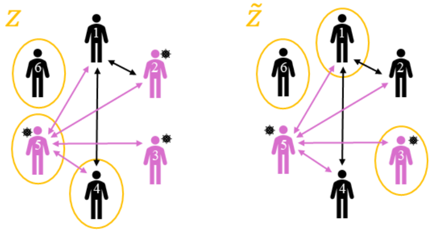

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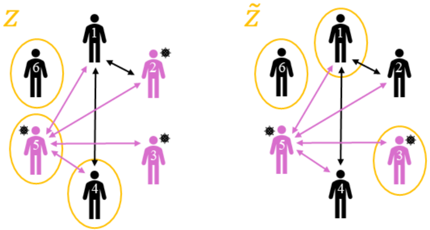

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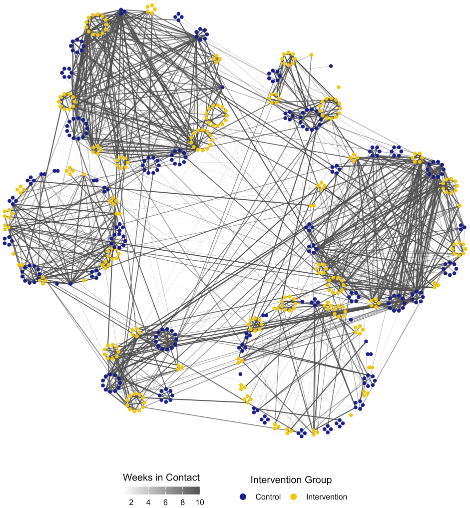
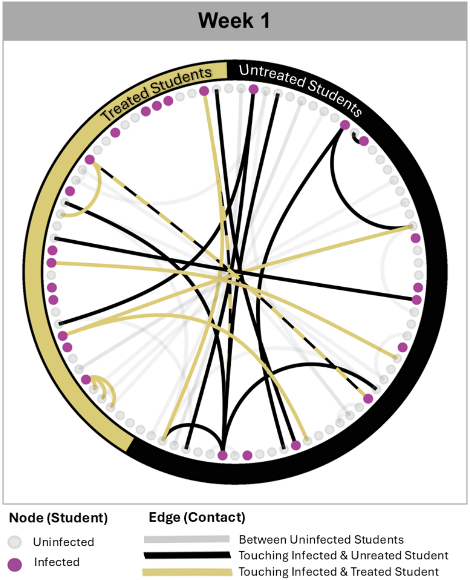
Previous analyses of the eX-FLU trial (Alexandria et al., 2023) tested $H_0^\sharp$, but no analyses have tested H_0^Y

eX-FLU: Descriptive Results



eX-FLU: Descriptive Results

- 93 (out of 579) students with at least one infection



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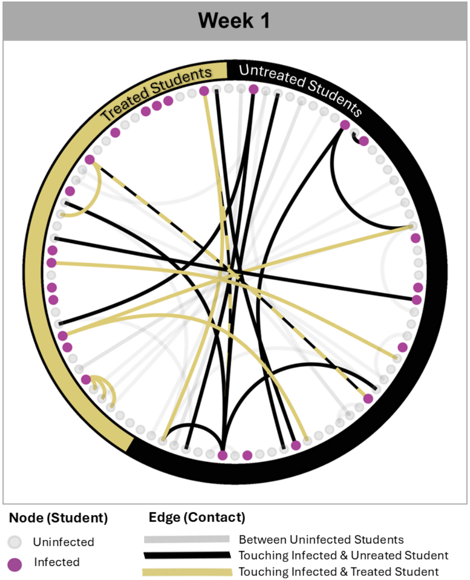

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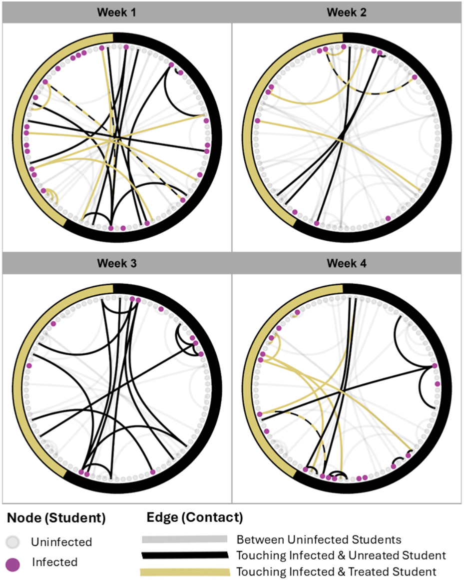
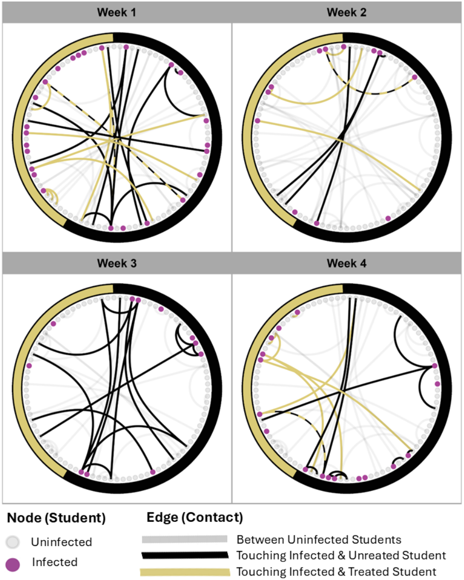


eX-FLU: Descriptive Results

- 93 (out of 579) students with at least one infection
- Bold edges represent possible transmission events
  - Proportion of possible transmission events attributable to students in the intervention group:

$$T = \frac{\text{number of yellow edges}}{\text{total number of edges}} = \frac{\sum_{k=2}^{\tau}\sum_{i=1}^{n}\sum_{j>i} Z_i Y_i^{k-1} A_{ij}^{k-1}}{\sum_{k=2}^{\tau}\sum_{i=1}^{n}\sum_{j>i} Y_i^{k-1} A_{ij}^{k-1}} = 0.359$$



