

Causal Mediation Using Stata

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Download Website

You can download all of the slides, datasets and do-files here:

https://tinyurl.com/stata-mediation

Acknowledgement



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- Aramayis Dallakyan, PhD is a Senior Statistician at StataCorp.
- My slides are heavily inspired by his talk about causal mediation.
- Many of the slides in my talk are literally copied from his talk.
- All errors are my own



Outline

- Causal Inference
 - Treatment effects with regress
 - Treatment effects with teffects ra
- Mediation
 - Mediation using **regress**
 - Mediation using **sem** and **estat teffects**
 - Mediation using **sem** and **bootstrap**
- Causal Mediation
 - Continuous outcomes with **mediate**
 - Binary outcomes with mediate
 - Count mediators with mediate



- Causal inference tackles the fundamental questions of cause and effect.
- The causal effect aims to compare the outcome when an action T is taken versus the outcome when the action T is withheld.



- We refer to action T as an intervention, an exposure, or a treatment.
 - Effect of a treatment/drug/vaccine on a disease;
 - Effect of social media on mental health;
 - Effect of genes on a disease, etc.



- Why do we need causality?
- Why association or statistical dependence is not enough?
- Association does not imply causation!
- The amount of association and the amount of causation can be different





- Suppose we analyze data where the "treatment" is sleeping with shoes on (or not), and the
 outcome is waking up with a headache (or not) the next day.
- We find that most times when someone wears shoes to bed, that person wakes up with a headache.
- Question: Can we interpret this relationship as causal?



- One possible explanations for association
 - Both treatment and outcome are caused by a common cause: drinking the night before.
 - Such variables are known as confounders and the association as confounding association.
 - Confounding is the main source of differentiating association from causation.



*Borrowed from Neal (2020)



- Our goal: Learn about causal effects
 - Represent the causal structure
 - Characterize the causal effect
- Notation:
 - $T \in \{0,1\}$ denotes treatment assignment: Wearing shoes vs not wearing shoes to bed
 - Y denotes the outcome: Headache vs no headache
 - X denotes potential confounders that affect both T and Y: Drinking the previous day

Directed Acyclic Graphs (DAGs)

Directed acyclic graphs (DAGs)

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- We use DAGs to represent causal relationships and structure.
- Arrows indicate a direct causal effect (not mediated) for at least one subject.
- Informally, the goal of causal inference is to estimate the causal part of the graph while controlling for the confounding part.

Potential Outcomes Framework

• To characterize the causal effect we use the potential outcomes framework.



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- The potential outcome Y(T = t) = Y(t) is the outcome we would have observed had T = t been assigned.
- The causal effect can be measured as Y(1) -Y(0), which is the change due to the treatment keeping everything else the same.



Potential Outcomes Framework

- Fundamental Problem of Causal Inference: Only one of **{Y(1), Y(0)}** is observed.
- The *observed* potential outcome is called **factual.**
- The *unobserved* potential outcome is called **counterfactual**.
- The causal effect is a contrast between two parallel worlds, which we imagine for the same subject.





Potential Outcomes Framework



 Note that compared to the observed world, in imaginary worlds the causal link between X and treatment T is broken.

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Causal Identification



• In general, the causal effect is not the association effect: $E[Y(1)] - E[Y(0)] \neq E[Y|T = 1] - E[Y|T = 0]$



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Treatment Effects With **regress**

. use NHANES2015.dta, clear (Example dataset based on NHANES 2015. Type 'notes _dta' for more information.)

. describe sbp weight meds_bp

Variable name	Storage type	Display format	Value label	Variable label
sbp weight	int double	%9.0g %10.0g		<pre>* Systolic Blood Pressure (mmHg) * Weight (kg)</pre>
meds_bp	byte	%10.0g	meds	* Taking prescription for hypertension

This is observational data, not clinical trial data!

Treatment Effects With **regress**

. list meds_bp weight sbp in 1/10

	meds_bp	weight	sbp
1.	No	53.9	127
2.	No	142.5	109
3.	No	121.2	114
4.	No	96.5	155
5.	No	74.9	112
6.	Yes	74.3	98
7.	Yes	120.7	116
8.	Yes	75.7	130
9.	Yes	62.2	166
10.	Yes	145.1	105

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Treatment Effects With **regress**

Systolic Blood Pressure By Medication Status 250 -Systolic Blood Pressure (mmHg) 200 -150 -100 -50 -Unmedicated

Medicated

Treatment Effects With **regress**

Relationship Between Systolic Blood Pressure and Weight Taking prescription blood pressure medication?



Graphs by Taking prescription for hypertension

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Treatment Effects With **regress**

. list meds_bp weight sbp obs_sbp0 obs_sbp1 in 1/10

	meds_bp	weight	sbp	obs_sbp0	obs_sbp1
1.	No	53.9	127	127	
2.	No	142.5	109	109	•
3.	No	121.2	114	114	
4.	No	96.5	155	155	
5.	No	74.9	112	112	
6.	Yes	74.3	98		98
7.	Yes	120.7	116		116
8.	Yes	75.7	130		130
9.	Yes	62.2	166		166
10.	Yes	145.1	105		105

Treatment Effects With **regress**

. regress sbp	weight if med	ds_bp==0					
Source	SS	df	MS	Numb	er of obs	=	219
				F(1,	217)	=	3.62
Model	872.466244	1	872.466244	Prob	> F	=	0.0583
Residual	52239.1867	217	240.733579	R-sq	uared	=	0.0164
				Adj	R-squared	=	0.0119
Total	53111.653	218	243.631436	Root	MSE	=	15.516
sbp	Coefficient	Std. err.	t	P> t	[95% c	onf.	interval]
weight	.0871461	.0457764	1.90	0.058	00307	73	.1773695
_cons	120.7801	4.152478	29.09	0.000	112.59	58	128.9645

. generate exp_sbp0 = 120.7801 + .0871461*weight

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Treatment Effects With **regress**

