Sensitivity analysis for unmeasured confounding in principal stratification with binary variables

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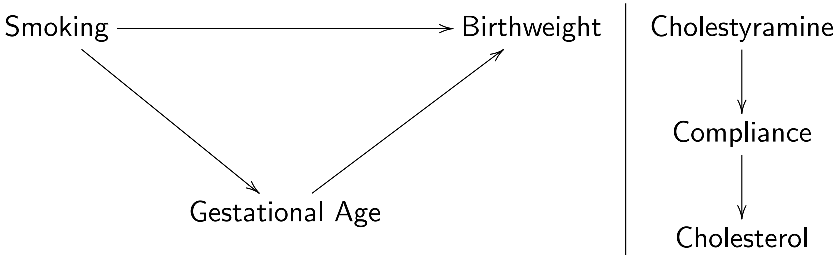
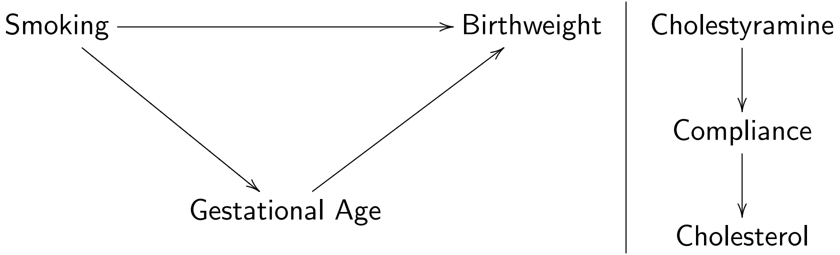
Intermediate Variables



Intermediate Variables



- <u>'Pathway' Intermediate Variables</u>: What role does gestational age play in the influence of smoking on birthweight?
- <u>'Instrument' Intermediate Variables</u>: What is the true efficacy of Cholestyramine in reducing Cholesterol?

Potential Outcomes and notations

$$
\begin{tikzcd}
T \arrow[rr] \arrow[dr] & & Y(t) \\
& D(t) \arrow[ur] &
\end{tikzcd}
$$

- T: Treatment (e.g., Smoking, Cholestyramine)
- D: Intermediate Variable (e.g., Gestational Age, Compliance)
- Y: Outcome (e.g., Birthweight, Cholesterol)
- $Y(t)$: Potential Outcome under $T = t$.

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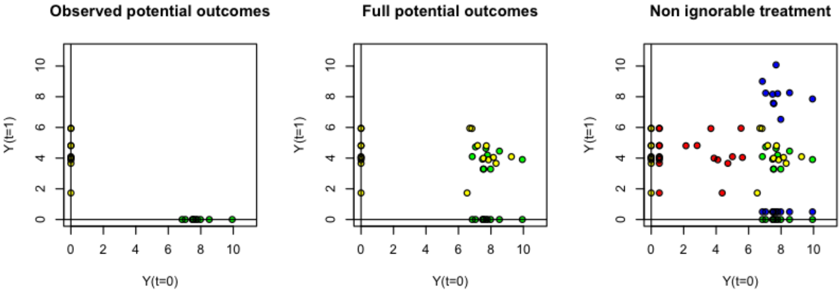
- $Y(t)$: Potential Outcome under $T = t$.

- $D(t)$: Intermediate Variables have potential outcomes too!

Causal (Volitional) Effects

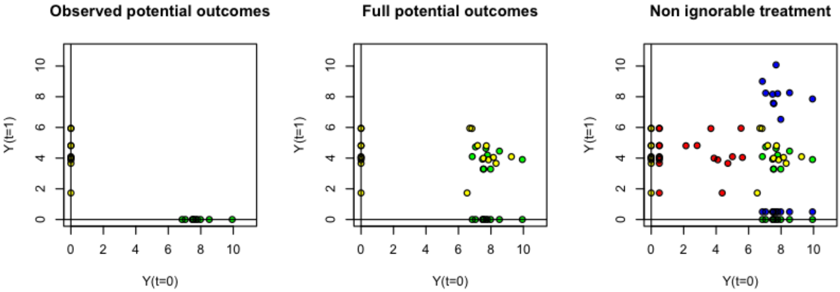
- Causal effects for 'causable' treatments T : $Y_i(1) - Y_i(0)$