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$\mathbf{z}_2$	$\overline{\mathbf{A}}(\mathbf{z}_2) =?$	$\overline{\mathbf{Y}}(\mathbf{z}_1) =?$	$T(\mathbf{z}_1, ?, ?)$
...	...	...	...
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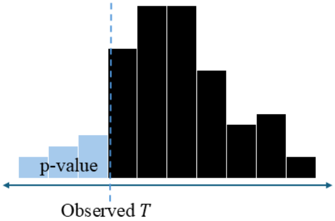
$$F_T(t|H_0^\sharp) = \Pr\left(T \leq t|H_0^\sharp\right) = \sum_{\mathbf{z}\in\mathcal{Z}} r(\mathbf{z})\mathbb{1}\{T(\mathbf{z}, \overline{\mathbf{A}}, \overline{\mathbf{Y}}) \leq t\}$$

  is the **cumulative distribution function** (CDF) of T



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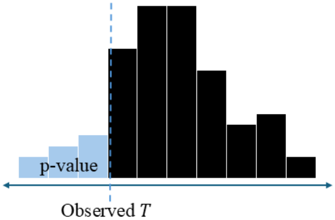
  is the **cumulative distribution function** (CDF) of T
- Reject $H_0^\sharp$ if $\rho^\sharp \leq 0.05$



Testing $H_0^\sharp$

- This test of $H_0^\sharp$ controls the **type I error rate** exactly:

$$\Pr\left(\rho^\sharp \leq \alpha | H_0^\sharp\right) \leq \alpha$$

for any $\alpha \in [0, 1]$, for any sample size, and for any choice of test statistic

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- The **power** of this test:

$$\Pr\left(\rho^\sharp \leq \alpha | H_1^\sharp\right)$$

depends on the choice of test statistic

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Proposition: This procedure will **asymptotically** control the type I error rate

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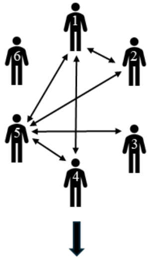

	1	2	3	4	5	6
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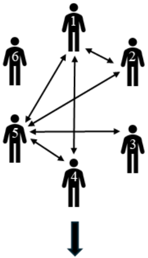

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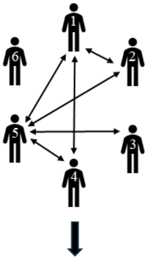

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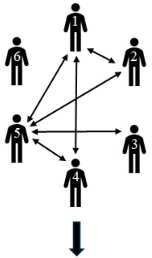

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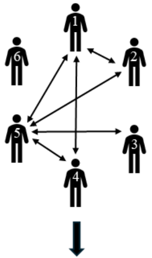

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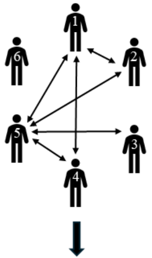

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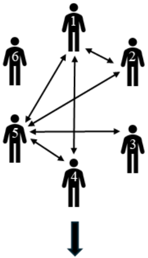

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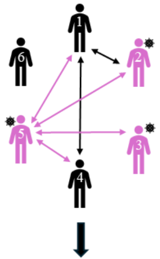

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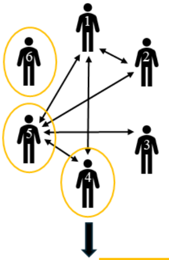

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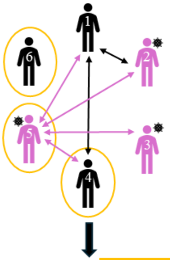

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Separable Temporal Exponential Family Random Graph Models

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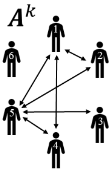

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A **STERGM** assumes that, at each time step $k = 1, \dots, \tau - 1$:

- New edges form according to a **formation** ERGM

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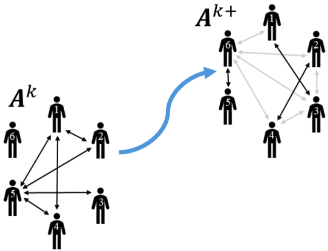

Separable Temporal Exponential Family Random Graph Models

A **STERGM** assumes that, at each time step $k = 1, \ldots, \tau - 1$:

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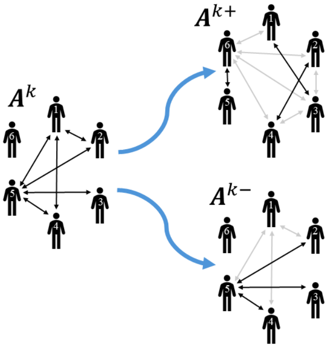
$$\Pr_{\theta^-}(\mathbf{A}^{k-} = \mathbf{a}^{k-} | \mathbf{A}^k = \mathbf{a}^k, \mathbf{X} = \mathbf{x}) = \frac{\exp\{\theta^- \cdot \mathbf{g}^-(\mathbf{a}^{k-}, \mathbf{x})\}}{\kappa\{\theta^-, \mathcal{A}^-(\mathbf{a}^k), \mathbf{x}\}}.$$

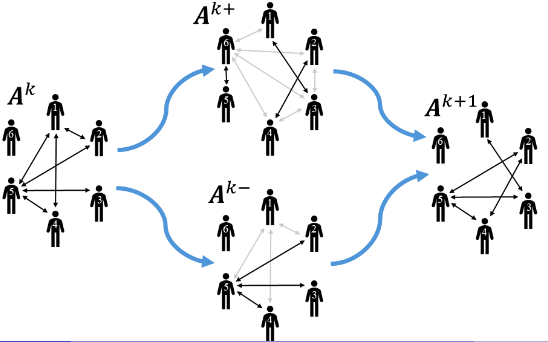


Separable Temporal Exponential Family Random Graph Models

A **STERGM** assumes that, at each time step $k = 1, \ldots, \tau - 1$:

- New edges form according to a **formation** ERGM
- Old edges persist according to a **persistence** ERGM
- The network at time step $k+1$ is the result of formation and persistence

$$\mathbf{A}^{k+1} = \underbrace{\mathbf{A}^{k}}_{\text{previous network}} \cup \underbrace{(\mathbf{A}^{k+} - \mathbf{A}^{k})}_{\text{new edges formed}} - \underbrace{(\mathbf{A}^{k} - \mathbf{A}^{k-})}_{\text{old edges not persisting}}$$



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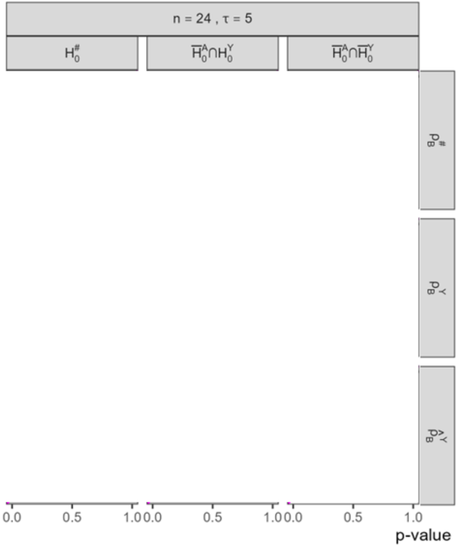
- Three testing procedures:
  1. $\rho_B^\sharp$: testing $H_0^\sharp$
  2. ρ_B^Y: testing H_0^Y using known q
  3. $\widehat{\rho}_B^Y$: testing H_0^Y using estimated q

Simulation Results: Empirical CDF of P-Values



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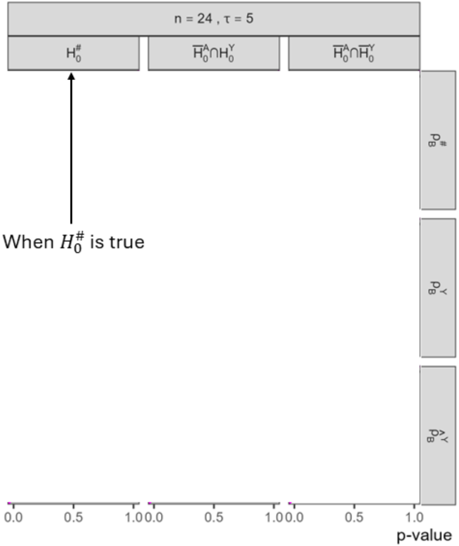

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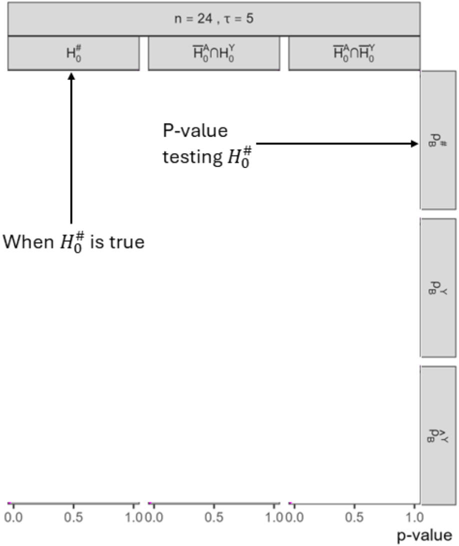

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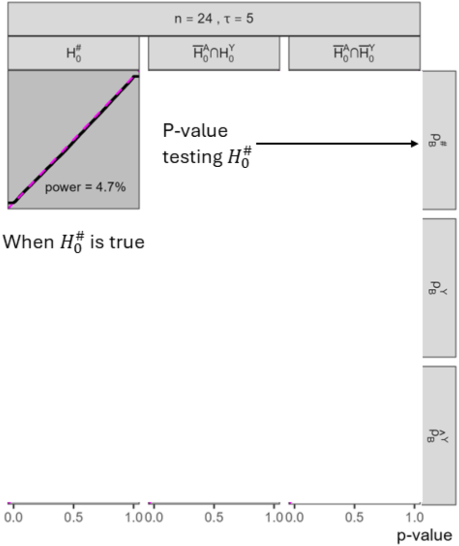

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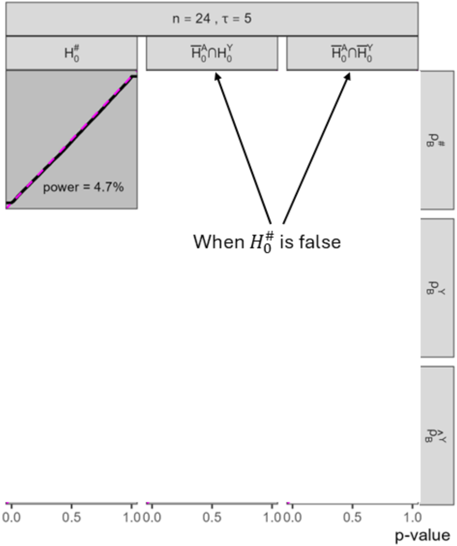

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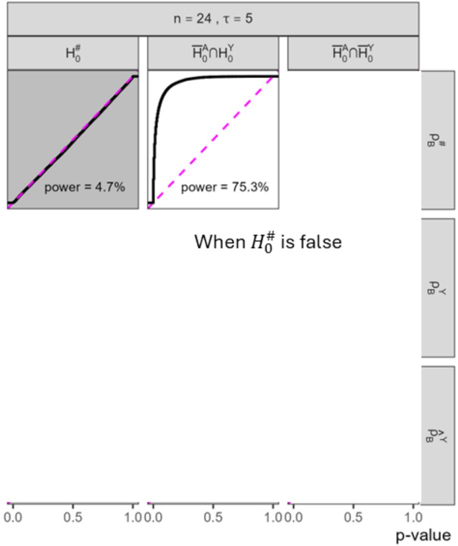

