Imputation strategies for natural effect models probing mediation

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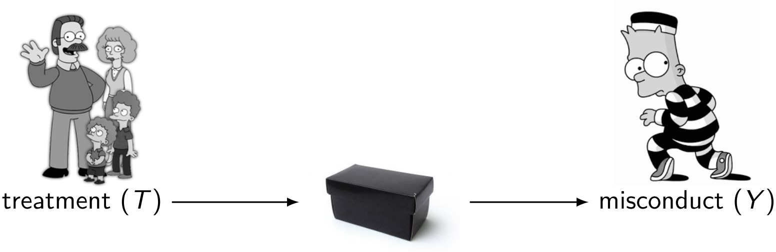
Unraveling causal mechanisms Eddy & Chamberlain (2000)



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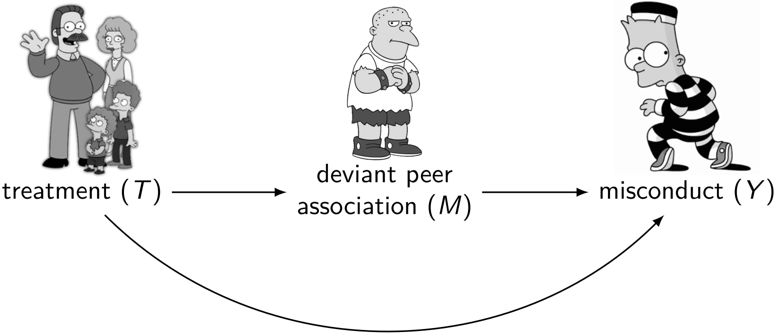

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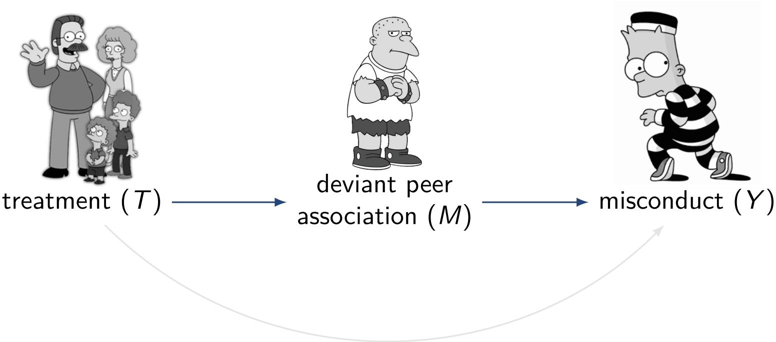
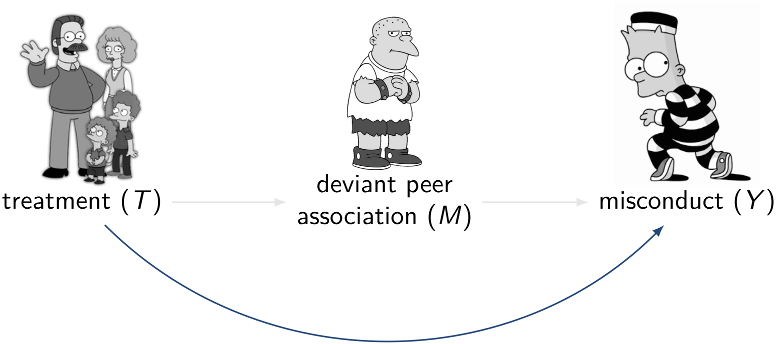


indirect or mediated effect

Unraveling causal mechanisms Eddy & Chamberlain (2000)

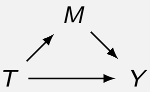


indirect or mediated effect

direct effect

Causal inference as a missing data problem

Counterfactual outcomes

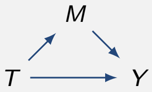


M^t	mediator level that we would have observed had T been set to t
$Y^{tM^{t'}}$	outcome that we would have observed had T been set to t and M to $M^{t'}$

