mediate multiple — Causal mediation analysis (two mediators)+

+The two-mediator version of this command is part of StataNow.

Description

mediate fits causal mediation models and estimates effects of a treatment on an outcome. The treatment effect can occur both directly and indirectly through other variables, mediators.

In this entry, we describe how mediate can be used to perform causal mediation analysis with two mediator variables. The relationship between the mediators can take one of two forms. Causal mediation models where there is no causal relationship between mediators are known as parallel mediation models. Causal mediation models where the mediators are causally ordered, with one mediator predicting the other, are known as sequential mediation models.

mediate estimates direct, indirect, and total effects. The natural direct and indirect effects reflect the finest possible decomposition of total effects into their path-specific components. Because the number of effects is potentially large with two mediators, mediate also offers coarser decompositions.

For an introduction to causal mediation analysis, see [CAUSAL] **mediate intro**. For the use of mediate to fit causal mediation models with one mediator, see [CAUSAL] **mediate**.

Quick start

Fit a parallel mediation model with two mediators m1 and m2, outcome variable y, and treatment t

```
mediate (y) (m2) (m1) (t)
```

Same as above, but with covariates in the outcome and mediator equations

```
mediate (y x1 x2) (m2 x1 x3) (m1 x1 x2 x3) (t)
```

Fit a sequential mediation model where m1 is a predictor of m2

```
mediate (y x1 x2) (m2 x1 x3) (m1 x1 x2 x3) (t), sequential
```

Same as above, but add treatment–mediator interactions in the equation for y

```
mediate (y x1 x2) (m2 x1 x3) (m1 x1 x2 x3) (t), sequential tinteraction
```

Same as above, but add the mediator–mediator interaction in the equation for y

```
mediate (y x1 x2) (m2 x1 x3) (m1 x1 x2 x3) (t), sequential tinteraction ///
minteraction
```

Same as above, but add the treatment–mediator interaction in the equation for m2

```
mediate (y x1 x2) (m2 x1 x3) (m1 x1 x2 x3) (t), sequential tinteraction ///
minteraction meqtinteraction
```

Same as above, but add covariate interactions with the treatment and mediators in the outcome equation

```
mediate (y x1 x2 i.t#c.(x1 x2) c.m2#c.(x1 x2) c.m1#c.(x1 x2))          ///
    (m2 x1 x3) (m1 x1 x2 x3) (t),                                      ///
    sequential tinteraction minteraction meqtinteraction
```

Sequential mediation model with type-1 mediator-specific effects

```
mediate (y x1 x2) (m2 x3) (m1 x1) (t), sequential mseffects(m1)
```

Fit sequential mediation model with continuous treatment t2, and evaluate at values 0 and 3 of the treatment with 0 as the control

```
mediate (y x1 x2) (m2 x3) (m1 x1) (t2, continuous(0 3)), sequential
```

Menu

Statistics > Causal inference/treatment effects > Continuous outcomes > Causal mediation

Syntax

mediate (*ovar* [*omvarlist*, noconstant])
  (*mvar*$_2$ [*mmvarlist*$_2$, noconstant])
  (*mvar*$_1$ [*mmvarlist*$_1$, noconstant])
  (*tvar* [, continuous(*numlist*)]) [*if*] [*in*] [*weight*] [, *stat options*]

ovar is a continuous outcome of interest.

omvarlist specifies the covariates in the outcome model.

mvar$_2$ is a continuous mediator variable (the second mediator for sequential mediators).

mmvarlist$_2$ specifies the covariates in the *mvar*$_2$ model.

mvar$_1$ is a continuous mediator variable (the first mediator for sequential mediators).

mmvarlist$_1$ specifies the covariates in the *mvar*$_1$ model.

tvar is the treatment variable and may be binary or continuous.

stat	Description
Stat	
nie	natural indirect effects
nde	natural direct effects
te	total effect
pomeans	potential-outcome means

Multiple effects may be specified. The default is nie nde te. You may not specify nie, nde, or te in combination with pomeans.

options	Description
Options	
parallel	fit a parallel mediation model; the default
sequential	fit a sequential mediation model
tinteraction[(*mvar*$_1$ | *mvar*$_2$)]	include interactions of mediators and treatment in outcome model
minteraction	include interaction among mediators in outcome model
meqtinteraction	include interaction of first mediator and treatment in second mediator model
mseffects(*mvar*$_1$ | *mvar*$_2$)	estimate mediator-specific natural effects for mediator *mvar*$_1$ or mediator *mvar*$_2$
control(# | *label*)	specify the level of *tvar* that is the control; default is first treatment level
SE/Robust	
vce(*vcetype*)	*vcetype* may be robust, cluster *clustvar*, bootstrap, or jackknife
nose	do not estimate standard errors
Reporting	
level(#)	set confidence level; default is level(95)
aequations	display auxiliary-equation results
nolegend	suppress table legend
display_options	control columns and column formats, row spacing, line width, display of omitted variables and base and empty cells, and factor-variable labeling
Optimization	
optimization_options	control the optimization process; seldom used
Advanced	
coeflegend	display legend instead of statistics

omvarlist and *mmvarlist* may contain factor variables; see [U] **11.4.3 Factor variables**.

bayesboot, bootstrap, by, collect, jackknife, and statsby are allowed; see [U] **11.1.10 Prefix commands**.

Weights are not allowed with the bootstrap prefix; see [R] **bootstrap**.

pweights, fweights, and iweights are allowed; see [U] **11.1.6 weight**.

coeflegend does not appear in the dialog box.