When $H_0^{\#}$ is false

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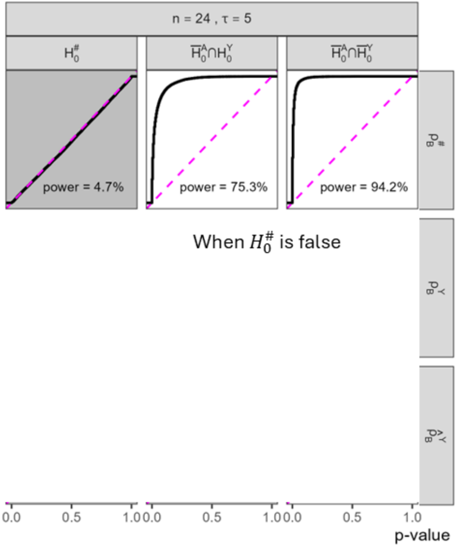

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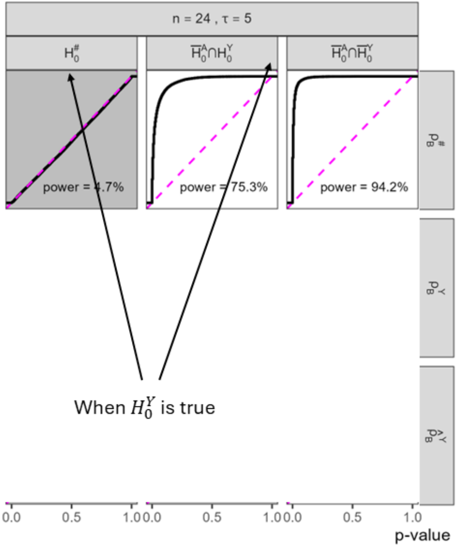

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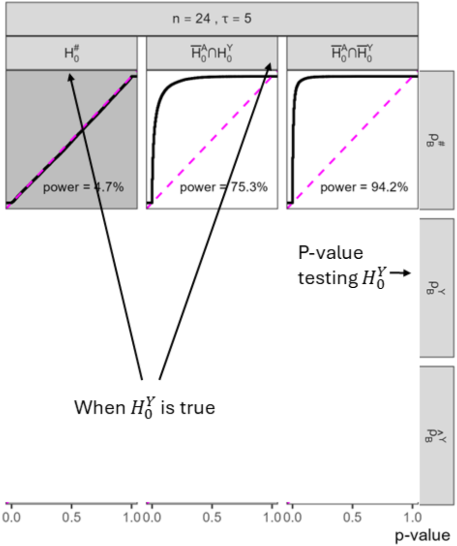

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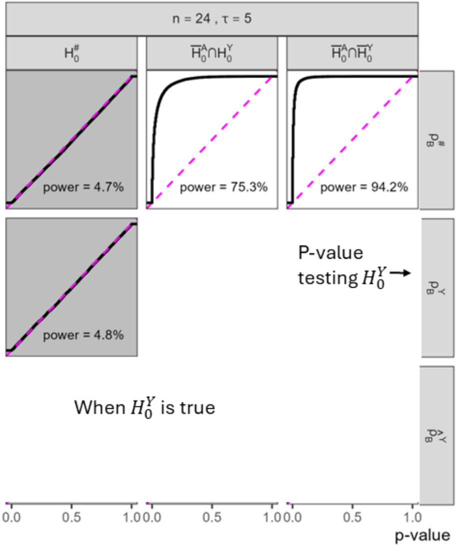

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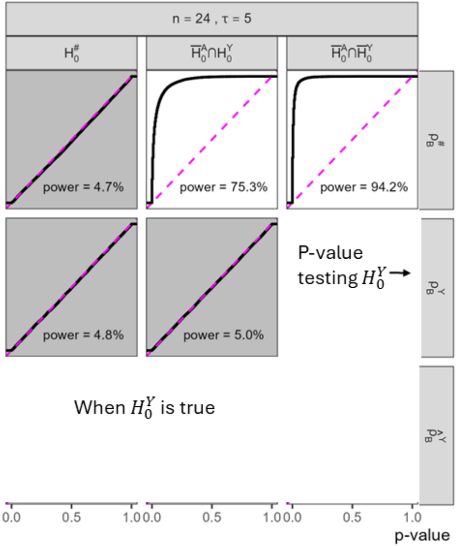

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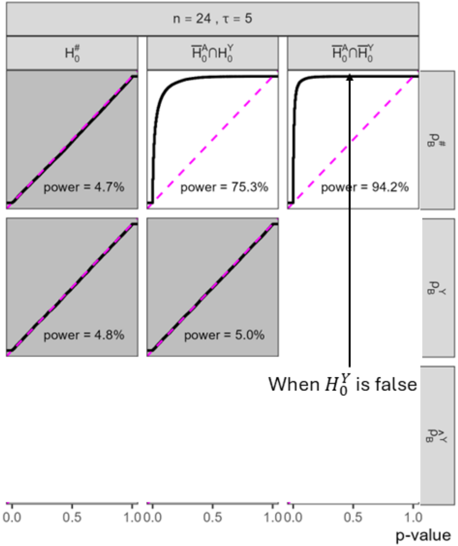

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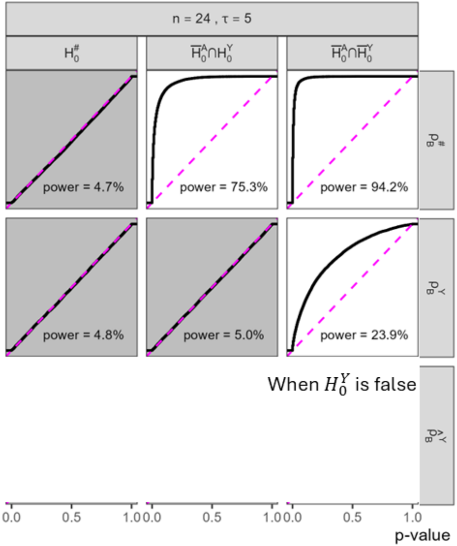