. list meds_bp obs_sbp0 obs_sbp1 exp_sbp0 in 1/10

meds_bp	obs_sbp0	obs_sbp1	exp_sbp0
No No	127 109	•	125.5 133.2
No	114		131.3
No	155	•	129.2
No	112	•	127.3
Yes	•	98	127.3
Yes	•	116	131.3
Yes	•	130	127.4
Yes	•	166	126.2
Yes	•	105	133.4
	meds_bp No No No No No Yes Yes Yes Yes Yes	meds_bpobs_sbp0No127No109No114No155No112Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.Yes.	meds_bp obs_sbp0 obs_sbp1 No 127 . No 109 . No 114 . No 155 . No 112 . Yes . 98 Yes . 116 Yes . 130 Yes . 166 Yes . 105

Potential Outcome Y(0)

Treatment Effects With **regress**

. regress sbp weight if meds_bp==1

Source	SS	df	MS	Number of obs	=	1,715
				F(1, 1/13)	=	8.75
Model	3409.90256	1	3409.90256	Prob > F	=	0.0031
Residual	667623.832	1,713	389.73954	R-squared	=	0.0051
				Adj R-squared	=	0.0045
Total	671033.734	1,714	391.501595	Root MSE	=	19.742

sbp	Coefficient	Std. err.	t	P> t	[95% conf.	interval]
weight	0612475	.0207064	-2.96	0.003	1018599	020635
_cons	140.2318	1.858353	75.46	0.000	136.587	143.8767

en exp_sbp1 = 140.2318 - .0612475*weight

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Treatment Effects With regress

. list meds_bp obs_sbp0 obs_sbp1 exp_sbp0 exp_sbp1 in 1/10

	meds_bp	obs_sbp0	obs_sbp1	exp_sbp0	exp_sbp1
1.	No	127	•	125.5	136.9
2.	No	109	•	133.2	131.5
3.	No	114	•	131.3	132.8
4.	No	155	•	129.2	134.3
5.	No	112	•	127.3	135.6
6.	Yes	•	98	127.3	135.7
7.	Yes	•	116	131.3	132.8
8.	Yes	•	130	127.4	135.6
9.	Yes	•	166	126.2	136.4
10.	Yes	•	105	133.4	131.3

Potential Outcome Y(1)

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Treatment Effects With regress

. list meds_bp obs_sbp0 obs_sbp1 exp_sbp0 exp_sbp1 in 1/10

	meds_bp	obs_sbp0	obs_sbp1	exp_sbp0	exp_sbp1
1.	No	127	•	125.5	136.9
2.	No	109	•	133.2	131.5
3.	No	114	•	131.3	132.8
4.	No	155	•	129.2	134.3
5.	No	112	•	127.3	135.6
6.	Yes	•	98	127.3	135.7
7.	Yes	•	116	131.3	132.8
8.	Yes	•	130	127.4	135.6
9.	Yes	•	166	126.2	136.4
10.	Yes	•	105	133.4	131.3

We have estimated the expected sbp assuming **everyone** took the medication and assuming **no one** took the medication.



Potential Outcome Means (POMs)

The potential-outcome means (POMs) are the means of Y_0 and Y_1 in the population.

. mean exp_sbp0 exp_sbp1

Mean estimation

	Mean	Std. err.	[95% conf. interval]
exp_sbp0	128.3497	.0456114	128.2603 128.4392
exp_sbp1	134.9118	.0320563	134.8489 134.9746



Average Treatment Effect (ATE)

- . generate te = exp_sbp1 exp_sbp0
- . mean te

Mean estimation

Number of obs = 1,934

	Mean	Std. err.	[95% conf.	interval]
te	6.562066	.0776677	6.409745	6.714387

The average treatment effect (ATE) is the mean of the difference Y(1) - Y(0).

Treatment Effects With teffects ra

😑 teffe	cts - Treati	ment-effec	ts estima	ation			-		×
Model	by/if/in	Weights	Stat	SE/Robust	Reporting	Maximization	Advanced		
Estimat	tor:								
Regres	sion adju	stment			\sim				
Outcor	ne model:								
Linear		~							
Outcor	ne depend	lent: Out	come in	dependent:					
sbp		~ we	ight					\sim	
			Suppress	constant terr	n from outc	ome model			
meds_	bp								
? C						OK (Cancel	Subm	nit

teffects ra (sbp weight) (meds_bp)

POMs With teffects ra

. teffects ra (sbp weight) (meds_bp), pomeans nolog

Treatment-effe	cts estimation	Number of obs	=	1,934
Estimator	: regression adjustment			
Outcome model	: linear			
Treatment mode	1: none			

sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
POmeans meds bp						
No	128.3498	1.048327	122.43	0.000	126.2951	130.4044
Yes	134.9118	.4772015	282.71	0.000	133.9765	135.8471

. mean exp_sbp0 exp_sbp1

Mean estimation

	Mean	Std. err.	[95% conf.	interval]
exp_sbp0	128.3497	.0456114	128.2603	128.4392
exp_sbp1	134.9118	.0320563	134.8489	134.9746

ATE With teffects ra

. teffects ra (sbp weight) (meds_bp), ate nolog

Treatment-effects estimationNumber of obs=1,934Estimator: regression adjustmentOutcome model: linearTreatment model: none

sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
ATE						
meds_bp (Yes vs No)	6.562067	1.153127	5.69	0.000	4.30198	8.822153
POmean meds_bp No	128.3498	1.048327	122.43	0.000	126.2951	130.4044

. mean te exp_sbp0

Mean estimation

	Mean	Std. err.	[95% conf.	interval]
te	6.562066	.0776677	6.409745	6.714387
exp_sbp0	128.3497	.0456114	128.2603	128.4392

Sneak Preview! ATE with mediate

. mediate (sbp) (weight) (meds_bp), ate nolog

Final EE criterion = 3.83e-29

Causal mediation analysis

Number of obs = 1,934

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Binary

	sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
ATE							
	meds_bp (Yes vs No)	6.489727	1.155656	5.62	0.000	4.224683	8.75477

Note: Outcome equation includes treatment-mediator interaction.