	T	M^1	M^0	Y^{1M^1}	Y^{0M^1}	Y^{1M^0}	Y^{0M^0}
1	1	M_1		Y_1			
2	1	M_2		Y_2			
⋮	⋮	⋮		⋮			
	⋮						
n	0		M_n				Y_n

Effect decomposition

Total causal effect

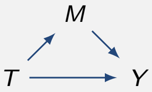


$$E\left[Y^{1M^1} - Y^{0M^0}\right]$$

	T	M^1	M^0	Y^{1M^1}	Y^{0M^1}	Y^{1M^0}	Y^{0M^0}
1	1						
2	1						
⋮							
	⋮						
n	0						

Effect decomposition

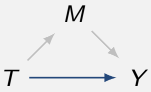
Total causal effect



$$E\left[Y^{1M^1} - Y^{0M^0}\right]$$

=

Natural direct effect

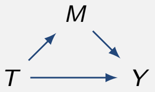


$$E\left[Y^{1M^1} - Y^{0M^1}\right]$$

	T	M^1	M^0	Y^{1M^1}	Y^{0M^1}	Y^{1M^0}	Y^{0M^0}
1	1						
2	1						
⋮							
	⋮						
n	0						

Effect decomposition

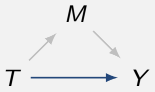
Total causal effect



$$E\left[Y^{1M^1} - Y^{0M^0}\right]$$

=

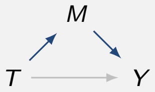
Natural direct effect



$$E\left[Y^{1M^1} - Y^{0M^1}\right]$$

+

Natural indirect effect



$$E\left[Y^{0M^1} - Y^{0M^0}\right]$$

	T	M^1	M^0	Y^{1M^1}	Y^{0M^1}	Y^{1M^0}	Y^{0M^0}
1	1						
2	1						
⋮							
	⋮						
n	0						

Natural effect models (Lange *et al.*, 2012; Vansteelandt *et al.*, 2012)

(Conditional) mean models for nested counterfactuals

$$g\left(E\left[Y^{tM^{t'}}\middle|X\right]\right) = \beta^\top W(t, t', X)$$

E.g., average linear model assuming no effect modification

$$E\left[Y^{tM^{t'}}\right] = \beta_0 + \beta_1 t + \beta_2 t',$$

with parameters β_1 and β_2 indexing the causal effects of interest:

Total causal effect		**Natural direct effect**		**Natural indirect effect**
$E\left[Y^{1M^1} - Y^{0M^0}\right] = \beta_1 + \beta_2$	$=$	$E\left[Y^{1M^1} - Y^{0M^1}\right] = \beta_1$	$+$	$E\left[Y^{0M^1} - Y^{0M^0}\right] = \beta_2$

How to fit natural effect models?

First 'replicate' the data according unobserved (t, t') combinations

	T	t	t'	M^t	$Y^{tM^{t'}}$
1	1	1	1	M_1	Y_1
2	1	1	1	M_2	Y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n

How to fit natural effect models?

First 'replicate' the data according unobserved (t, t') combinations

	T	t	t'	M^t	$Y^{tM^{t'}}$
1	1	1	1	M_1	Y_1
1	1	1	**0**	M_1	.
2	1	1	1	M_2	Y_2
2	1	1	**0**	M_2	.
⋮	⋮	⋮	⋮	⋮	⋮
n	0	0	0	M_n	Y_n
n	0	0	**1**	M_n	.

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First 'replicate' the data according unobserved (t,t') combinations

	T	t	t'	M^t	$Y^{tM^{t'}}$
1	1	1	1	M_1	Y_1
1	1	1	**0**	M_1	.
2	1	1	1	M_2	Y_2
2	1	1	**0**	M_2	.
⋮	⋮	⋮	⋮	⋮	⋮
n	0	0	0	M_n	Y_n
n	0	0	**1**	M_n	.