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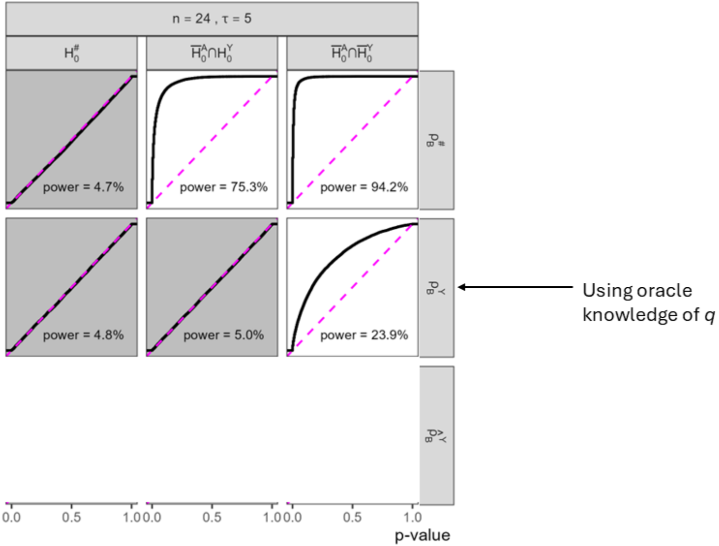

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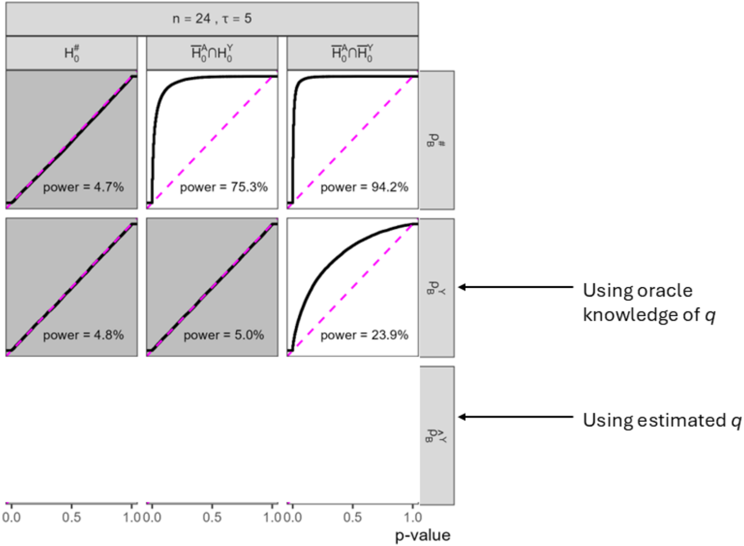

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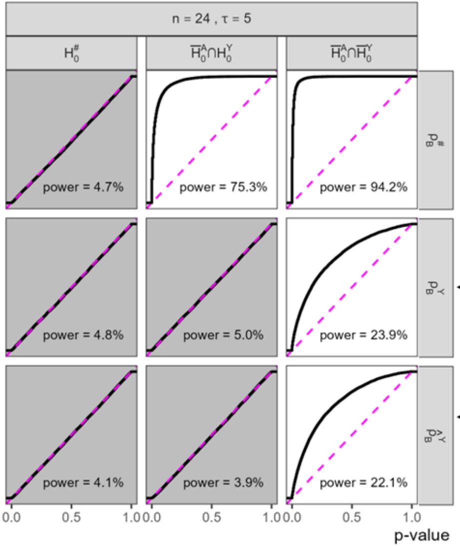
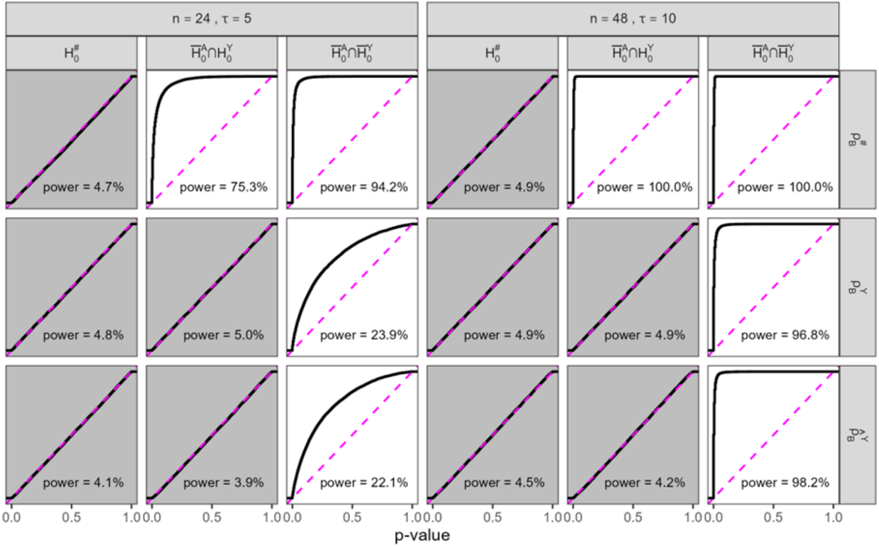


Using oracle knowledge of q

Using estimated q

Simulation Results: Empirical CDF of P-Values



eX-FLU: Hypothesis Test Results

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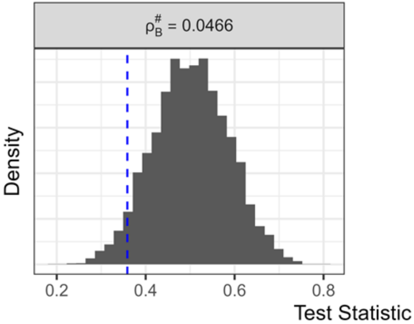