See [U] **20 Estimation and postestimation commands** for more capabilities of estimation commands.

Options

Model

`noconstant`; see [R] **Estimation options**.

`continuous(`*numlist*`)` specifies that the treatment variable is continuous; *numlist* specifies the values at which the potential-outcome means are to be evaluated, where the first value in the list is taken as the control.

Options

`parallel` fits a parallel mediation model where there is no causal relationship between mediators; this is the default.

`sequential` fits a sequential mediation model where there is a causal order among mediators. In this case, the mediators should be specified such that $mvar_1$ is assumed to predict $mvar_2$.

`tinteraction[(`$mvar_1$ | $mvar_2$`)]` includes the interaction between the treatment and one or both mediators in the model for the outcome. If one of the mediator names, $mvar_1$ or $mvar_2$, is specified, only the interaction with that mediator is included. If `tinteraction` is specified without a mediator name, the model includes treatment–mediator interactions for both mediator variables.

`minteraction` includes the interaction between two mediators in the model for the outcome.

When `minteraction` is specified with `tinteraction`, the three-way interaction between the treatment and both mediators is also included in the model for the outcome.

`meqtinteraction` includes the interaction between the treatment and the first mediator in the model for the second mediator. This option is available only when the `sequential` option is specified to fit a sequential mediation model.

`mseffects(`$mvar_1$ | $mvar_2$`)` specifies that mediator-specific natural effects for the specified mediator be reported. Specifying $mvar_1$ yields type-1 mediator-specific natural effects. Specifying $mvar_2$ yields type-2 mediator-specific natural effects. This option is available only when the `sequential` option is specified to fit a sequential mediation model.

`control(`# | *label*`)` specifies the level of *tvar* that is the control. The default is the first treatment level. You may specify the numeric level # (a nonnegative integer) or the label associated with the numeric level. `control()` may not be specified with continuous treatments.

Stat

stat specifies the statistics to be estimated. In addition to natural 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 effects
`nde`	natural direct effects
`te`	total effect
`pomeans`	potential-outcome means

Multiple effects may be specified. You may not specify `nie`, `nde`, or `te` in combination with `pomeans`.

SE/Robust

`vce(`*vcetype*`)` specifies the type of standard error reported, which includes types that are robust to some kinds of misspecification (`robust`), that allow for intragroup correlation (`cluster` *clustvar*), and that use bootstrap or jackknife methods (`bootstrap`, `jackknife`); see [R] ***vce_option***.

`nose` suppresses calculation of the variance–covariance matrix and standard errors.

Reporting

`level(#)`; see [R] **Estimation options**.

`aequations` specifies that the estimation results for the outcome model and the mediator model be displayed. By default, they are not displayed.

`nolegend` suppresses the display of the table legend.

display_options: `noci`, `nopvalues`, `noomitted`, `vsquish`, `noemptycells`, `baselevels`, `allbaselevels`, `nofvlabel`, `fvwrap(#)`, `fvwrapon(`*style*`)`, `cformat(%`*fmt*`)`, `pformat(%`*fmt*`)`, `sformat(%`*fmt*`)`, and `nolstretch`; see [R] **Estimation options**.

Optimization

optimization_options: `conv_maxiter()`, `conv_ptol()`, `conv_vtol()`, `tracelevel()`, and [`no`]`log`. See [M-5] **optimize( )**.

`conv_maxiter(#)` specifies the maximum number of iterations. The default is the number set using `set maxiter`, which by default is 300.

`conv_ptol(#)` specifies the convergence criteria for the parameters. The default is `conv_ptol(1e-6)`.

`conv_vtol(#)` specifies the convergence criteria for the gradient. The default is `conv_vtol(1e-7)`.

`tracelevel(`*tracelevel*`)` allows you to display additional information about the iterative process in the iteration log. *tracelevel* may be `none`, `value`, `tolerance`, `step`, `params`, or `gradient`. See *tracelevel* in [M-5] **optimize( )** for details.

`log` and `nolog` specify whether to display the iteration log. The iteration log is displayed by default unless you used `set iterlog off` to suppress it; see `set iterlog` in [R] ***set iter***.

Advanced

The following option is available with `mediate` but is not shown in the dialog box:

`coeflegend`; see [R] **Estimation options**.

Remarks and examples

Remarks are presented under the following headings:

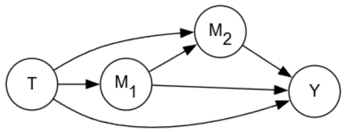
Introduction

In this entry, we discuss practical and theoretical aspects of causal mediation with two mediators, and we provide examples of fitting these models with the `mediate` command. For a general introduction to causal mediation, we recommend that you first read [CAUSAL] **mediate intro**.

In causal mediation analysis with two mediators, we first need to consider the relationship among the mediators. When one mediator is presumed to predict the other, we refer to them as sequential mediators. When there is no presumption of one mediator predicting the other, we refer to them as parallel mediators. The `mediate` command allows us to estimate total, direct, and indirect effects of interest when mediators are sequential or parallel. The estimates are derived from a potential-outcomes framework, and the framework for the two-mediator case is an extension of the framework for the one-mediator case that is described in [CAUSAL] **mediate**. With two mediators, however, the number and complexity of potential outcomes increases. In the following sections, we provide an introduction into the intricacies of causal mediation with multiple mediators that is more technical than the one in [CAUSAL] **mediate intro**. For both sequential and parallel mediation models, we formally define the potential outcomes and the effects and discuss how to estimate them. We also show all of the ways that the total effects can be decomposed into the direct and indirect effects. We follow the derivations and definitions presented in Daniel et al. (2015). You may prefer to read this technical introduction and then the examples demonstrating `mediate`, or if you are already familiar with technical concepts of mediation analysis for multiple mediators, you may prefer to go directly to *Examples* and then refer back to the definitions and decompositions as they relate to the examples at hand.