Then regress either

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	T	t	t'	M^t	$Y^{tM^{t'}}$
1	1	1	1	M_1	Y_1
1	1	1	**0**	M_1	Y_1
2	1	1	1	M_2	Y_2
2	1	1	**0**	M_2	Y_2
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$
n	0	0	0	M_n	Y_n
n	0	0	**1**	M_n	Y_n

Then regress either

1. the observed outcomes Y, weighted by $\frac{\Pr(M = M_i | T = t', X)}{\Pr(M = M_i | T = t, X)}$
   Lange, Vansteelandt and Bekaert (2012)

How to fit natural effect models?

First ‘replicate’ the data according unobserved (t, t') combinations

	T	t	t'	$M^{t'}$	$Y^{tM^{t'}}$
1	1	1	1	M_1	Y_1
1	1	**0**	1	M_1	$\hat{Y}_1^{0M^1}$
2	1	1	1	M_2	Y_2
2	1	**0**	1	M_2	$\hat{Y}_2^{0M^1}$
⋮	⋮	⋮	⋮	⋮	⋮
n	0	0	0	M_n	Y_n
n	0	**1**	0	M_n	$\hat{Y}_n^{1M^0}$

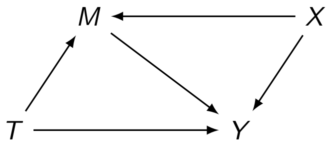
Then regress either

1. the observed outcomes Y, weighted by $\frac{\Pr(M = M_i | T = t', X)}{\Pr(M = M_i | T = t, X)}$ or
   Lange, Vansteelandt and Bekaert (2012)
2. imputed counterfactual outcomes $\hat{Y}^{tM^{t'}}$
   Vansteelandt, Bekaert and Lange (2012)

How to impute ‘missing’ counterfactuals?

Key idea

$$M^{t'} = M \text{ for individuals with } T = t' \Longrightarrow Y^{tM^{t'}} = Y^{tM}$$



Then, given a set of covariates X such that

$$(Y^{tM^{t'}}, M^{t'} : t, t' \in \{0,1\}) \perp\!\!\!\perp T | X \quad (1)$$

$$Y^{tM^{t'}} : t, t' \in \{0,1\} \perp\!\!\!\perp M^t | T, X \quad (2)$$

$Y_i^{tM^{t'}}$ can be imputed by any appropriate model $\hat{E}(Y_i | T = t, M_i, X_i)$

Congeniality concerns

Key concern

finding a coherent model specification between

1. imputer's model for Y
2. analyst's (natural effect) model for $Y^{tM^{t'}}$

Guideline (Loeys *et al.*, 2013)
*"... We thus favor here a **rich imputation model** and a **parsimonious natural effects model** that allows answering the researcher's main questions in a transparent way. We believe that by following this guideline, model incongeniality may have limited impact... [on bias]"*

$\Longrightarrow$ case for routine application of machine learning techniques for imputation model, while keeping natural effect model as parsimonious as possible?

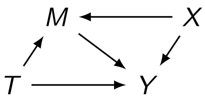
Simulation study

Aim

assess utility of machine learning techniques for imputing $Y^{tM^{t'}}$
wrt potential bias reduction in natural effect model parameters

- Super Learner (van der Laan et al., 2007; Polley et al., 2010)
  loss-based prediction algorithm that combines predictions from a set of machine learning algorithms by optimally weighting them using cross-validation
- recently used for imputing counterfactual outcomes Y^t (Kreif et al., 2014)

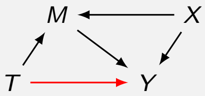
Simulation study



- Data generating mechanism (DGM): $(T, X) \sim N(0, 1)$
- Imputation models
  1. naive: $\hat{E}(Y|T, M, X) = \hat{\theta}_0 + \hat{\theta}_1 T + \hat{\theta}_2 M + \hat{\theta}_3 X$
  2. SL: SuperLearner (machine learning)
  3. correct: consistent with DGM
- Natural effect models
  1. $\hat{E}\left[Y^{tM^{t'}}\right] = \hat{\beta}_0 + \hat{\beta}_1 t + \hat{\beta}_2 t'$
  2. $\hat{E}\left[Y^{tM^{t'}}\middle|X\right] = \hat{\beta}'_0 + \hat{\beta}'_1 t + \hat{\beta}'_2 t' + \hat{\beta}'_3 X$