- Encouragement to isolate affects the social network and/or influenze-like illness ($\rho_B^\sharp = 0.0466$)

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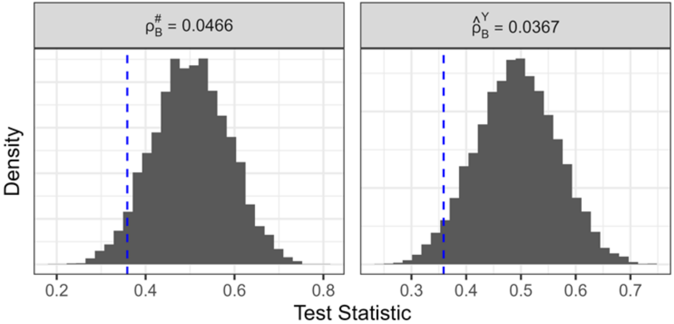

- Encouragement to isolate affects the social network and/or influenze-like illness ($\rho_B^\sharp = 0.0466$)
- Encouragement to isolate specifically affects influenze-like illness ($\widehat{\rho}_B^Y = 0.0367$)

Future Directions

1. Account for **measurement error** in the self-reported social networks

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3. **Design future trials** with independent clusters
   - can allow **identification** of more causal estimands

Thank you!

Questions?

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Choice of Test Statistic

Test statistics: "proportion of possible transmission events attributable to students in the intervention group:"

$$T^{**}(\mathbf{Z}, \overline{\mathbf{A}}, \overline{\mathbf{Y}}) = \frac{\sum_{k=2}^{\tau} \sum_{i=1}^{n} \sum_{j>i} Z_i E_{ijk}^{**}}{\sum_{k=2}^{\tau} \sum_{i=1}^{n} \sum_{j>i} E_{ijk}^{**}}.$$

	From Infected to Infected	**From Infected**
Contact at $k-1$	$E_{ijk}^{11} = Y_i^{k-1} A_{ij}^{k-1} Y_j^k$	$E_{ijk}^{12} = Y_i^{k-1} A_{ij}^{k-1}$
Contact at k	$E_{ijk}^{21} = Y_i^{k-1} A_{ij}^{k} Y_j^k$	$E_{ijk}^{22} = Y_i^{k-1} A_{ij}^{k}$
Contact at $k-1$ **or** k	$E_{ijk}^{31} = Y_i^{k-1} (A_{ij}^{k-1} \vee A_{ij}^{k}) Y_j^k$	$E_{ijk}^{32} = Y_i^{k-1} (A_{ij}^{k-1} \vee A_{ij}^{k})$
Contact at $k-1$ **and** k	$E_{ijk}^{41} = Y_i^{k-1} (A_{ij}^{k-1} * A_{ij}^{k}) Y_j^k$	$E_{ijk}^{42} = Y_i^{k-1} (A_{ij}^{k-1} * A_{ij}^{k})$

Table: Definitions of a possible transmission event E_{ijk} from student i to student j at time k. Y_i^k is an indicator for student i being infected at week k, A_{ij}^k is an indicator for students i and j being in contact at week k, and $a \vee b$ denotes the maximum of a and b.

ERGM Model Formulation

$$\Pr_\theta(\mathbf{A} = \mathbf{a} | \mathbf{X} = \mathbf{x}) = \frac{\exp\{\theta \cdot \mathbf{g}(\mathbf{a}, \mathbf{x})\}}{\kappa(\theta, \mathcal{A}, \mathbf{x})},$$

$$\kappa(\theta, \mathcal{A}, \mathbf{x}) = \sum_{\mathbf{a} \in \mathcal{A}} \exp\{\theta \cdot \mathbf{g}(\mathbf{a}, \mathbf{x})\}$$

For example, in the simulation study and eX-FLU application,

$$\mathbf{g}(\mathbf{a}, \mathbf{x}) = \begin{bmatrix} \text{\# edges} \\ \text{\# edges touching a treated node} \\ \text{\# edges touching an infected node} \\ \text{\# edges touching a treated and infected node} \\ \text{\# edges between roommate pairs} \end{bmatrix} = \begin{bmatrix} \sum_{i,j} a_{ij} \\ \sum_{i,j} a_{ij}(z_i + z_j) \\ \sum_{i,j} a_{ij}(y_i + y_j) \\ \sum_{i,j} a_{ij}(z_i y_i + z_j y_j) \\ \sum_{i,j} a_{ij} \mathbb{1}(i, j \text{ roomates}) \end{bmatrix}$$

ERGM Change Statistic Model Formulation

- **Change statistic**: $\delta_{\mathbf{g}}(\mathbf{a},\mathbf{x})_{ij} = \mathbf{g}(\mathbf{a}_{ij}^{+},\mathbf{x}) - \mathbf{g}(\mathbf{a}_{ij}^{-},\mathbf{x})$ is the change in network statistic that would occur if a_{ij} were changed from 0 to 1
  - where $\mathbf{a}_{ij}^{+}$ and $\mathbf{a}_{ij}^{-}$ represent the network $\mathbf{a}$ with dyad a_{ij} set to 1 or 0, respectively
- Then the equivalent ERGM specification is

$$\text{logit}\{\Pr_{\theta}(A_{ij} = 1 | \mathbf{A}_{ij}^{C} = \mathbf{a}_{ij}^{C}, \mathbf{X} = \mathbf{x})\} = \theta^{k}\delta_{\mathbf{g}}(\mathbf{a},\mathbf{x})_{ij}$$