Causal (Volitional) Effects

- Causal effects for 'causable' treatments $T: Y_i(1) - Y_i(0)$
-

$$
\begin{aligned}
E[Y_i(1) - Y_i(0)] &= E_X[E[Y_i(1) - Y_i(0)|X_i]] \\
\textit{no confounding?} &\stackrel{?}{=} E_X[E[Y_i(1) - Y_i(0)|T_i, X_i]] \\
&= E[Y_i(1)|T_i = 1] - E[Y_i(0)|T_i = 0]
\end{aligned}
$$



Ignorability

- Ignorability of assignment $(Y_i(1), Y_i(0)) \perp\!\!\!\perp T_i | X_i$ allows causal estimation based on observed data:

$$E[Y_i(1) - Y_i(0) | X_i] = E[Y_i(1) | T_i = 1, X_i] - E[Y_i(0) | T_i = 0, X_i]$$

- But by definition when D is an intermediate variable

$$E[Y_i(1) - Y_i(0) | D_i, X_i] \neq E[Y_i(1) | T_i = 1, D_i, X_i] - E[Y_i(0) | T_i = 0, D_i, X_i]$$

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- But by definition when D is an intermediate variable

$$E[Y_i(1) - Y_i(0) | D_i, X_i] \neq E[Y_i(1) | T_i = 1, D_i, X_i] - E[Y_i(0) | T_i = 0, D_i, X_i]$$

- **Intermediate variables kinda mess things up**

$$(Y_i(1), Y_i(0)) \not\perp\!\!\!\perp T_i | D_i, X_i$$

Posttreatment selection bias

- Conditioning on D, e.g., matching, subclassification, or regression, results in **posttreatment selection bias**:

$$\{Y_i(1) : D_i(1) = d, T_i = 1\} \text{ versus } \{Y_i(0) : D_i(0) = d, T_i = 0\}$$

does not estimate a causal effect because it compares different individuals (D is affected by T by definition):

$$\{i : D_i(1) = d, T_i = 1\} \neq \{i : D_i(0) = d, T_i = 0\}$$

- **Individuals are not exchangeable wrt T conditional on D.**

ITT and PP analyses in Instrument settings

- Ignoring intermediate variables, as in intention to treat (ITT) analysis, does not capture efficacy:

$$\{Y_i(0)\colon T_i = 0\} \text{ versus } \{Y_i(1)\colon T_i = 1\}$$

- Using 'compliant' intermediate variables, as in per-protocol (PP) analysis, induces posttreatment selection bias:

$$\{Y_i(0)\colon D_i(0) = T_i = 0\} \text{ versus } \{Y_i(1)\colon D_i(1) = T_i = 1\}$$

Principal Stratification (PS)

- Principal strata are joint potential intermediate outcomes

$$S_i = (D_i(1), D_i(0))$$

- Principal strata are not affected by the treatment
- Thus, they may be conditioned on as pretreatment variables

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- So, if strong ignorability holds, $(Y_i(1) - Y_i(0)) \perp\!\!\!\perp T_i | S_i, X_i$, comparisons within principal stratum capture causal effects:

$$\{Y_i(1) : S_i = s, X_i, T_i = 1\} \text{ versus } \{Y_i(0) : S_i = s, X_i, T_i = 0\}$$

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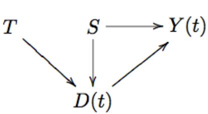
$$\{Y_i(1) : S_i = s, X_i, T_i = 1\} \text{ versus } \{Y_i(0) : S_i = s, X_i, T_i = 0\}$$

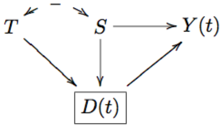
- **Principal strata not fully observed...** that's a bit of an issue

Confounding in PS

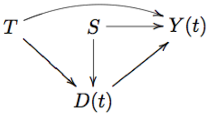
Principal Stratification Framework



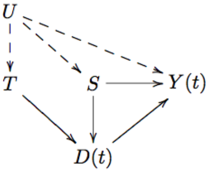
Posttreatment selection bias Back door criteria violation



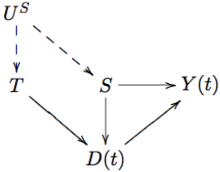
Principal Stratification with Direct Effects



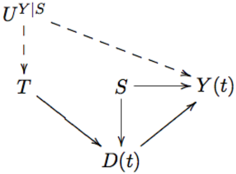
General confounding



S-confounding



Y-confounding



Conditional Independence in DAGs

(1) Intermediate Variable Case: $Y \perp\!\!\!\perp Z | D$

$$\boxed{Z \longrightarrow D \longrightarrow Y}$$

(2) Confounder Case: $Y \perp\!\!\!\perp Z | X$

$$\begin{tikzcd} & X \arrow[dl] \arrow[dr] & \\ Z & & Y \end{tikzcd}$$

(3) Ancestors Case: $Z \perp\!\!\!\perp X$ but $Z \not\perp\!\!\!\perp X | D$ or Y

$$\begin{tikzcd} Z \arrow[r] \arrow[rr, dash, dashed, bend left] & D \arrow[d] & X \arrow[l] \\ & Y & \end{tikzcd}$$