Sequential mediators

Suppose we have the following causal model involving treatment T, first mediator M_1, second mediator M_2, and outcome Y:



There are four path-specific effects of interest: the direct effect from T to Y (that is, the effect of T on Y not mediated by either M_1 or M_2); one effect through M_1 alone; one through M_2 alone; and one through both M_1 and M_2. These four effects combined will sum to the total causal effect.

We define the effects based on potential outcomes. When we had a single mediator, our potential outcomes took the form $Y_i\{t, M_i(t')\}$, where t can be counterfactually set in two places. Multiple mediators increase the complexity and number of the potential outcomes. With these two mediators, and given the two are causally ordered, our potential outcomes of interest take on the form $Y_i[t, M_{1i}(t'), M_{2i}\{t'', M_{1i}(t''')\}]$. Notice that we can counterfactually set t in four places now: with respect to the outcome, with respect to the first mediator, with respect to the second mediator, and with respect to the first mediator as component of the potential outcomes of the second mediator. The direct and indirect effects are derived as expected differences in these potential outcomes. This leads to eight variations of each path-specific effect rather than the two variations (pure and total) in the single-mediator case. With 4 path-specific effects of interest and 8 variations of each one, we can estimate a maximum of 32 effects (plus the total effect) for 2 causally ordered mediators.

With a single mediator, there were two possible decompositions of the total effect into direct and indirect effects. With multiple mediators, there are many ways that total effect can be decomposed into sums of its path-specific components. In fact, with k mediators, there are $2^k!$ decompositions. Thus, for models with a single mediator, we have only two decompositions. However, in the case with 2 sequential mediators, we have 24 distinct decompositions of the total causal effect. This becomes infeasible quickly if we want to add more mediators. With only 3 mediators, the number of distinct decompositions grows to 40,320, and with 4 mediators, we would be looking at over 20 trillion decompositions.

The following table shows an overview of all possible effect estimands as well as their corresponding potential-outcome means contrast. When you use `mediate` to estimate effects, you can refer to this table to see how each effect is defined in terms of the potential outcomes.

Table 1

Path	Effect	Definition
Direct (through neither M_1 nor M_2)	NDE-000	$E(Y[1, M_1(0), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
	NDE-100	$E(Y[1, M_1(1), M_2\{0, M_1(0)\}] - Y[0, M_1(1), M_2\{0, M_1(0)\}])$
	NDE-010	$E(Y[1, M_1(0), M_2\{1, M_1(0)\}] - Y[0, M_1(0), M_2\{1, M_1(0)\}])$
	NDE-001	$E(Y[1, M_1(0), M_2\{0, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(1)\}])$
	NDE-110	$E(Y[1, M_1(1), M_2\{1, M_1(0)\}] - Y[0, M_1(1), M_2\{1, M_1(0)\}])$
	NDE-101	$E(Y[1, M_1(1), M_2\{0, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(1)\}])$
	NDE-011	$E(Y[1, M_1(0), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(1)\}])$
	NDE-111	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{1, M_1(1)\}])$
Indirect through M_1 only	NIE_1-000	$E(Y[0, M_1(1), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_1-100	$E(Y[1, M_1(1), M_2\{0, M_1(0)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_1-010	$E(Y[0, M_1(1), M_2\{1, M_1(0)\}] - Y[0, M_1(0), M_2\{1, M_1(0)\}])$
	NIE_1-001	$E(Y[0, M_1(1), M_2\{0, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(1)\}])$
	NIE_1-110	$E(Y[1, M_1(1), M_2\{1, M_1(0)\}] - Y[1, M_1(0), M_2\{1, M_1(0)\}])$
	NIE_1-101	$E(Y[1, M_1(1), M_2\{0, M_1(1)\}] - Y[1, M_1(0), M_2\{0, M_1(1)\}])$
	NIE_1-011	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(1)\}])$
	NIE_1-111	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{1, M_1(1)\}])$
Indirect through M_2 only	NIE_2-000	$E(Y[0, M_1(0), M_2\{1, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_2-100	$E(Y[1, M_1(0), M_2\{1, M_1(0)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_2-010	$E(Y[0, M_1(1), M_2\{1, M_1(0)\}] - Y[0, M_1(1), M_2\{0, M_1(0)\}])$
	NIE_2-001	$E(Y[0, M_1(0), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(1)\}])$
	NIE_2-110	$E(Y[1, M_1(1), M_2\{1, M_1(0)\}] - Y[1, M_1(1), M_2\{0, M_1(0)\}])$
	NIE_2-101	$E(Y[1, M_1(0), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{0, M_1(1)\}])$
	NIE_2-011	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(1)\}])$
	NIE_2-111	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(1), M_2\{0, M_1(1)\}])$
Indirect through M_1 and M_2	NIE_{12}-000	$E(Y[0, M_1(0), M_2\{0, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_{12}-100	$E(Y[1, M_1(0), M_2\{0, M_1(1)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
	NIE_{12}-010	$E(Y[0, M_1(1), M_2\{0, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(0)\}])$
	NIE_{12}-001	$E(Y[0, M_1(0), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(0)\}])$
	NIE_{12}-110	$E(Y[1, M_1(1), M_2\{0, M_1(1)\}] - Y[1, M_1(1), M_2\{0, M_1(0)\}])$
	NIE_{12}-101	$E(Y[1, M_1(0), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{1, M_1(0)\}])$
	NIE_{12}-011	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{1, M_1(0)\}])$
	NIE_{12}-111	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(1), M_2\{1, M_1(0)\}])$

Source: Definitions from Daniel et al. (2015).