. mean te

Mean estimation

	Mean	Std. err.	[95% conf.	interval]
te	6.562066	.0776677	6.409745	6.714387



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What is Mediation?

"In general, a given variable may be said to function as a mediator to the extent that it accounts for the relation between the predictor and the criterion. Mediators explain how external physical events take on internal psychological significance. Whereas moderator variables specify when certain effects will hold, mediators speak to how or why such effects occur." (Baron & Kenny, 1986, pg 1176).

Stat



Example: Systolic blood pressure (SBP) tends to increase with age. Weight also tends to increase with age. And weight gain is associated with higher SBP. Thus age has a <u>direct effect</u> on SBP but age also has an <u>indirect effect</u> on SBP through its effect on the mediating variable weight.

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What is Mediation?



Direct Effect = c'Indirect Effect $= a^*b$ Total Effect $= c' + a^*b$



Mediation Using **regress**

. use NHANES2015.dta, clear (Example dataset based on NHANES 2015. Type 'notes _dta' for more information.)

. describe sbp weight age

Variable name	Storage type	Display format	Value label	Variable label	
sbp	int	%9.0g		* Systolic Blood Pressure (mmHg)	
weight	double	%10.0g		* Weight (kg)	
age	byte	%10.0g		* Age in years at screening	
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Mediation Using **regress**



weight = $\beta_w + a(age) + e_w$ $sbp = \beta_s + c'(age) + b(weight) + e_s$

Estimate a

. regress weight age if !missing(sbp)

Source	SS	df	MS	Numb	er of obs	; =	7,299
				– F(1,	7297)	=	1054.97
Model	567192.719	1	567192.719	9 Prob) > F	=	0.0000
Residual	3923147.98	7,297	537.638479	9 R-so	uared	=	0.1263
				- Adj	R-squared	1 =	0.1262
Total	4490340.7	7,298	615.28373	5 Root	MSE	=	23.187
	I						
weight	Coefficient	Std. err.	t	P> t	[95% c	conf.	interval]
age	➡.395699	.0121827	32.48	0.000	.37181	.73	.4195807
_cons	58.89463	.5508451	106.92	0.000	57.814	81	59.97444

. scalar a = 0.395699

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a = 0.395699

Estimate **b** and **c'**

. regress sbp age weight

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Source	SS	df	MS	Number of obs	=	7,299
				F(2, 7296)	=	2183.07
Model	915467.252	2	457733.626	Prob > F	=	0.0000
Residual	1529784.89	7,296	209.674464	R-squared	=	0.3744
				Adj R-squared	=	0.3742
Total	2445252.14	7,298	335.057844	Root MSE	=	14.48

sbp	Coefficient	Std. err.	t	P> t	[95% conf.	interval]
age	 .4293534 .1348724 .07427 	.0081394	52.75	0.000	.4133978	.4453091
weight		.0073106	18.45	0.000	.1205414	.1492034
_cons		.5511034	168.89	0.000	91.99395	94.15459

c' = 0.4293534 b = 0.1348724

 \cdot scalar cprime = 0.4293534

. scalar b = 0.1348724

Direct, Indirect and Total Effects

. // DIRECT EFFECT OF age ON sbp

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. display "The Direct Effect of age on sbp is " cprime The Direct Effect of age on sbp is .4293534

- . // INDIRECT EFFECT OF age ON sbp
- . scalar IE = scalar(a)*scalar(b)

. display "The Indirect effect of age on sbp is " IE The Indirect effect of age on sbp is .05336887

- . // TOTAL EFFECT OF age ON sbp
- . scalar c = cprime + scalar(a)*scalar(b)

. display "The Total Effect of age on sbp is " c The Total Effect of age on sbp is .48272227

STa



The <u>direct effect</u> of age on SBP is the estimated coefficient for path c' which is 0.429. Each additional year of age is associated with a 0.429 mm/Hg increase of SBP.

The <u>indirect effect</u> of age on SBP through weight is more subtle. Each additional year of age is associated with a 0.396 kg increase in weight. And each additional kilogram increase of weight is associated with a 0.135 mm/Hg increase in SBP. So the estimate of the indirect effect is the product of the coefficients a and b which equals 0.053.

The **total effect** of age on SBP is the sum of the direct and indirect effects. Thus each year of age is associated with a 0.483 mm/Hg increase in SBP.



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Mediation Using **sem**



Mediation Using **sem**

E SEM	estimatio	on option	IS			_		×
Model	Group	if/in	Weights	SE/Robust	Reporting	Maximization	Advanced	
Model Meth M As	Group od aximum aximum symptotic	if/in likelihood ikelihood	Weights d d with miss tion free	SE/Robust	Reporting	Maximization	Advanced	
? C						ОК	Cano	el

Mediation Using **sem**



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SEM Parameter Estimates

sem (sbp <- age weight) (weight <- age)</pre>

	Coefficient	OIM std. err.	Z	P> z	[95% conf.	interval]
Structural						
sbp						
weight		.0073091	18.45	0.000	.1205467	.149198
age	➡.4293534	.0081378	52.76	0.000	.4134037	.4453032
_cons	93.07427	.5509902	168.92	0.000	91.99435	94.15419
weight						
age	.395699	.0121811	32.48	0.000	.3718246	.4195735
_cons	58.89463	.5507696	106.93	0.000	57.81514	59.97412
<pre>var(e.sbp)</pre>	209.5883	3.469368			202.8976	216.4996
<pre>var(e.weight)</pre>	537.4912	8.897226			520.3328	555.2154

LR test of model vs. saturated: chi2(0) = 0.00

Prob > chi2 = .