  - where $\mathbf{A}_{ij}^{C}$ represents all dyads in $\mathbf{A}$ except A_{ij}
- **Interpretation of θ**: the change in conditional log-odds of the network associated with a one-unit increase in the corresponding component of $\mathbf{g}(\mathbf{a},\mathbf{x})$ resulting from switching a particular dyad A_{ij} from 0 to 1 and leaving the rest of the network fixed at $\mathbf{A}_{ij}^{C}$

Dyadic Independence EGRMs

- **Dyadic independence term**: a component g of $\mathbf{g}$ in an ERGM for which the corresponding change statistic $\delta_g(\mathbf{a}, \mathbf{x})_{ij}$ can be calculated for any i, j without knowing $\mathbf{a}$
  - For example, if $g(\mathbf{a}, \mathbf{x}) = \sum_{i,j} a_{ij}(Z_i + Z_j)$ counts the number of edges touching treated nodes, then $\delta_g(\mathbf{a}, \mathbf{x})_{ij} = z_i + z_j$ doesn't depend on $\mathbf{a}$
- **Dyadic independence ERGM**: an ERGM with only dyadic independence terms
  - replace $\delta_g(\mathbf{a}, \mathbf{x})_{ij}$ with $\delta_g(\mathbf{x})_{ij}$ and write the model as

$$\text{logit}\{\Pr\big(A_{ij} = 1 | \mathbf{X} = \mathbf{x}\big)\} = \theta \cdot \delta_g(\mathbf{x})_{ij}$$

- **Interpretation of θ**: the change in log-odds of the network associated with a one-unit increase in the corresponding component of $\mathbf{g}(\mathbf{a}, \mathbf{x})$ resulting from switching a particular dyad A_{ij} from 0 to 1

STERGM Model Formulation

- **Formation model** is an ERGM conditional on only adding edges:

$$\Pr_{\theta^+}(\mathbf{A}^{k+} = \mathbf{a}^{k+} | \mathbf{A}^k = \mathbf{a}^k, \mathbf{X} = \mathbf{x}) = \frac{\exp\{\theta^+ \cdot \mathbf{g}^+(\mathbf{a}^{k+}, \mathbf{x})\}}{\kappa\{\theta^+, \mathcal{A}^+(\mathbf{a}^k), \mathbf{x}\}}$$

  - $\mathcal{A}^+(\mathbf{a})$: space of possible networks that can be formed by adding edges to $\mathbf{a}$

- **Persistence model** is an ERGM conditional on only removing edges:

$$\Pr_{\theta^-}(\mathbf{A}^{k-} = \mathbf{a}^{k-} | \mathbf{A}^k = \mathbf{a}^k, \mathbf{X} = \mathbf{x}) = \frac{\exp\{\theta^- \cdot \mathbf{g}^-(\mathbf{a}^{k-}, \mathbf{x})\}}{\kappa\{\theta^-, \mathcal{A}^-(\mathbf{a}^k), \mathbf{x}\}}$$

  - $\mathcal{A}^-(\mathbf{a})$: space of possible networks that can be formed by removing edges to $\mathbf{a}$

- A **STERGM** assumes the network at time $k+1$ is then the result of applying the changes in $\mathbf{A}^{k+}$ and $\mathbf{A}^{k-}$ to $\mathbf{A}^k$:

$$\mathbf{A}^{k+1} = \underbrace{\mathbf{A}^k}_{\text{previous network}} \cup \underbrace{(\mathbf{A}^{k+} - \mathbf{A}^k)}_{\text{new edges formed}} - \underbrace{(\mathbf{A}^k - \mathbf{A}^{k-})}_{\text{old edges not persisting}}$$

Separability of STERGMs

1. $\mathbf{A}^{k+} \perp\!\!\!\perp \mathbf{A}^{k-} | \mathbf{A}^{k}$, i.e., the formation and persistence processes are conditionally independent give the network at time k

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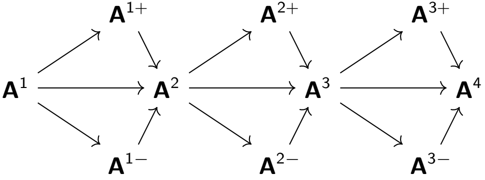
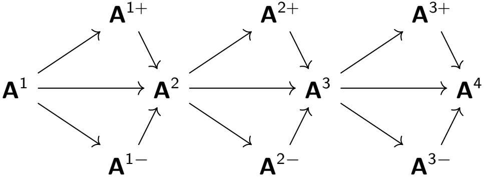


Separability of STERGMs

1. $\mathbf{A}^{k+} \perp\!\!\!\perp \mathbf{A}^{k-} | \mathbf{A}^{k}$, i.e., the formation and persistence processes are conditionally independent give the network at time k
2. the parameter space for $\theta = (\theta^+, \theta^-)$ is the product of the parameter spaces for θ^+ and θ^-



Simulation Setup

- $n \in \{24, 48\}$ students were equally divided into two residence halls, each with six clusters of equal size
- Within each residence hall group, the clusters were randomized using a 50:50 allocation to either the intervention group or the control group
- Five pairs of students were randomly selected to be roommates, meaning they had contact with each other each week
- Baseline $(k = 1)$ social contacts were simulated between each pair of students with probability 0.5
- Baseline infection statuses were simulated for each student with probability 0.5
- Social networks were simulated over the remaining $\tau \in \{5, 10\}$ weeks according to a STERGM with both formation and persistence models including edge count, intervention assignment Z, infection status Y, $Z \times Y$ interaction, and an offset to force constant edges between roommates
- Infection statuses were simulated for each student i at each week $k \in \{2, \ldots, \tau\}$ with probability $\Pr\left(Y_i^k = 1 | \overline{\mathbf{A}}^{k-1}, \overline{\mathbf{Y}}^{k-1}\right) = g(\sum_{j=1}^n A_{ij}^{k-1} Y_j^{k-1})$, where $\sum_{j=1}^n A_{ij}^{k-1} Y_j^{k-1}$ is the number of infected contacts at the previous week, and $g : [0, \infty) \to [0, 1]$ is a non-decreasing function