This defines all eight estimands for each of the four path-specific effects. Each estimand is defined as the expected value of a particular contrast of potential outcomes.

The first block shows estimands related to the natural direct effect. Notice that the contrasts of potential outcomes take on the form $Y[1, M_1(t'), M_2\{t'', M_1(t''')\}] - Y[0, M_1(t'), M_2\{t'', M_1(t''')\}]$. That is, for each difference in potential outcomes, the first argument is fixed to 1 in the first potential outcome and is fixed to 0 in the second, while the remaining arguments consist of permutations of 0s and 1s. Fixing the first argument is what makes them direct effects. Zooming in on the first effect, NDE-000, we see the corresponding contrast is $Y[1, M_1(0), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}]$. Here all the remaining arguments are fixed at 0, which is why it is labeled 000. This is an extension of the pure natural direct effect because the potential values of the mediators are based on fixing the treatment at the level it would naturally take had there been no treatment. However, unlike in the single-mediator case where we have only 2 variations of effects, pure and total, here we have 8 types of effects: 000, 100, 010, 001, 110, 101, 011, and 111. The NDE-111 effect can be considered an extension of the total natural direct effect because the potential mediators are held at the level that they would be observed at had everyone in the population been exposed to treatment.

The second block of estimands reflects natural indirect effects through M_1 alone. Notice that here we fix the second argument of the potential outcomes to 1 and 0, while the remaining arguments again consist of 0/1 permutations. For example, the NIE$_1$-100 natural indirect effect is defined based on the contrast $Y[1, M_1(1), M_2\{0, M_1(0)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}]$, where the free arguments are 1, 0, and 0, hence the label 100.

Similarly, the third block shows the indirect effects through the second mediator alone. Here it is the third argument of the potential outcomes that is fixed. For example, the NIE$_2$-110 effect is defined as based on the contrast $Y[1, M_1(1), M_2\{1, M_1(0)\}] - Y[1, M_1(1), M_2\{0, M_1(0)\}]$.

Finally, the NIE$_{12}$ effects are indirect effects through both the first and second mediator. The natural NIE$_{12}$-111 indirect effect, for instance, is defined based on the contrast $Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(1), M_2\{1, M_1(0)\}]$.

The effects discussed above constitute a single decomposition of the total causal effect into its path-specific components. That is, if we let TE be the total effect, we have that

$$\text{TE} = \text{NDE-000} + \text{NIE}_1\text{-100} + \text{NIE}_2\text{-110} + \text{NIE}_{12}\text{-111}$$

Recall that, in the single-mediator case, we had only two decompositions (pure natural direct effect plus total natural indirect effect and total natural direct effect plus pure natural indirect effect). With 2 sequential mediators, however, there are 24 ways to decompose the total effect into a sum of path-specific effects. The possible decompositions of the total effect into sums of its path-specific components are listed in the table below. When you use `mediate` to fit a model with two sequential mediators, you can refer back to this table to see all the ways the reported effects can be summed to the total effect.

Table 2

Decomposition	Total effect
1	NDE-000 + NIE_1-100 + NIE_2-110 + NIE_{12}-111
2	NDE-000 + NIE_1-100 + NIE_2-111 + NIE_{12}-110
3	NDE-000 + NIE_1-110 + NIE_2-100 + NIE_{12}-111
4	NDE-000 + NIE_1-101 + NIE_2-111 + NIE_{12}-100
5	NDE-000 + NIE_1-111 + NIE_2-100 + NIE_{12}-101
6	NDE-000 + NIE_1-111 + NIE_2-101 + NIE_{12}-100
7	NDE-100 + NIE_1-000 + NIE_2-110 + NIE_{12}-111
8	NDE-100 + NIE_1-000 + NIE_2-111 + NIE_{12}-110
9	NDE-010 + NIE_1-110 + NIE_2-000 + NIE_{12}-111
10	NDE-010 + NIE_1-111 + NIE_2-000 + NIE_{12}-101
11	NDE-001 + NIE_1-101 + NIE_2-111 + NIE_{12}-000
12	NDE-001 + NIE_1-111 + NIE_2-101 + NIE_{12}-000
13	NDE-110 + NIE_1-000 + NIE_2-010 + NIE_{12}-111
14	NDE-110 + NIE_1-010 + NIE_2-000 + NIE_{12}-111
15	NDE-101 + NIE_1-000 + NIE_2-111 + NIE_{12}-010
16	NDE-101 + NIE_1-001 + NIE_2-111 + NIE_{12}-000
17	NDE-011 + NIE_1-111 + NIE_2-000 + NIE_{12}-001
18	NDE-011 + NIE_1-111 + NIE_2-001 + NIE_{12}-000
19	NDE-111 + NIE_1-000 + NIE_2-010 + NIE_{12}-011
20	NDE-111 + NIE_1-000 + NIE_2-011 + NIE_{12}-010
21	NDE-111 + NIE_1-010 + NIE_2-000 + NIE_{12}-011
22	NDE-111 + NIE_1-001 + NIE_2-011 + NIE_{12}-000
23	NDE-111 + NIE_1-011 + NIE_2-000 + NIE_{12}-001
24	NDE-111 + NIE_1-011 + NIE_2-001 + NIE_{12}-000

Source: Decompositions from Daniel et al. (2015).