. estat teffects

Direct effects

	Coefficient	OIM std. err.	z	P> z	[95% conf.	interval]
Structural sbp						
weight	.1348724	.0073091	18.45	0.000	.1205467	.149198
age	.4293534	.0081378	52.76	0.000	.4134037	.4453032
weight						
age	.395699	.0121811	32.48	0.000	.3718246	.4195735

Indirect effects

	Coefficient	OIM std. err.	z	P> z	[95% conf.	interval]
Structural sbp						
weight	0	(no path)				
age	.0533689	.0033263	16.04	0.000	.0468495	.0598882
weight age	0	(no path)				

Total effects

	Coefficient	OIM std. err.	z	P> z	[95% conf.	interval]
Structural						
sbp						
weight	.1348724	.0073091	18.45	0.000	.1205467	.149198
age	.4827223	.0077819	62.03	0.000	.4674701	.4979745
weight						
age	.395699	.0121811	32.48	0.000	.3718246	.4195735

Direct effects

- Indirect effects

Total effects



estat teffects



Direct effects

	Coefficient	OIM std. err.	Z	P> z	[95% conf.	interval]
Structural sbp						
weight	.1348724	.0073091	18.45	0.000	.1205467	.149198
age	.4293534	.0081378	52.76	0.000	.4134037	.4453032
weight						
age	.395699	.0121811	32.48	0.000	.3718246	.4195735



estat teffects





estat teffects



Total effects

	Coefficient	OIM std. err.	Z	P> z	[95% conf.	interval]
 Structural						
weight age	.1348724 .4827223	.0073091 .0077819	18.45 62.03	0.000 0.000	.1205467 .4674701	.149198 .4979745
weight age	. 395699	.0121811	32.48	0.000	.3718246	.4195735



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The coeflegend option

sem (sbp <- age weight) (weight <- age), coeflegend</pre>

	Coefficient	Legend
Structural sbp		
weight age _cons	.1348724 .4293534 93.07427	_b[sbp:weight] _b[sbp:age] _b[sbp:_cons]
weight age _cons	.395699 58.89463	_b[weight:age] _b[weight:_cons]
<pre>var(e.sbp) var(e.weight)</pre>	209.5883 537.4912	_b[/var(e.sbp)] _b[/var(e.weight)]



The bootstrap prefix

bootstrap direct = (_b[sbp:age]) ///
indirect = (_b[weight:age] * _b[sbp:weight]) ///
total = (_b[sbp:age] + _b[weight:age] * _b[sbp:weight]) ///
, nodots : sem (sbp <- age weight) (weight <- age)</pre>

The bootstrap prefix

```
. bootstrap direct = (_b[sbp:age]) ///
> indirect = (_b[weight:age] * _b[sbp:weight]) ///
> total = (_b[sbp:age] + _b[weight:age] * _b[sbp:weight]) ///
> , nodots reps(500) : sem (sbp <- age weight) (weight <- age)</pre>
```

Bootstrap results

Stata

```
Number of obs = 7,299
Replications = 500
```

```
Command: sem (sbp <- age weight) (weight <- age)
direct: _b[sbp:age]
indirect: _b[weight:age] * _b[sbp:weight]
   total: _b[sbp:age] + _b[weight:age] * _b[sbp:weight]</pre>
```

	Observed coefficient	Bootstrap std. err.	Z	P> z	Normal [95% conf.	-based interval]
direct	.4293534	.0099233	43.27	0.000	.4099041	.4488027
indirect	.0533689	.0034491	15.47	0.000	.0466088	.060129
total	.4827223	.0085877	56.21	0.000	.4658908	.4995538

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😑 mediat	🛿 mediate — Causal mediation analysis – 🗆 🗙									
Model Ł	oy/if/in	Weights	Stat	SE/Robust	Reporting	Optimization	Advanced			
Outcon	Outcome equation									
Model:	Model:									
Linear	Linear 🗸									
Depend	dent vari	able: li	ndepende	nt variables:						
sbp		\sim					~			
		Γ	Suppres	s constant te	rm from out	tcome model				
Madiat										
Medal	or equat	ion								
Linear		~								
- Incor										
Depend	dent vari	able: Ir	ndepende	nt variables:						
weigh	L		٦ с			بالمعمد محماما	×			
		L		is constant te	rm from me	diator model				
Treatme	ent equa	tion								
Variable	e:		Continu	ious treatme	nt	(Examples)				
age		\sim	30 31			Values to es	timate PON	1		
Option	Options									
⊠ No t	No treatment-mediator interaction in the outcome equation									
	Level of treatment variable that is the control									
? C					ОК	Cancel	Subm	it		

Continuous Outcomes With mediate

Final EE criterion = 3.34e-28

Causal mediation analysis

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

sbp	Coefficient	Robust std. err.	z	P> z	[95% conf.	interval]	
AITE							
age (1 vs 0)	.0533689	.0034635	15.41	0.000	.0465805	.0601573	Direct effect
ADTE							
age (1 vs 0)	.4293534	.0094489	45.44	0.000	.4108339	.447873	Indirect effect
ATE							
age (1 vs 0)	.4827223	.0082838	58.27	0.000	.4664864	.4989582	Total effect

Note: Outcome equation does not include treatment-mediator interaction.

Auxiliary Equations With aequations

. mediate (sbp) (weight) (age, continuous(30 31)), ///

> ate nolog nolegend aequations

Final EE criterion = 8.07e-29

Causal mediation analysis

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
ATE						
age						
(1 vs 0)	.4846903	.008329	58.19	0.000	.4683657	.5010148
sbp						
age	.67264	.0288097	23.35	0.000	.6161741	.7291059
weight	.2547316	.0115282	22.10	0.000	.2321367	.2773265
c.weight#c.age	0034775	.0003704	-9.39	0.000	0042035	0027515
_cons	85.44831	.7316597	116.79	0.000	84.01428	86.88233
weight						
age	.395699	.0118989	33.25	0.000	.3723775	.4190205
_cons	58.89463	.5597933	105.21	0.000	57.79745	59.9918

Note: Outcome equation includes treatment-mediator interaction.