Binary PS

- When the treatment T and intermediate variable D are binary, the principal strata $S_i = (D_i(1), D_i(0))$ are interpretable as compliers, always and never takers, and defiers.
- Defier behavior is absent under monotonicity $(D(1) \geq D(0))$.

a: Always takers	$S = (1, 1)$
c: Compliers	$S = (1, 0)$
n: Never takers	$S = (0, 0)$
d: Defiers	$S = (0, 1)$

S: $D(1) \geq D(0)$

	$T = 0$	$T = 1$
$D = 0$	n/c	n
$D = 1$	a	a/c

- Principal stratification requires resolving the Y mixtures

Influenza vaccination: McDonald (1992)

- Randomized encouragement design
- Z: Patients received encouragement for vaccination, or not
- D: Receipt of vaccination recorded
- Y: Incidence of flu like symptoms recorded
- Age, chronic obstructive pulmonary disease, heart disease

$p_{00} = .088$	$p_{10} = .112$	$p_{01} = .083$	$p_{11} = .069$
$\pi_{00} = .88$	$\pi_{10} = .12$	$\pi_{01} = .69$	$\pi_{11} = .31$

$$p_{dz} = \Pr(Y = 1 | z, d) \qquad \pi_{dz} = \Pr(D = d | z)$$

S	$T = 0$	$T = 1$
$D = 0$	n/c	n
$D = 1$	a	a/c

π_{dz}	$T = 0$	$T = 1$
$D = 0$	.88	.69
$D = 1$	.12	.31

p_{dz}	$T = 0$	$T = 1$
$D = 0$	.088	.083
$D = 1$	.112	.069

Monotonicity: $D(1) \geq D(0)$

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$\left.\begin{matrix} p_{00}=.088 \\ \pi_{00}=.88 \end{matrix}\right\}$		p_{1n} π_{1n}	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$				$\left\}\begin{matrix} p_{11}=.069 \\ \pi_{11}=.31 \end{matrix}\right.$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	p_{0a} π_{0a}		
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1|D=d,T=t) \qquad \pi_{td} = \Pr(D=d|T=t)$$
$$p_{ts} = \Pr(Y^{obs}=1|S=s,T=t) \qquad \pi_{ts} = \Pr(S=s|T=t)$$

McDonald 1992 flu vaccination encouragement study

No S-confounding: $S = (D(0), D(1)) \perp\!\!\!\perp T$

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	p_{00}=.088 π_{00}=.88	$\boxed{\pi_{0n}}$	p_{1n} $\boxed{\pi_{1n}}$	p_{10}=.083 π_{10}=.69
$c=(0,1)$				p_{11}=.069 π_{11}=.31
$a=(1,1)$	p_{01}=.112 π_{01}=.12	p_{0a} $\boxed{\pi_{0a}}$	$\boxed{\pi_{1a}}$	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1|D=d, T=t) \qquad \pi_{td} = \Pr(D=d|T=t)$$
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$$\pi_{0n} \stackrel{?}{=} \pi_{1n} \qquad \pi_{0a} \stackrel{?}{=} \pi_{1a}$$

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$n=(0,0)$	$p_{00}{=}.088$ $\pi_{00}{=}.88$	$\boxed{\pi_{0n}}$	p_{1n} $\boxed{\pi_{1n}}$	$p_{10}{=}.083$ $\pi_{10}{=}.69$
$c=(0,1)$		$\pi_{0c}{=}.19$	$\pi_{1c}{=}.19$	$p_{11}{=}.069$ $\pi_{11}{=}.31$
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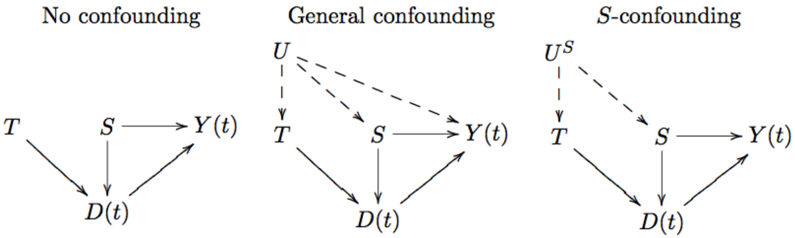
S-confounding