Modeling and estimation

So far, we have concerned ourselves only with the nonparametric part of identification of treatment effects based on potential outcomes but not with how to estimate these. In what follows, we use linear models with interaction effects to approximate our effects of interest.

Given the causal mediation model with two causally ordered mediators, and ignoring covariates, we can specify the following system of three equations:

$$
\begin{aligned}
Y &= \beta_0 + \beta_1 T + \beta_2 M_1 + \beta_3 M_2 + \beta_4 T M_1 + \beta_5 T M_2 + \beta_6 M_1 M_2 + \beta_7 T M_1 M_2 + \epsilon_Y \\
M_2 &= \gamma_0 + \gamma_1 T + \gamma_2 M_1 + \gamma_3 T M_1 + \epsilon_{M_2} \\
M_1 &= \alpha_0 + \alpha_1 T + \epsilon_{M_1}
\end{aligned}
$$

Here Y is our outcome variable, M_1 and M_2 are our first and second mediators, respectively, and T is our treatment variable. Error terms ϵ_{M_1}, ϵ_{M_2}, and ϵ_Y are assumed to have zero mean and be independent. Parameters $\boldsymbol{\beta} \equiv (\beta_0, \ldots, \beta_7)$, $\boldsymbol{\gamma} \equiv (\gamma_0, \ldots, \gamma_3)$, and $\boldsymbol{\alpha} \equiv (\alpha_0, \alpha_1)$ are to be estimated. Notice that the equations contain all possible interactions among treatment and mediators to retain model flexibility. Looking at the equation for the first mediator (M_1), we see that this includes only the treatment variable on the right-hand side. The equation for M_2 contains M_1, T, and a $T \times M_1$ interaction term. That is, we allow the effect of the first mediator on the second to vary by treatment group. Finally, the outcome equation contains both mediators and treatment as well as their interactions, a mediator–mediator interaction term, and the three-way interaction $T \times M_1 \times M_2$.

To estimate the coefficients for each of the equations, we can simply fit each equation separately and solve for the coefficients by ordinary least squares (OLS). We can then work out the form for our potential-outcomes of interest. Plugging the equations for M_1 and M_2 into the outcome equation, we get

$$
\begin{aligned}
Y[t, M_1(t'), M_2\{t'', M_1(t''')\}] =& \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)(\alpha_0 + \alpha_1 t' + \epsilon_{M_1}) + \\
& (\beta_3 + \beta_5 t)(\gamma_0 + \gamma_1 t'' + (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t''' + \epsilon_{M_1}) + \epsilon_{M_2}) + \\
& (\beta_6 + \beta_7 t)\Big\{(\alpha_0 + \alpha_1 t' + \epsilon_{M_1})(\gamma_0 + \gamma_1 t'' + (\gamma_2 + \gamma_3 t'') \\
& (\alpha_0 + \alpha_1 t''' + \epsilon_{M_1}) + \epsilon_{M_2})\Big\} + \epsilon_Y
\end{aligned}
$$

Replacing error terms with their expectations yields

$$
\begin{aligned}
E(Y[t, M_1(t'), M_2\{t'', M_1(t''')\}]) =& \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)(\alpha_0 + \alpha_1 t') + \\
& (\beta_3 + \beta_5 t)(\gamma_0 + \gamma_1 t'' + (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t''')) + \\
& (\beta_6 + \beta_7 t)\Big\{(\alpha_0 + \alpha_1 t')(\gamma_0 + \gamma_1 t'' + \\
& (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t'''))\Big\} + \\
& (\beta_6 + \beta_7 t)(\gamma_2 + \gamma_3 t'')E[\epsilon_{M_1}\epsilon_{M_1}] \\
=& \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)(\alpha_0 + \alpha_1 t') + \\
& (\beta_3 + \beta_5 t)(\gamma_0 + \gamma_1 t'' + (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t''')) + \\
& (\beta_6 + \beta_7 t)\Big\{(\alpha_0 + \alpha_1 t')(\gamma_0 + \gamma_1 t'' + \\
& (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t'''))\Big\} + \\
& (\beta_6 + \beta_7 t)(\gamma_2 + \gamma_3 t'')\sigma^2_{M_1} \qquad (1)
\end{aligned}
$$

At this point, we could simply plug in values for t, t', t'', and t''' according to which potential-outcome mean we wish to compute. For example, to compute natural direct effect NDE-000, we need the difference of potential outcome means $E[Y_i(1, M_1(0), M_2(0, M_1(0)))] - E[Y_i(0, M_1(0), M_2(0, M_1(0)))]$. Taking the first, we have

$$
\begin{aligned}
E[Y_i(1, M_1(0), M_2(0, M_1(0)))] =& \beta_0 + \beta_1 + (\beta_2 + \beta_4)\alpha_0 + (\beta_3 + \beta_5)(\gamma_0 + \gamma_2\alpha_0) + \\
& (\beta_6 + \beta_7)\Big\{\alpha_0(\gamma_0 + \gamma_2\alpha_0) + \gamma_2\sigma^2_{M_1}\Big\}
\end{aligned}
$$

And for the second potential-outcome mean, we have

$$
\begin{aligned}
E[Y_i(0, M_1(0), M_2(0, M_1(0)))] =& \beta_0 + \beta_2\alpha_0 + \beta_3(\gamma_0 + \gamma_2\alpha_0) + \\
& \beta_6\Big\{\alpha_0(\gamma_0 + \gamma_2\alpha_0) + \gamma_2\sigma^2_{M_1}\Big\}
\end{aligned}
$$

We could now plug in our OLS estimates for $\boldsymbol{\beta}$, $\boldsymbol{\gamma}$, and $\boldsymbol{\alpha}$ for both potential-outcome means and then take the difference to get an estimate of NDE-000.