😑 mediate — Causal mediation analysis 🦳 🗌									
s Stat	SE/Robust	Reporting	Optimization	Advanced					
Outcome equation									
Linear V									
Independe	ent variables:								
				~					
Suppre	ss constant te	rm from ou	tcome model						
Independe	ent variables:								
				~					
Suppre	ss constant te	erm from me	diator model						
Contin	uous treatme	nt	(Examples)						
			Values to es	timate PON	л				
No treatment-mediator interaction in the outcome equation									
Level of treatment variable that is the control									
		OK	Cancel	Subm	nit				
	liation anal ts Stat Independe Suppre Independe	diation analysis Independent variables: Suppress constant te Continuous treatmee ator interaction in the ou Level of treatment varia	diation analysis ts Stat SE/Robust Reporting Independent variables: Suppress constant term from out Independent variables: Suppress constant term from me Continuous treatment Continuous treatment Level of treatment variable that is the OK	diation analysis — ts Stat SE/Robust Reporting Optimization Independent variables:	diation analysis — □ ts Stat SE/Robust Reporting Optimization Advanced Independent variables:				

mediate (ovar [omvarlist, omodel noconstant])
 (mvar [mmvarlist, mmodel noconstant])
 (tvar [, continuous(numlist)]) [if] [in] [weight] [, stat options]

ovar is a continuous, binary, or count outcome of interest.
omvarlist specifies the covariates in the outcome model.
mvar is the mediator variable and may be continuous, binary, or count.
mmvarlist specifies the covariates in the mediator model.
tvar is the treatment variable and may be binary, multivalued, or continuous.

Mediator	linear	logit	probit	Poisson	exp. mean
Outcome					
linear	Х	Х	Х	Х	Х
logit		Х	Х	Х	
probit	Х	Х	Х	Х	Х
Poisson	Х	Х	Х	Х	Х
exp. mean	Х	Х	Х	Х	Х

Note: X indicates a supported model combination

😑 med	iate — Cau	usal media	tion anal	ysis		_		×			
Model	Model by/if/in Weights Stat SE/Robust Reporting Optimization Advanced										
Statis	Statistics labeled with Pearl's terminology Natural indirect effect Natural direct effect Total effect Pure natural indirect effect Total natural direct effect Statistics labeled with ATE terminology Average indirect treatment effect Average direct treatment effect										
	tal averag	e treatmer	t effect								
	verage ind	irect treatr	nent effe	ct with respe	ct to control	s					
	verage dire	ect treatme	ent effect	with respect	to the treate	d					
Pote Estin	ential-outo mate all ef	come mean fects and p	ns ootential-	outcome me	ans						
? C					OK	Cancel	Subm	it			

Continuous Outcomes With mediate

Stat

stata

stat specifies the statistics to be estimated. You may select from among five effects, each of which can be labeled according to terminology used by Pearl and others or by ATE terminology. In addition to effects, you may request that potential-outcome means be reported. The default is nie nde te.

stat may be one or more of the following:

stat	Definition
nie	natural indirect effect
nde	natural direct effect
te	total effect
pnie	pure natural indirect effect
tnde	total natural direct effect
aite	average indirect treatment effect; synonym for nie
adte	average direct treatment effect; synonym for nde
ate	average treatment effect; synonym for te
aitec	average indirect treatment effect with respect to controls; synonym for pnie
adtet	average direct treatment effect with respect to the treated; synonym for tnde
pomeans	potential-outcome means

all specifies that all effects and potential-outcome means be estimated; specifying all is equivalent to specifying nie nde te pnie tnde pomeans. When option ateterms is specified, all is equivalent to specifying aite adte ate aitec adtet pomeans.



Causal Mediation



Suppose using the Fundamental Steps of Causal Analysis (FSCA), a researcher concluded that age has a causal effect on SBP.



But the researcher wonders whether the increase in SBP is a consequence of the effect of age (T) on weight (M) which increases SBP (Y)

That is, the researcher is interested in decomposing the total effect of T on Y into the indirect causal pathway mediated by M and the direct pathway not mediated by M.



Preparing For Causal Identification



- Recall that our interest is in the contrast Y(1) Y(0)
- For mediation, the idea is to split the contrast Y(1) Y(0) into two other contrasts using a third potential outcome M(t).



- We introduce a new type of outcome Y(t,m), which corresponds to the potential outcome when we set T = t and M=m.
- Note the familiar Y(1) = Y[1, M(1)] and Y(0) = Y[0, M(0)].

Potential Outcome Means With mediate

. mediate (sbp) (weight) (age, continuous(30 31)), pomeans nolegend

Iteration 0: EE criterion = 3.203e-25 Iteration 1: EE criterion = 2.057e-28

Causal mediation analysis

stata

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

Robust Coefficient std. err. P>|z| [95% conf. interval] sbp Z POmeans YOMO 116.2711 .1742669 667.20 0.000 115.9295 116.6126 Y1M0 116.6976 .1751862 666.13 0.000 116.3543 117.041 Y0M1 116.3306 .1740157 668.51 0.000 115.9895 116.6716 Y1M1 116.7558 .1747872 667.99 0.000 116.4132 117.0983

Note: Outcome equation includes treatment-mediator interaction.