S-confounding

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	p_{00}=.088 π_{00}=.88	$\pi_{0n} = \boxed{\pi_{1n}}$	p_{1n} $\boxed{\pi_{1n}}$	p_{10}=.083 π_{10}=.69
$c=(0,1)$		$.19 = \pi_{0c}$	$.19 = \pi_{1c}$	p_{11}=.069 π_{11}=.31
$a=(1,1)$	p_{01}=.112 π_{01}=.12	p_{0a} $\boxed{\pi_{0a}}$	$\pi_{1a} = \boxed{\pi_{0a}}$	
$\cancel{d=(1,0)}$				

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S-confounding

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}=.088$ $\pi_{00}=.88$	$\pi_{0n} = \boxed{\pi_{1n}} + \xi_n$	p_{1n} $\boxed{\pi_{1n}}$	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$		$.19 = \pi_{0c} - \xi_n$	$.19 = \pi_{1c} - \xi_a$	$p_{11}=.069$ $\pi_{11}=.31$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	p_{0a} $\boxed{\pi_{0a}}$	$\pi_{1a} = \boxed{\pi_{0a}} + \xi_a$	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1 \mid D=d, T=t) \qquad \pi_{td} = \Pr(D=d \mid T=t)$$
$$p_{ts} = \Pr(Y^{obs}=1 \mid S=s, T=t) \qquad \pi_{ts} = \Pr(S=s \mid T=t)$$

Y-confounding & Exclusion Restriction (ER)

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}{=}.088$ $\pi_{00}{=}.88$	$\boxed{p_{0n}}$ π_{0n}	$\boxed{p_{1n}}$ π_{1n}	$p_{10}{=}.083$ $\pi_{10}{=}.69$
$c=(0,1)$		$\pi_{0c}{=}.19$	$\pi_{1c}{=}.19$	$p_{11}{=}.069$ $\pi_{11}{=}.31$
$a=(1,1)$	$p_{01}{=}.112$ $\pi_{01}{=}.12$	$\boxed{p_{0a}}$ π_{0a}	$\boxed{p_{1a}}$ π_{1a}	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1|D=d, T=t) \qquad \pi_{td} = \Pr(D=d|T=t)$$
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$$p_{0n} \stackrel{?}{=} p_{1n} \qquad p_{0a} \stackrel{?}{=} p_{1a}$$

Y-confounding & Exclusion Restriction (ER)

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}=.088$	$\boxed{p_{0n}}$ π_{0n}	$\boxed{p_{1n}}$ π_{1n}	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$	$\pi_{00}=.88$	$p_{0c}=.117$ $\pi_{0c}=.19$	$p_{1c}=.001$ $\pi_{1c}=.19$	$p_{11}=.069$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	$\boxed{p_{0a}}$ π_{0a}	$\boxed{p_{1a}}$ π_{1a}	$\pi_{11}=.31$
$\cancel{d=(1,0)}$				

$$p_{td}=\Pr(Y^{obs}=1|D=d,T=t) \qquad \pi_{td}=\Pr(D=d|T=t)$$
$$p_{ts}=\Pr(Y^{obs}=1|S=s,T=t) \qquad \pi_{ts}=\Pr(S=s|T=t)$$

$$p_{0n}=p_{1n} \qquad p_{0a}=p_{1a}$$

Y-confounding & Exclusion Restriction (ER)

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	p_{00}=.088 π_{00}=.88	$\boxed{p_{0n}}$ π_{0n}	$\boxed{p_{1n}}$ π_{1n}	p_{10}=.083 π_{10}=.69
$c=(0,1)$		p_{0c}=.117 π_{0c}=.19	p_{1c}=.001 π_{1c}=.19	p_{11}=.069 π_{11}=.31
$a=(1,1)$	p_{01}=.112 π_{01}=.12	$\boxed{p_{0a}}$ π_{0a}	$\boxed{p_{1a}}$ π_{1a}	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1|D=d, T=t) \qquad \pi_{td} = \Pr(D=d|T=t)$$
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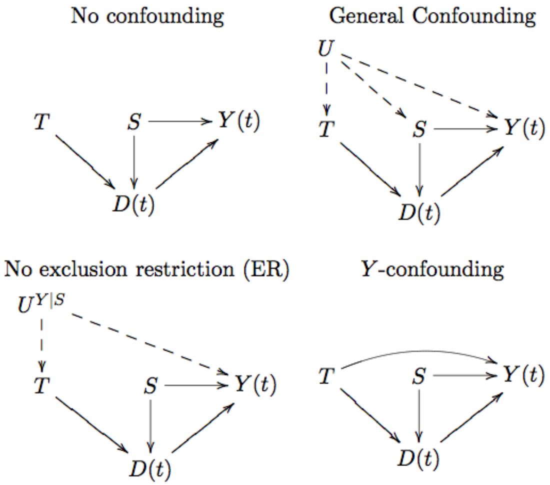
No Y-confounding: $\big(Y(0), Y(1)\big) \perp\!\!\!\perp T \big| \big(D(0), D(1)\big)$