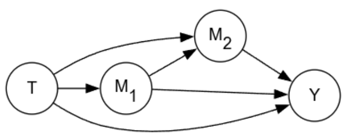
In addition to the coefficients, however, we also need to plug in an estimate of $\sigma^2_{M_1}$, which is the residual variance of the M_1 equation. Notice that our reduced form in (1) contains the expected value of the product of two error terms. Following Daniel et al. (2015), we can think of the error terms as arising from the fact that $M_1(t)$ can be evaluated at a different t when $t' \neq t'''$. If we set $t' = 0$ and $t''' = 1$, for example, we can write the potential outcomes for mediator M_1 as

$$M_1(t') = M_1(0) = \alpha_0 + \epsilon^{t'}_{M_1}$$
$$M_1(t''') = M_1(1) = \alpha_0 + \alpha_1 + \epsilon^{t'''}_{M_1}$$

Here, to calculate the expected value of the product $\epsilon^{t'}_{M_1}\epsilon^{t'''}_{M_1}$, we would need to have information about their covariance, which is not available from the data. Therefore, this conditional correlation between $M_1(0)$ and $M_1(1)$ has to be set by assumption. A reasonable assumption is that the unobservables $\epsilon^{t'}_{M_1}$ and $\epsilon^{t'''}_{M_1}$ are the same regardless of how treatment is set counterfactually. Under this assumption, $\epsilon^{t'}_{M_1}$ and $\epsilon^{t'''}_{M_1}$ are perfectly correlated with correlation coefficient $\rho_{M_1^{t'} M_1^{t'''}} = 1$, and the expected value of the error term product yields $\sigma^2_{M_1}$. However, the value of $\rho_{M_1^{t'} M_1^{t'''}}$ can be varied to perform a sensitivity analysis. After we run `mediate`, this can be done using the `estat smsensitivity` postestimation command. *Example 12: Sensitivity analysis* shows an example of this type of sensitivity analysis.

Mediator-specific natural effects

As we have seen, a causal mediation model with two causally ordered mediators and a full set of interactions yields a complex set of estimands. One option to reduce this complexity is to perform a coarser decomposition. So far, we have focused on the finest possible decomposition along four path-specific effects. However, we could combine some of the paths, which reduces the number of estimands at the expense of the decomposition being coarser. Consider again the following causal diagram:



The four path-specific effects we considered so far are $T \rightarrow Y$, $T \rightarrow M_1 \rightarrow Y$, $T \rightarrow M_2 \rightarrow Y$, and $T \rightarrow M_1 \rightarrow M_2 \rightarrow Y$. However, if, for example, we were primarily interested in the indirect effect $T \rightarrow M_1 \rightarrow Y$, we could combine the paths $T \rightarrow M_2 \rightarrow Y$ and $T \rightarrow M_1 \rightarrow M_2 \rightarrow Y$. Because here we put a focus on M_1, that is, the first mediator in the causal sequence, the resulting indirect effects are referred to as type-1 mediator-specific effects. Likewise, if our focus is on the second mediator M_2, we can combine the paths $T \rightarrow M_1 \rightarrow Y$ and $T \rightarrow M_1 \rightarrow M_2 \rightarrow Y$ to obtain type-2 mediator-specific effects. Here are the definitions of all type-1 and type-2 mediator-specific natural effects that result from this coarser decomposition:

Table 3

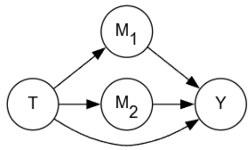
Effect	Definition
MS^1-NDE-00	$E(Y[1, M_1(0), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^1-NDE-01	$E(Y[1, M_1(0), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(1)\}])$
MS^1-NDE-10	$E(Y[1, M_1(1), M_2\{0, M_1(0)\}] - Y[0, M_1(1), M_2\{0, M_1(0)\}])$
MS^1-NDE-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{1, M_1(1)\}])$
MS^1-NIE_1-00	$E(Y[0, M_1(1), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^1-NIE_1-01	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(1)\}])$
MS^1-NIE_1-10	$E(Y[1, M_1(1), M_2\{0, M_1(0)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
MS^1-NIE_1-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{1, M_1(1)\}])$
MS^1-NIE_2-00	$E(Y[0, M_1(0), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^1-NIE_2-01	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(0)\}])$
MS^1-NIE_2-10	$E(Y[1, M_1(0), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
MS^1-NIE_2-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(1), M_2\{0, M_1(0)\}])$
MS^2-NDE-00	$E(Y[1, M_1(0), M_2\{0, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^2-NDE-01	$E(Y[1, M_1(0), M_2\{1, M_1(0)\}] - Y[0, M_1(0), M_2\{1, M_1(0)\}])$
MS^2-NDE-10	$E(Y[1, M_1(1), M_2\{0, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(1)\}])$
MS^2-NDE-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{1, M_1(1)\}])$
MS^2-NIE_1-00	$E(Y[0, M_1(1), M_2\{0, M_1(1)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^2-NIE_1-01	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(0), M_2\{1, M_1(0)\}])$
MS^2-NIE_1-10	$E(Y[1, M_1(1), M_2\{0, M_1(1)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
MS^2-NIE_1-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(0), M_2\{1, M_1(0)\}])$
MS^2-NIE_2-00	$E(Y[0, M_1(0), M_2\{1, M_1(0)\}] - Y[0, M_1(0), M_2\{0, M_1(0)\}])$
MS^2-NIE_2-01	$E(Y[0, M_1(1), M_2\{1, M_1(1)\}] - Y[0, M_1(1), M_2\{0, M_1(1)\}])$
MS^2-NIE_2-10	$E(Y[1, M_1(0), M_2\{1, M_1(0)\}] - Y[1, M_1(0), M_2\{0, M_1(0)\}])$
MS^2-NIE_2-11	$E(Y[1, M_1(1), M_2\{1, M_1(1)\}] - Y[1, M_1(1), M_2\{0, M_1(1)\}])$