Number of obs = 7,299

POMs With gsem and nlcom

. gsem (sbp <- c.age##c.weight) (weight <- age), ///
> nolog noheader listwise coeflegend

stata

	Coefficient	Legend
sbp		
weight age	.2547316 .67264	_b[sbp:weight] _b[sbp:age]
c.age#c.weight	0034775	_b[sbp:c.age#c.weight]
cons	85.44831	_b[sbp:_cons]
weight		
age	.395699	_b[weight:age]
_cons	58.89463	_b[weight:_cons]
<pre>var(e.sbp) var(e.weight)</pre>	206.705 537.4912	_b[/var(e.sbp)] _b[/var(e.weight)]



POMs With gsem and nlcom

Expected value of SBP assuming everyone is 30 years old (not treated)



	Coefficient	Std. err.	Z	P> z	[95% conf.	interval]
YOMO	116.2711	.2027684	573.42	0.000	115.8737	116.6685



POMs With gsem and nlcom

Expected value of SBP assuming everyone is 31 years old (treated)



	Coefficient	Std. err.	z	P> z	[95% conf.	interval]
Y1M1	116.7558	.1999727	583.86	0.000	116.3638	117.1477

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. nlcom		///
<pre>> (Y0M0: _b[sbp:_cons]</pre>		///
<pre>> + _b[sbp:age]*30</pre>		///
<pre>> + _b[sbp:weight]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*30)</pre>	///
<pre>> + _b[sbp:c.weight#c.age]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*30) *</pre>	30) ///
<pre>> (Y1M0: _b[sbp:_cons]</pre>		///
<pre>> + _b[sbp:age]*31</pre>		///
<pre>> + _b[sbp:weight]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*30)</pre>	///
<pre>> + _b[sbp:c.weight#c.age]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*30) *</pre>	31) ///
<pre>> (Y0M1: _b[sbp:_cons]</pre>		///
<pre>> + _b[sbp:age]*30</pre>		///
<pre>> + _b[sbp:weight]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*31)</pre>	///
<pre>> + _b[sbp:c.weight#c.age]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*31) *</pre>	30) ///
<pre>> (Y1M1: _b[sbp:_cons]</pre>		
<pre>> + _b[sbp:age]*31</pre>		
<pre>> + _b[sbp:weight]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*31)</pre>	
<pre>> + _b[sbp:c.weight#c.age]</pre>	<pre>* (_b[weight:_cons] + _b[weight:age]*31) *</pre>	31)

	Coefficient	Std. err.	Z	P> z	[95% conf.	interval]
YOMO	116.2711	.2027684	573.42	0.000	115.8737	116.6685
Y1M0	116.6976	.1999543	583.62	0.000	116.3057	117.0895
YOM1	116.3306	.202873	573.42	0.000	115.933	116.7282
Y1M1	116.7558	.1999727	583.86	0.000	116.3638	117.1477



Different Treatment Effects

• Denoting E[Y(t,M(t'))] as $Y_{tM_{t'}}$, we define the following treatment effects of interest:

(Total) natural indirect effect (NIE)	$Y_{1M_1} - Y_{1M_0}$	δ(1)
(Pure) natural direct effect (NDE)	$Y_{1M_0} - Y_{0M_0}$	ζ (0)
(Pure) natural indirect effect (PNIE)	$Y_{0M_1} - Y_{0M_0}$	δ(0)
(Total) natural direct effect (TNDE)	$Y_{1M_1} - Y_{0M_1}$	ζ(1)
Total effect (TE)	$Y_{1M_1} - Y_{0M_0}$	τ

. mediate (sbp) (weight) (age, continuous(30 31)), all nolegend

Iteration 0: EE criterion = 3.266e-25 Iteration 1: EE criterion = 6.029e-28

Causal mediation analysis

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

			Robust					
	sbp	Coefficient	std. err.	z	P> z	[95% conf.	interval]	
POmea	ans							
	YØMØ	116.2711	.1742669	667.20	0.000	115.9295	116.6126	
	Y1M0	116.6976	.1751862	666.13	0.000	116.3543	117.041	
	YØM1	116.3306	.1740157	668.51	0.000	115.9895	116.6716	
	Y1M1	116.7558	.1747872	667.99	0.000	116.4132	117.0983	
NIE								
	age (1 vs 0)	.0581394	.0033109	17.56	0.000	.0516503	.0646286	Total Natural Indirect Effect Y1M1 - Y1M0
NDE								
	age							Pure Natural Direct Effect V1N/0 V0N/0
	(1 vs 0)	.4265509	.0092994	45.87	0.000	.4083243	.4447774	
PNIE								
	age							Pure Natural Indirect Effect YOM1 - YOM0
	(1 vs 0)	.0595155	.0032948	18.06	0.000	.0530577	.0659732	
TNDE								
	age							Total Natural Direct Effect Y1M1 - Y0M1
	(1 vs 0)	.4251748	.0092848	45.79	0.000	.4069769	.4433727	
TE								
	age							Total Effect V1N11 - V0N10
	(1 vs 0)	.4846903	.008329	58.19	0.000	.4683657	.5010148	
		I						

Note: Outcome equation includes treatment-mediator interaction.


- Practical question remains: For a specific analysis, which decomposition should be used? $\tau = \delta(1) + \zeta(0)$ or $\tau = \delta(0) + \zeta(1)$
- Or should both be used?
- We follow Nguyen et al. (2020) and propose three answers for three cases.



Case 1: Is there a mediated effect? Or, is the causal effect partly mediated by this mediator?

- We propose using $\tau = \delta(1) + \zeta(0)$ decomposition (NIE and NDE)
- Rational: Here, we are not questioning the existence of a direct effect.
- We are researching the possibility of a mediated effect to the direct effect.
- If there is no mediated effect, then the total effect $\tau = \zeta(0)$ is the direct effect.

. mediate (sbp) (weight) (age, continuous(30 31)), nie nde nolegend

Iteration 0: EE criterion = 3.193e-25 Iteration 1: EE criterion = 7.329e-29

Causal mediation analysis

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

		sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
NIE								
		age						
	(1 vs	0)	.0581394	.0033109	17.56	0.000	.0516503	.0646286
NDE								
		age						
	(1 vs	0)	.4265509	.0092994	45.87	0.000	.4083243	.4447774



Case 2: In addition to the mediated effect, is there a direct effect?

- We propose using $\tau = \delta(0) + \zeta(1)$ decomposition (PNIE and TNDE).
- This is a mirror image of the Case 1.
- Rational: Here, we are not questioning the existence of a mediator effect.
- We are researching the possibility of treatment affecting the outcome through other mechanisms.
- If there is no direct effect, then the total effect $\tau = \delta(0)$ is the indirect effect.