Exclusion Restriction (ER): $D(0) = D(1) \implies Y(0) = Y(1)$.

Indistinguishable ER and Y-confounding



Y-confounding & Exclusion Restriction (ER)

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}=.088$ $\pi_{00}=.88$	$p_{0n}:p_{1n}$ π_{0n}	$\boxed{p_{1n}}$ π_{1n}	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$		$p_{0c}=f$ $\pi_{0c}=.19$	$p_{1c}=g$ $\pi_{1c}=.19$	$p_{11}=.069$ $\pi_{11}=.31$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	$\boxed{p_{0a}}$ π_{0a}	$p_{1a}:p_{1a}$ π_{1a}	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1 \mid D=d, T=t) \qquad \pi_{td} = \Pr(D=d \mid T=t)$$
$$p_{ts} = \Pr(Y^{obs}=1 \mid S=s, T=t) \qquad \pi_{ts} = \Pr(S=s \mid T=t)$$

No Y-confounding: $\big(Y(0), Y(1)\big) \perp\!\!\!\perp T \mid \big(D(0), D(1)\big)$
Exclusion Restriction (ER): $D(0)=D(1) \Longrightarrow Y(0)=Y(1)$.

Y-confounding & Exclusion Restriction (ER)

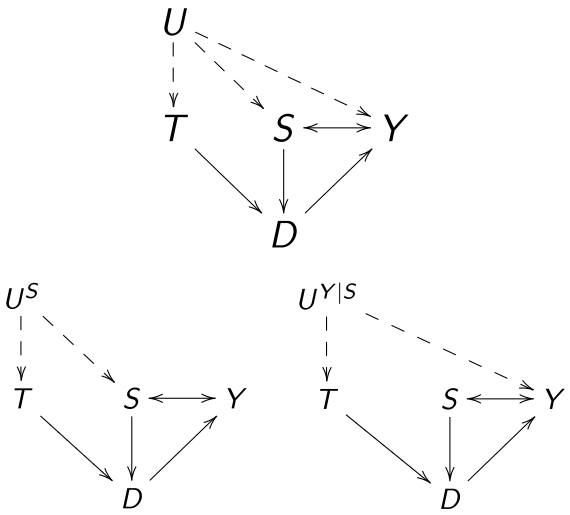
$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}{=}.088$ $\pi_{00}{=}.88$	$p_{0n}{:}p_{1n}{+}\delta_n$ π_{0n}	$\boxed{p_{1n}}$ π_{1n}	$p_{10}{=}.083$ $\pi_{10}{=}.69$
$c=(0,1)$		$p_{0c}{=}f$ $\pi_{0c}{=}.19$	$p_{1c}{=}g{+}\eta_n$ $\pi_{1c}{=}.19$	$p_{11}{=}.069$ $\pi_{11}{=}.31$
$a=(1,1)$	$p_{01}{=}.112$ $\pi_{01}{=}.12$	$\boxed{p_{0a}}$ π_{0a}	$p_{1a}{:}p_{1a}{+}\delta_a$ π_{1a}	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1 \mid D=d, T=t) \qquad \pi_{td} = \Pr(D=d \mid T=t)$$
$$p_{ts} = \Pr(Y^{obs}=1 \mid S=s, T=t) \qquad \pi_{ts} = \Pr(S=s \mid T=t)$$

No Y-confounding: $\big(Y(0), Y(1)\big) \perp\!\!\!\perp T \big| \big(D(0), D(1)\big)$

Exclusion Restriction (ER): $D(0) = D(1) \Longrightarrow Y(0) = Y(1)$.