TY misspecification

Data generating mechanism



$$M|T,X \sim N(1+2T-5X,1)$$

$$Y|T,M,X \sim N(0.5+1.5T+0.8T^2+0.75M+1.5X,1)$$

natural direct effect

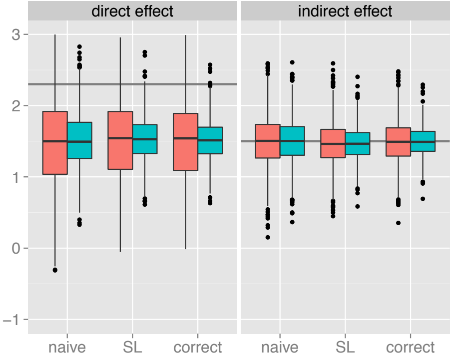
$$E\left[Y^{T+1,M^T}-Y^{TM^T}\middle|X\right]$$

$$=2.3+1.6T$$

natural indirect effect

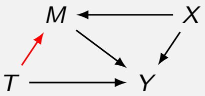
$$E\left[Y^{TM^{T+1}}-Y^{TM^T}\middle|X\right]$$

$$=1.5$$



TM misspecification

Data generating mechanism



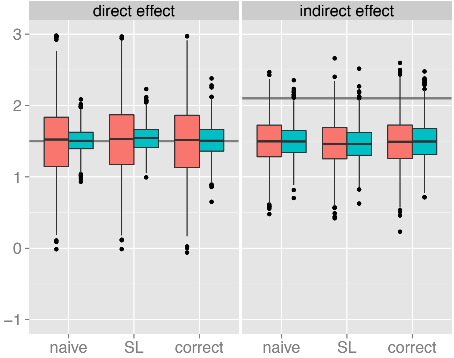
$$M|T,X \sim N(1 + 2T + 0.8T^2 - 5X, 1)$$
$$Y|T,M,X \sim N(0.5 + 1.5T + 0.75M + 1.5X, 1)$$

natural direct effect

$$E\left[Y^{T+1,M^T} - Y^{TM^T}\middle|X\right] = 1.5$$

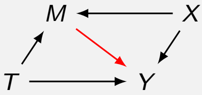
natural indirect effect

$$E\left[Y^{T+1,M^{T+1}} - Y^{T+1,M^T}\middle|X\right] = 2.1 + 1.2T$$



MY misspecification

Data generating mechanism



$$M|T, X \sim N(1 + 2T - 5X, 1)$$

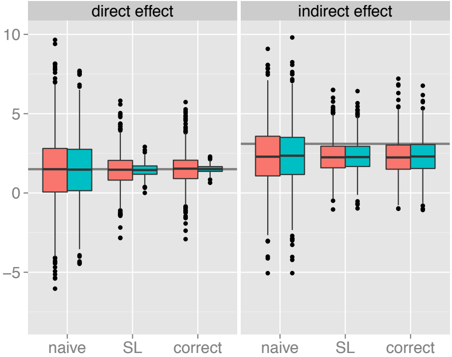
$$Y|T, M, X \sim N(0.5 + 1.5T + 0.75M + 0.2M^2 + 1.5X, 1)$$

natural direct effect

$$E\left[Y^{T+1,M^T} - Y^{TM^T}\middle|X\right] = 1.5$$

natural indirect effect

$$E\left[Y^{T+1,M^{T+1}} - Y^{T+1,M^T}\middle|X\right] = 3.1 + 1.6T - 4X$$



Results and further food for thought

- Biased estimates for effects whose constituent paths are misspecified, irrespective of imputation algorithm
- No implications for other effects
  $\longrightarrow$ what about non-linear models?
- Unbiased estimates under the null, even when natural effect model misspecified
- (Generally) reduced variance for machine learning imputation
  $\longrightarrow$ enhanced power?
- High-dimensional covariates + machine learning = overfitting?
- Application of machine learning: asset compared to direct application of the mediation formula for estimating natural effects

Thanks for listening!
Questions?

thanks to

fwo Research Foundation Flanders
Opening new horizons