. mediate (sbp) (weight) (age, continuous(30 31)), pnie tnde nolegend

Iteration 0: EE criterion = 3.218e-25 Iteration 1: EE criterion = 2.812e-28

Causal mediation analysis

stata

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

		sbp	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
PNIE								
		age						
	(1 v	50)	.0595155	.0032948	18.06	0.000	.0530577	.0659732
TNDE								
		age						
	(1 v	50)	.4251748	.0092848	45.79	0.000	.4069769	.4433727



Case 3: No prior assumption or preferred question about either direct or indirect effect

- We propose reporting both $\tau = \delta(1) + \zeta(0)$ and $\tau = \delta(0) + \zeta(1)$ decompositions.
- **Rational:** If the purpose is to describe all we can learn, there is no reason to prefer wither decomposition over the other.

. mediate (sbp) (weight) (age, continuous(30 31)), nie nde pnie tnde nolegend

Iteration 0: EE criterion = 3.228e-25 Iteration 1: EE criterion = 3.507e-28

Causal mediation analysis

Number of obs = 7,299

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

-									
			sbp	Coefficient	Robust std. err.	z	P> z	[95% conf.	interval]
NIE									
	(1	vs	age 0)	.0581394	.0033109	17.56	0.000	.0516503	.0646286
NDE									
	(1	vs	age 0)	.4265509	.0092994	45.87	0.000	.4083243	.4447774
PNIE									
	(1	vs	age 0)	.0595155	.0032948	18.06	0.000	.0530577	.0659732
TNDE									
	(1	vs	age 0)	.4251748	.0092848	45.79	0.000	.4069769	.4433727

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Causal Identification: Assumptions



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Sequential ignorabilty

- 1. No unobserved confounding in the treatment-outcome relationship.
- 2. No unobserved confounding in the mediator-outcome relationship.
- 3. No unmeasured confounding in the treatmentmediator relationship
- 4. No (observed) confounders in the mediator-outcome relationship that are caused by the treatment.

In addition to sequential ignorability, we need SUTVA and overlap assumptions.

STATA Data Analysis and Statistical Software

Continuous Outcomes With mediate

. mediate (sbp i.healthstat calories) /// (weight i.healthstat calories) >

111

(age, continuous(30 31)), nolegend >

Iteration 0: EE criterion = 2.881e-26 Iteration 1: EE criterion = 9.487e-29

Causal mediation analysis

Number of obs = 4,876

Outcome model: Linear Mediator model: Linear Mediator variable: weight Treatment type: Continuous

		sbp	Coefficient	Robust std. err.	z	P> z	[95% conf.	interval]
NIE								
		age						
	(1 vs	5 Ø)	.0201403	.0026806	7.51	0.000	.0148864	.0253943
NDE								
		age						
	(1 vs	50)	.4048525	.0109781	36.88	0.000	.3833358	.4263692
TE								
		age						
	(1 vs	5 0)	.4249928	.0110645	38.41	0.000	.4033068	.4466788



Continuous Outcomes With mediate

. estat proportion

Proportion mediated

Number of obs = 4,876

Continuous treatment levels: 0: age = 30 (control) 1: age = 31

sbp	Proportion	Robust std. err.	Z	P> z	[95% conf.	interval]
age (1 vs 0)	.0473898	.0062387	7.60	0.000	.0351623	.0596174

Outline

- Causal Inference
- Treatment effects with regress
- ✓ Treatment effects with teffects ra
- Mediation
- Mediation using regress
- Mediation using sem and estat teffects
- Mediation using sem and bootstrap
- Causal Mediation
- Continuous outcomes with mediate
 - Binary outcomes with mediate
 - Count mediators with mediate

STATA Data Analysis and Statistical Software

Binary Outcomes With mediate

. mediate (hypertension i.healthstat calories, logit) ///

> (hx_overweight i.healthstat calories, logit) ///

> (age, continuous(30 31)), nolegend

Iteration 0: EE criterion = 4.470e-21 Iteration 1: EE criterion = 3.422e-32

Causal mediation analysis

Number of obs = 4,459

Outcome model: Logit Mediator model: Logit Mediator variable: hx_overweight Treatment type: Continuous

			Robust				
	hypertension	Coefficient	std. err.	Z	P> z	[95% conf.	interval]
NIE							
	age						
	(1 vs 0)	.0002823	.000064	4.41	0.000	.0001569	.0004077
NDE							
	age						
	(1 vs 0)	.0118771	.0003093	38.40	0.000	.0112708	.0124834
TE							
	age						
	(1 vs 0)	.0121594	.0002964	41.03	0.000	.0115785	.0127403



Risk Ratios

- If the outcome is binary, and if the outcome model is either logit or probit, we can express the treatment effects as risk ratios or odds ratios.
- The treatment effects on risk-ratio are ratios of potential-outcome means:

$$NIE^{RR} = \frac{Y_{1M_{1}}}{Y_{1M_{0}}}$$
$$NDE^{RR} = \frac{Y_{1M_{0}}}{Y_{0M_{0}}}$$
$$PNIE^{RR} = \frac{Y_{0M_{1}}}{Y_{0M_{0}}}$$
$$TNDE^{RR} = \frac{Y_{1M_{1}}}{Y_{0M_{1}}}$$
$$TE^{RR} = \frac{Y_{1M_{1}}}{Y_{0M_{0}}}$$



Risk Ratios With estat rr

. estat rr estat rr requires potential-outcome means; refitting model ...