General Confounding



Pathways of Confounding and their Effects

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}=.088$ $\pi_{00}=.88$	$p_{0n}:p_{1n}$ $\pi_{0n}:\pi_{1n}$	p_{1n} π_{1n}	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$		$p_{0c}=f$ $\pi_{0c}=.19$	$p_{1c}=g$ $\pi_{1c}=.19$	$p_{11}=.069$ $\pi_{11}=.31$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	p_{0a} π_{0a}	$p_{1a}:p_{1a}$ $\pi_{1a}:\pi_{0a}$	
$\cancel{d=(1,0)}$				

$$p_{td}=\Pr(Y^{obs}=1|D=d,T=t) \qquad \pi_{td}=\Pr(D=d|T=t)$$
$$p_{ts}=\Pr(Y^{obs}=1|S=s,T=t) \qquad \pi_{ts}=\Pr(S=s|T=t)$$

S-confounding & Y-confounding (No Exclusion Restriction)...
(Monotonicity)

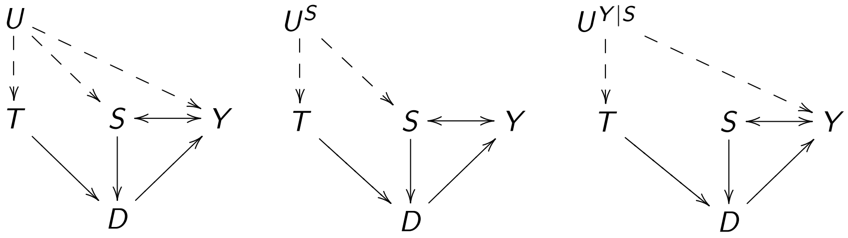
Pathways of Confounding and their Effects

$S_{=(D(0),D(1))}$		$T=0$	$T=1$	
$n=(0,0)$	$p_{00}=.088$ $\pi_{00}=.88$	$p_{0n}:p_{1n}+\delta_n$ $\pi_{0n}:\pi_{1n}+\xi_n$	p_{1n} π_{1n}	$p_{10}=.083$ $\pi_{10}=.69$
$c=(0,1)$		$p_{0c}=f$ $\pi_{0c}:19-\xi_n$	$p_{1c}=g+\eta_n$ $\pi_{1c}:19-\xi_a$	$p_{11}=.069$ $\pi_{11}=.31$
$a=(1,1)$	$p_{01}=.112$ $\pi_{01}=.12$	p_{0a} π_{0a}	$p_{1a}:p_{1a}+\delta_a$ $\pi_{1a}:\pi_{0a}+\xi_a$	
$\cancel{d=(1,0)}$				

$$p_{td} = \Pr(Y^{obs}=1|D=d,T=t) \qquad \pi_{td} = \Pr(D=d|T=t)$$
$$p_{ts} = \Pr(Y^{obs}=1|S=s,T=t) \qquad \pi_{ts} = \Pr(S=s|T=t)$$

S-confounding & Y-confounding (No Exclusion Restriction)...
(Monotonicity)

Confounding in PS



- Factoring confounding

$$
\begin{aligned}
\Pr(Y_i(t), S_i | T_i, U_i) &= \Pr(Y_i(t)|S_i, T_i, U_i) \quad \Pr(S_i|T_i, U_i) \\
&= \Pr(Y_i(t)|S_i, T_t, U_i^{Y|S}) \Pr(S_i|T_i, U_i^S)
\end{aligned}
$$

Model based PS sensitivity analysis

$$\Pr(Y_i, S_i | T_i, X_i, U_i) = \underset{\text{(Logistic)}}{\Pr(Y_i | S_i, T_i, X_i, U_i^{Y|S})} \underset{\text{(Multinomial)}}{\Pr(S_i | T_i, X_i, U_i^S)}$$

$$\log \frac{\Pr(S_i = s | T_i, X_i)}{\Pr(S_i = c | T_i, X_i)} = X_i \beta^S + T_i \xi_s, \quad s \in \{a, n\}$$

$$\text{logit} \Pr(Y_i(t) = 1 | T_i, S_i, X_i) = X_i \beta^Y + I_{S_i=c} T_i(\theta_c + \eta_c) + \sum_{s' \in \{a,n\}} I_{S_i=s'}(\beta^Y_{s'} + T_i \delta_{s'})$$

log relative ratio:

$$\exp(\xi_s) = \frac{\frac{\Pr(S_i=s|T_i=1,x_i)}{\Pr(S_i=c|T_i=1,x_i)}}{\frac{\Pr(S_i=s|T_i=0,x_i)}{\Pr(S_i=c|T_i=0,x_i)}}$$

log odds ratio:

$$\exp([\delta/\eta/\theta]_s) = \frac{\frac{\Pr(Y(1)=1|S_i=s,T_i=1,x_i)}{\Pr(Y(1)=0|S_i=s,T_i=1,x_i)}}{\frac{\Pr(Y(0)=1|S_i=s,T_i=0,x_i)}{\Pr(Y(0)=0|S_i=s,T_i=0,x_i)}}$$