Simulation Setup

Three scenarios:

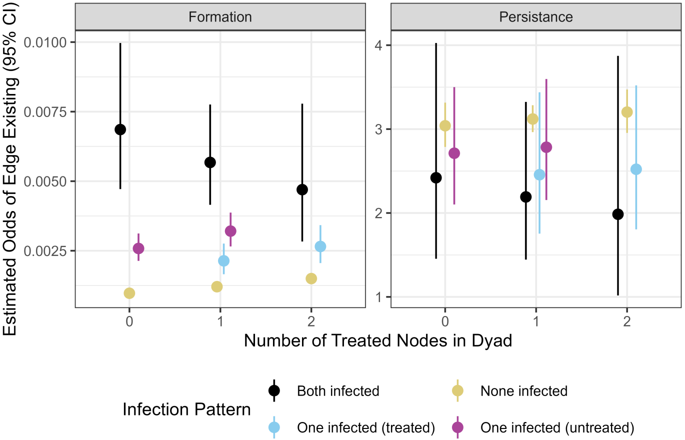
Null Hypothesis	Formation Model Parameters θ^+	Persistence Model Parameters θ^-	Infection Probability Function g
$H_0^\sharp$	$(-0.5, 0, 0, 0)$	$(-0.5, 0, 0, 0)$	$g(s) = 0.5$
$\overline{H}_0^A \cap H_0^Y$	$(-0.2, 0, 0, -1)$	$(-0.2, 0, 0, -1)$	$g(s) = 0.5$
$\overline{H}_0^A \cap \overline{H}_0^Y$	$(-0.2, 0, 0, -1)$	$(-0.2, 0, 0, -1)$	$g(s)$ increasing in s

Table: Data generating process for the simulation study. The null hypothesis refers to the null hypothesis that is true under the data generating process, formation model parameters are $\theta^+ = (\theta^+_{\text{edges}}, \theta^+_Z, \theta^+_Y, \theta^+_{ZY})$, persistence model parameters are $\theta^- = (\theta^-_{\text{edges}}, \theta^-_Z, \theta^-_Y, \theta^-_{ZY})$, and the infection probability function g provides a unit's probability of being infected at week k given their number of infected neighbors at week $k-1$.

Three p-values:

- $\rho_B^\sharp$: testing the sharp null
- ρ_B^Y: testing H_0^Y using known q
- $\widehat{\rho}_B^Y$: testing H_0^Y using estimated q

eX-FLU: STERGM Results



Type I Error Control

- **Proposition 2.1**: Let T_N be a test statistic with CDF F_N under H_0.
  1. Under H_0, $F_N(T_N)$ stochastically dominates a Uniform$(0,1)$ distribution for any N.
  2. If the test statistic T_N has a continuous limiting distribution, then $F_N(T_N) \to^d$ Uniform$(0,1)$.
- **Corollary 2.2**:
  1. Under $H_0^\sharp$, the sharp null p-value $\rho_N^\sharp$ stochastically dominates a Uniform$(0,1)$ distribution for any N.
  2. Under H_0^Y, the oracle p-value ρ_N^Y stochastically dominates a Uniform$(0,1)$ distribution for any N.
  3. If the test statistic T_N has a continuous limiting distribution, then $\rho_N^\sharp \to^d$ Uniform$(0,1)$ under $H_0^\sharp$ and $\rho_N^Y \to^d$ Uniform$(0,1)$ under H_0^Y.

Type I Error Control

- **Proposition 2.3**: Let $q(\mathbf{a}, \mathbf{z}, \theta) \equiv \Pr\{\mathbf{A}(\mathbf{z}) = \mathbf{a}; \theta\}$ denote the PMF of the distribution of stochastic potential networks $\mathbf{A}(\mathbf{z})$ at parameter value θ, let $\widehat{\theta}_N$ denote the estimator of θ, and let $F_N(\cdot; \theta)$ denote the CDF of the test statistic T_N at θ, with limiting CDF $F(\cdot; \theta)$. Let θ_0 denote the true value of θ. Assume the following:

(A1) $\widehat{\theta}_N \to^p \theta_0$

(A2) $F(t; \theta_0)$ is continuous in t on $\mathbb{R}$

(A3) there exists a $\delta_0 > 0$ such that

$$\sup_{\theta \in B_{\delta_0}(\theta_0)} \sup_{t \in \mathbb{R}} |F_N(t; \theta) - F(t; \theta)| \to 0$$

(A4) $F(t; \theta)$ is continuous in θ at θ_0 uniformly in t, i.e.,

$$\lim_{\theta \to \theta_0} \sup_{t \in \mathbb{R}} |F(t; \theta) - F(t; \theta_0)| = 0$$

Then the plug-in p-value $\widehat{\rho}_N^Y$ converges in distribution to Uniform$(0, 1)$.

Type I Error Control

- **Proposition 2.4**: Let $\rho_N = F_N(T_N)$ for test statistic T_N and CDF F_N (not necessarily the true CDF of T_N). Let $T_N^* = h_N(T_N)$ for a sequence of deterministic, strictly increasing functions h_N. Define $F_N^*(t) = F_N\{h_N^{-1}(t)\}$, the (not necessarily true) CDF of the transformed test statistic, and let $\rho_N^* = F_N^*(T_N^*)$. Then $\rho_N^* = \rho_N$.
- **Corollary 2.5**: Let h_N be a sequence of deterministic, strictly increasing functions.
  1. If the hypotheses of Proposition 2.1 are met for a test statistic T_N, then the results also hold for $T_N^* = h_N(T_N)$.
  2. If the hypotheses of Proposition 2.3 are met for $T_N, F_N(\cdot;\theta)$, then the results also hold for $T_N^* = h_N(T_N), F_N^*(\cdot;\theta) = F_N\{h_N^{-1}(\cdot);\theta\}$.