Transformed treatment effects

Number of obs = 4,459

Continuous treatment levels:

0: age = 30 (control) 1: age = 31

stata

hypertension	Risk ratio	Robust std. err.	z	P> z	[95% conf.	interval]
NIE						
age						
(1 vs 0)	1.001121	.0002547	4.40	0.000	1.000622	1.00162
NDE						
age						
(1 vs 0)	1.049488	.002289	22.15	0.000	1.045011	1.053984
TE						
age						
(1 vs 0)	1.050664	.0022799	22.78	0.000	1.046205	1.055142



Odds Ratios

• For logit and probit outcome models, Y_{tM_t} , are probabilities, and so the treatment effects on the odds-ratio scale are

$$\begin{split} NIE^{OR} &= \frac{Y_{1M_1}/(1-Y_{1M_1})}{Y_{1M_0}/(1-Y_{1M_0})} \\ NDE^{OR} &= \frac{Y_{1M_0}(1-Y_{1M_0})}{Y_{0M_0}(1-Y_{0M_0})} \\ PNIE^{OR} &= \frac{Y_{0M_1}(1-Y_{0M_1})}{Y_{0M_0}(1-Y_{0M_0})} \\ TNDE^{OR} &= \frac{Y_{1M_1}(1-Y_{1M_1})}{Y_{0M_1}(1-Y_{0M_1})} \\ TE^{OR} &= \frac{Y_{1M_1}(1-Y_{1M_1})}{Y_{0M_0}(1-Y_{0M_0})} \end{split}$$

• Similar to risk-ratio, the total effect is the **product** of direct and indirect effect.



Odds Ratios With estat or

. estat or

estat or requires potential-outcome means; refitting model ...

Transformed treatment effects

Number of obs = 4,459

Continuous treatment levels:

0: age = 30 (control)

1: age = 31

hypertension	Odds ratio	Robust std. err.	Z	P> z	[95% conf.	interval]
NIE						
age						
(1 vs 0)	1.001499	.0003395	4.42	0.000	1.000833	1.002164
NDE						
age						
(1 vs 0)	1.066149	.0024518	27.85	0.000	1.061355	1.070966
TE						
age						
(1 vs 0)	1.067747	.0024108	29.03	0.000	1.063032	1.072483

Data Analysis and Statistical Software

Continuous Treatment With Multiple Values

> (age, continuous(30 31 35)), nolegend

stata

	hypertension	Coefficient	Robust std. err.	Z	P> z	[95% conf.	interval]
	21					L.	
NIE							
	age						
	(1 vs 0)	.0002823	.000064	4.41	0.000	.0001569	.0004077
	(2 vs 0)	.001543	.0003315	4.65	0.000	.0008933	.0021927
NDE							
	age						
	(1 vs 0)	.0118771	.0003093	38.40	0.000	.0112708	.0124834
	(2 vs 0)	.0630108	.0017107	36.83	0.000	.0596579	.0663637
TE							
	age						
	(1 vs 0)	.0121594	.0002964	41.03	0.000	.0115785	.0127403
	(2 vs 0)	.0645538	.0016592	38.91	0.000	.0613019	.0678057

[.] mediate (hypertension i.healthstat calories, logit) ///

> (hx_overweight i.healthstat calories, logit) ///

Continuous Treatment With Multiple Values

. estat or estat or requires potential-outcome means; refitting model ...

Transformed treatment effects

Number of obs = 4,459

Continuous treatment levels:

0: age = 30 (control)

- 1: age = 31
- 2: age = 35

hypertension	0dds ratio	Robust std. err.	Z	P> z	[95% conf	. interval]
NIE						
age	2					
(1 vs 0)	1.001499	.0003395	4.42	0.000	1.000833	1.002164
(2 vs 0)	1.007322	.0015833	4.64	0.000	1.004224	1.01043
NDE						
age	2					
(1 vs 0)	1.066149	.0024518	27.85	0.000	1.061355	1.070966
(2 vs 0)	1.376683	.0155514	28.30	0.000	1.346538	1.407503
TE						
age	•					
(1 vs 0)	1.067747	.0024108	29.03	0.000	1.063032	1.072483
(2 vs 0)	1.386763	.0154809	29.29	0.000	1.356751	1.41744



estat effectplot



Outline

- Causal Inference
- Treatment effects with regress
- ✓ Treatment effects with teffects ra
- Mediation
- Mediation using regress
- Mediation using sem and estat teffects
- Mediation using sem and bootstrap
- Causal Mediation
- Continuous outcomes with mediate
- Binary outcomes with mediate
 - Count mediators with mediate

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Count Mediators With mediate

. mediate (sbp) (smokenum, poisson) (age, continuous(30 31)), ///
> nolog nolegend

Final EE criterion = 4.60e-29

Causal mediation analysis

Number of obs = 1,035

Outcome model: Linear Mediator model: Poisson Mediator variable: smokenum Treatment type: Continuous

		sbp	Coefficient	Robust std. err.	z	P> z	[95% conf.	interval]
NIE								
		age						
	(1 vs	5 0)	.0024086	.0066381	0.36	0.717	0106018	.015419
NDE								
		age						
	(1 vs	50)	.4576963	.0339078	13.50	0.000	.3912383	.5241544
TE								
		age						
	(1 vs	5 0)	.4601049	.0333714	13.79	0.000	.3946983	.5255116



Count Mediators With mediate

```
. estat cde, mvalue(20)
```

Controlled direct effect

Mediator variable: smokenum Mediator value = 20

```
Continuous treatment levels:
    0: age = 30 (control)
    1: age = 31
```

Number of obs = 1,035

	CDE	Delta-method std. err.	z	P> z	[95% conf.	interval]
age (1 vs 0)	.4478632	.051657	8.67	0.000	.3466173	.549109

Outline

- Causal Inference
- Treatment effects with regress
- ✓ Treatment effects with teffects ra
- Mediation
- Mediation using regress
- Mediation using sem and estat teffects
- Mediation using sem and bootstrap
- Causal Mediation
- Continuous outcomes with mediate
- Binary outcomes with mediate
- Count mediators with mediate



References

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Thank you!

Questions?

You can download the slides, datasets, and do-files here: https://tinyurl.com/stata-mediation

You can contact me anytime at <u>chuber@stata.com</u>