Influenza vaccination McDonald (1992)

- Randomized encouragement design
- Z: Patients received encouragement for vaccination, or not
- D: Receipt of vaccination recorded
- Y: Incidence of flu like symptoms recorded
- Age, chronic obstructive pulmonary disease, heart disease

$p_{00} = .088$	$p_{10} = .112$	$p_{01} = .083$	$p_{11} = .069$
$\pi_{00} = .88$	$\pi_{10} = .12$	$\pi_{01} = .69$	$\pi_{11} = .31$

- Proportion of always/compliers increases with Age
- Proportion of flu incidence is higher among HD population
- COPD associates with both Age and HD

Influenza Vaccination: McDonald et. al. (1992)

	$T=0$	$T=1$
Age < 41	$74/1405 \approx 5.3\%$	$76/1486 \approx 5.1\%$
$40 <$ Age < 61	$315/1405 \approx 22.4\%$	$292/1486 \approx 19.7\%$
$60 <$ Age < 81	$922/1405 \approx 65.6\%$	$1018/1486 \approx 68.5\%$
$80 <$ Age	$94/1405 \approx 6.7\%$	$100/1486 \approx 6.7\%$
COPD	$406/1405 \approx 28.9\%$	$412/1486 \approx 27.7\%$
Heart Disease	$790/1405 \approx 56.2\%$	$862/1486 \approx 58.0\%$
D	$265/1405 \approx 18.8\%$	$456/1486 \approx 30.7\%$
Y	$127/1405 \approx 9.04\%$	$116/1486 \approx 7.81\%$

Y Model MLE's		S Model MLE's			
$\hat{\alpha}_1$	-2.61	$\hat{\beta}_a$	-0.09	$\hat{\beta}_n$	2.06
$\hat{\alpha}_{COPD}$	0.38	$\hat{\beta}_{a:COPD}$	0.32	$\hat{\beta}_{n:COPD}$	-0.19
$\hat{\alpha}_{HEARTD}$	0.79	$\hat{\beta}_{a:AGE=0}$		$\hat{\beta}_{n:AGE=0}$	
$\hat{\theta}_c$	-1.87	$\hat{\beta}_{a:AGE=1}$	0.23	$\hat{\beta}_{n:AGE=1}$	-0.17
$\hat{\alpha}_a$	-0.23	$\hat{\beta}_{a:AGE=2}$	0.43	$\hat{\beta}_{n:AGE=2}$	-0.37
$\hat{\alpha}_n$	-0.43	$\hat{\beta}_{a:AGE=3}$	0.54	$\hat{\beta}_{n:AGE=3}$	-0.28

Influenza Vaccination: McDonald et. al. (1992)

- We manipulate the original data set to induce S-confounding and Y-confounding in a known way.

	$T = 0$	$T = 1$
Age < 41	$74/1405 \approx 5.3\%$	$76/1486 \approx 5.1\%$
$40 <$ Age < 61	$315/1405 \approx 22.4\%$	$292/1486 \approx 19.7\%$
$60 <$ Age < 81	$922/1405 \approx 65.6\%$	$1018/1486 \approx 68.5\%$
$80 <$ Age	$94/1405 \approx 6.7\%$	$100/1486 \approx 6.7\%$
COPD	$406/1405 \approx 28.9\%$	$412/1486 \approx 27.7\%$
Heart Disease	$790/1405 \approx 56.2\%$	$862/1486 \approx 58.0\%$
D	$265/1405 \approx 18.8\%$	$456/1486 \approx 30.7\%$
Y	$127/1405 \approx 9.04\%$	$116/1486 \approx 7.81\%$

Influenza Vaccination: McDonald et. al. (1992)

- Half of always-takers in $Z = 1$ and half of never-takers in $Z = 0$ removed to induce S-confounding

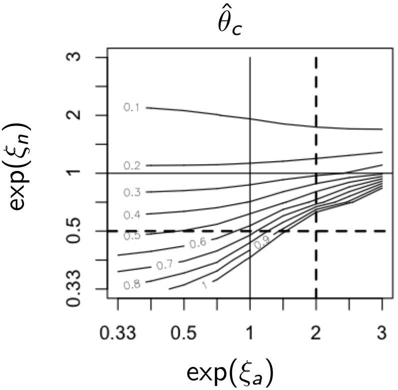
	$T = 0$	$T = 1$
Age < 41	$71/1273 \approx 5.5\%$	$42/972 \approx 4.3\%$
$40 <$ Age < 61	$287/1273 \approx 22.6\%$	$190/972 \approx 19.5\%$
$60 <$ Age < 81	$835/1273 \approx 65.6\%$	$675/972 \approx 69.5\%$
$80 <$ Age	$80/1273 \approx 6.3\%$	$65/972 \approx 6.7\%$
COPD	$355/1273 \approx 27.9\%$	$262/972 \approx 26.9\%$
Heart Disease	$714/1273 \approx 56.1\%$	$566/972 \approx 58.2\%$
D	$133/1273 \approx 10.5\%$	$456/972 \approx 46.9\%$
Y	$113/1273 \approx 8.88\%$	$74/972 \approx 7.61\%$

Influenza Vaccination: McDonald et. al. (1992)

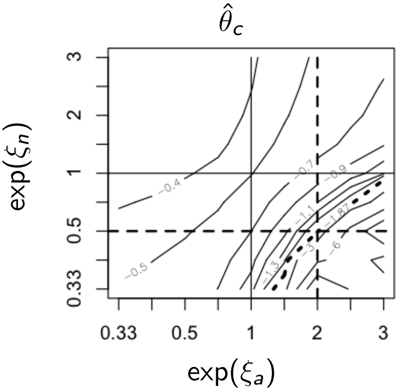
- Only heart disease (HD) cases kept in $Z = 1$. HD was not seen to differentially associate with observed principal stata

	$T = 0$	$T = 1$
Age < 41	$71/1273 \approx 5.5\%$	$24/862 \approx 2.8\%$
$40 <$ Age < 61	$287/1273 \approx 22.6\%$	$198/862 \approx 22.9\%$
$60 <$ Age < 81	$835/1273 \approx 65.6\%$	$577/862 \approx 66.9\%$
$80 <$ Age	$80/1273 \approx 6.3\%$	$63/862 \approx 7.9\%$
COPD	$355/1273 \approx 27.9\%$	$248/862 \approx 28.7\%$
Heart Disease	$714/1273 \approx 56.1\%$	$862/862 = 100\%$
D	$133/1273 \approx 10.5\%$	$272/862 \approx 31.6\%$
Y	$113/1273 \approx 8.88\%$	$83/862 \approx 9.63\%$

Sensitivity Analysis Works...



$\eta_c = \delta_{\{a,n\}} = 0$



$\eta_c = \delta_{\{a,n\}} = 0.25$

Swedish national March cohort: Lagerros (2006)

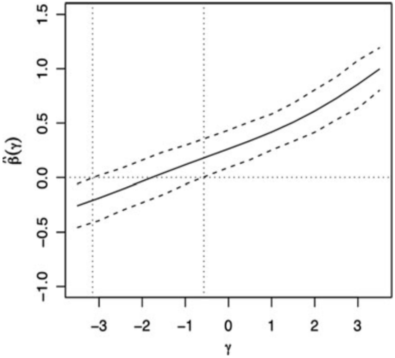
- Self report questionnaire
- Z: Physical activity (high or low)
- D: BMI (dichotomized as obese or not)
- Y: Incidence of CVD during 5 year follow up period
- Age was the only covariate made available

- Sjölander et al. (2009) wondered: *Does exercise help regardless of BMI reduction?*

- We are asking: *What portion of (potential) benefit of exercise is a result of reduction in BMI?*

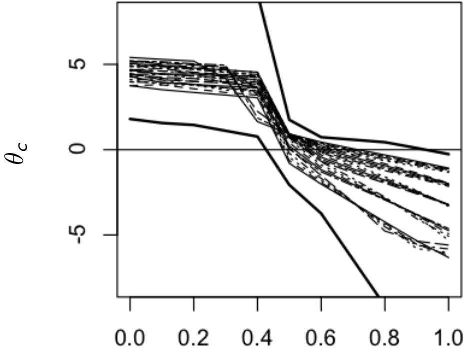
Swedish national March cohort: Lagerros (2006)

Sjölander et al. (2009)
Direct effect w/o confounding



Examine sensitivity to something like
$$\gamma = p_{c0} - p_{n0} = p_{a0} - p_{c1}$$

Sensitivity of θ_c to
$\delta_a = \delta_n$, η_c, ξ_a, and ξ_n



$$(\xi_a, \xi_n) \in [-0.66, 0.66] \times [-.90, 1.00]$$

That's it –

Thanks!