Source: Definitions from Daniel et al. (2015).

In the table above, the effects that start with MS^1 correspond to type-1 mediator-specific effects and those that start with MS^2 to type-2 mediator-specific effects. In *Example 10: Estimating mediator-specific natural effects*, we illustrate how to estimate mediator-specific effects.

Parallel mediators

The estimand complexity is also reduced if we have a causal mediation model with two parallel mediators, which are not causally ordered. In this case, we have at most 4 estimands over 3 effects for a total of 12 estimands. The complexity is reduced because mediator potential outcomes are no longer nested. That is, instead of potential outcomes of the form $Y[t, M_1(t'), M_2\{t'', M_1(t''')\}]$, with a parallel rather than sequential design, we simply have $Y\{t, M_1(t'), M_2(t'')\}$. Consider the following causal diagram:



In contrast to the sequential mediation model we have discussed so far, with the parallel mediation model, we have only three path-specific effects of interest: the effect through neither M_1 nor M_2 (that is, the natural direct effect), the effect through M_1 only, and the effect through M_2 only. Using linear models with interactions, and again ignoring covariates, we can specify our system of equations as follows:

$$
\begin{aligned}
Y &= \beta_0 + \beta_1 T + \beta_2 M_1 + \beta_3 M_2 + \beta_4 T M_1 + \beta_5 T M_2 + \beta_6 M_1 M_2 + \beta_7 T M_1 M_2 + \epsilon_Y \\
M_2 &= \gamma_0 + \gamma_1 T + \epsilon_{M_2} \\
M_1 &= \alpha_0 + \alpha_1 T + \epsilon_{M_1}
\end{aligned}
$$

Again, we can use OLS to estimate the coefficients of the above equations and work out the form for the potential-outcome means of interest. Plugging the equations for M_1 and M_2 into the outcome equation yields

$$
\begin{aligned}
Y\{t, M_1(t'), M_2(t'')\} =& \beta_0 + \beta_1 T + \beta_2(\alpha_0 + \alpha_1 T + \epsilon_{M_1}) + \beta_3(\gamma_0 + \gamma_1 T + \epsilon_{M_2}) + \\
& \beta_4 T(\alpha_0 + \alpha_1 T + \epsilon_{M_1}) + \beta_5 T(\gamma_0 + \gamma_1 T + \epsilon_{M_2}) + \\
& \beta_6(\alpha_0 + \alpha_1 T + \epsilon_{M_1})(\gamma_0 + \gamma_1 T + \epsilon_{M_2}) + \\
& \beta_7 T(\alpha_0 + \alpha_1 T + \epsilon_{M_1})(\gamma_0 + \gamma_1 T + \epsilon_{M_2}) + \epsilon_Y
\end{aligned}
$$

Simplifying and replacing error terms with their expectations yields

$$
\begin{aligned}
E[Y\{t, M_1(t'), M_2(t'')\}] =& \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)(\alpha_0 + \alpha_1 t') + (\beta_3 + \beta_5 t)(\gamma_0 + \gamma_1 t'') + \\
& (\beta_6 + \beta_7 t)(\alpha_0 + \alpha_1 t')(\gamma_0 + \gamma_1 t'')
\end{aligned}
$$

Suppose now that we wanted to calculate the natural direct effect NDE-00. This effect is defined as the contrast $E[Y\{1, M_1(0), M_2(0)\}] - E[Y\{0, M_1(0), M_2(0)\}]$. We can write out each potential-outcome mean as

$$
\begin{aligned}
E[Y\{1, M_1(0), M_2(0)\}] &= \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)\alpha_0 + (\beta_3 + \beta_5 t)\gamma_0 + (\beta_6 + \beta_7 t)\alpha_0\gamma_0 \\
E[Y\{0, M_1(0), M_2(0)\}] &= \beta_0 + \beta_2\alpha_0 + \beta_3\gamma_0 + \beta_6\alpha_0\gamma_0
\end{aligned}
$$

We could now simply plug in our OLS estimates of $\boldsymbol{\beta}$, $\boldsymbol{\alpha}$, and $\boldsymbol{\gamma}$ to calculate NDE-00. The following table provides an overview of all parallel mediation estimands:

Table 4

Path	Effect	Definition
Direct	NDE-00	$E[Y\{1, M_1(0), M_2(0)\} - Y\{0, M_1(0), M_2(0)\}]$
(through	NDE-10	$E[Y\{1, M_1(1), M_2(0)\} - Y\{0, M_1(1), M_2(0)\}]$
neither M_1 nor M_2)	NDE-01	$E[Y\{1, M_1(0), M_2(1)\} - Y\{0, M_1(0), M_2(1)\}]$
	NDE-11	$E[Y\{1, M_1(1), M_2(1)\} - Y\{0, M_1(1), M_2(1)\}]$
Indirect	NIE_1-00	$E[Y\{0, M_1(1), M_2(0)\} - Y\{0, M_1(0), M_2(0)\}]$
through M_1	NIE_1-10	$E[Y\{1, M_1(1), M_2(0)\} - Y\{1, M_1(0), M_2(0)\}]$
	NIE_1-01	$E[Y\{0, M_1(1), M_2(1)\} - Y\{0, M_1(0), M_2(1)\}]$
	NIE_1-11	$E[Y\{1, M_1(1), M_2(1)\} - Y\{1, M_1(0), M_2(1)\}]$
Indirect	NIE_2-00	$E[Y\{0, M_1(0), M_2(1)\} - Y\{0, M_1(0), M_2(0)\}]$
through M_2	NIE_2-10	$E[Y\{1, M_1(0), M_2(1)\} - Y\{1, M_1(0), M_2(0)\}]$
	NIE_2-01	$E[Y\{0, M_1(1), M_2(1)\} - Y\{0, M_1(1), M_2(0)\}]$
	NIE_2-11	$E[Y\{1, M_1(1), M_2(1)\} - Y\{1, M_1(1), M_2(0)\}]$

Source: Definitions from Daniel et al. (2015).

Because we have fewer estimands under the parallel design, we also have fewer decompositions. The number of distinct decompositions in this case is six:

Table 5

Decomposition	Total effect
1	NDE-00 + NIE_1-10 + NIE_2-11
2	NDE-00 + NIE_1-11 + NIE_2-10
3	NDE-10 + NIE_1-00 + NIE_2-11
4	NDE-01 + NIE_1-11 + NIE_2-00
5	NDE-11 + NIE_1-00 + NIE_2-01
6	NDE-11 + NIE_1-01 + NIE_2-00

Source: Decompositions from Daniel et al. (2015).

Notice that these decompositions also apply to the mediator-specific effects discussed in the previous section.

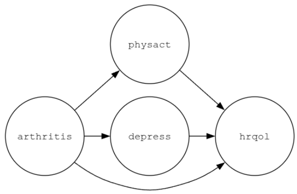
Identification assumptions

Assumptions that allow identification of causal effects are principally the same as in the single-mediator case; see *Evaluating assumptions for causal inference* in [CAUSAL] **mediate**. Perhaps most prominently, there must not be any unmeasured confounding anywhere in the system. That is, no treatment–mediator confounding, no treatment–outcome confounding, no mediator–mediator confounding, and no mediator–outcome confounding. In other words, all model equations have to be correctly specified. For a detailed discussion of identification assumptions for models with multiple mediators, see Daniel et al. (2015, sec. 4).

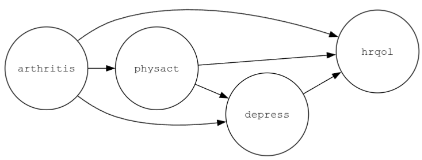
Examples

Example 1: Parallel causal mediation model

Suppose we wish to evaluate whether suffering from arthritis affects an individuals' health-related quality of life. If so, we also wish to disentangle, at least partially, the causal mechanisms through which the arthritis affects quality of life. We consider two mediator variables: physical activity and depression. We hypothesize that suffering from arthritis leads to a reduction of physical activity, which in turn leads to a reduction of health-related quality of life. We also hypothesize that arthritis leads to an increase in depression, which also leads to a reduction in health-related quality of life. Ignoring other covariates, we could depict our causal model in the following causal diagram:



We have three causal pathways from arthritis (`arthritis`) to health-related quality of life (`hrqol`): a direct path, a path through physical activity (`physact`), and path through depression (`depress`). Notice that there is no path between the two mediators. That is, our hypothesized causal model does not assume causal ordering among mediators. We refer to this design as parallel mediation. We could instead argue that there is a causal path between the two mediators. For instance, we could hypothesize the following model,



where we assume that physical activity, or lack thereof, affects depression. In this case, we have four causal pathways from `arthritis` to `hrqol`: one direct path, one indirect path through `physact`, one indirect path through `depress`, and one indirect path through both `physact` and `depress`. We refer to this design as sequential mediation.

We start with a parallel design. The following shows an excerpt of a fictional dataset where hrqol is a scale measuring health-related quality of life, physact records hours of physical activity in the last month, depress is a scale measuring depression, and arthritis is an indicator for having arthritis. The dataset also contains confounding variables male and age, which are used in later examples.

```
. use https://www.stata-press.com/data/r19/qoflife
Artificial quality-of-life data
. list hrqol depress physact arthritis male age in 1/5
```

	hrqol	depress	physact	arthri~s	male	age
1.	33.58646	6.161322	4	No	Yes	34
2.	33.09237	6.321835	4	Yes	Yes	35
3.	40.68521	5.355282	9	No	Yes	30
4.	34.04324	6.025885	3	No	No	38
5.	28.16133	6.586061	0	No	Yes	48

To estimate the total treatment effect of arthritis on quality of life as well as the three path-specific effects, we use mediate with four sets of parentheses. The first set specifies the outcome equation, the middle two specify the mediator equations, and the last one specifies our treatment variable. Because we do not include covariates in this example, we simply specify the outcome, mediator, and treatment variables accordingly:

```
. mediate (hrqol) (depress) (physact) (arthritis)
Iteration 0:  EE criterion = 1.537e-27
Iteration 1:  EE criterion = 8.303e-30
Causal mediation analysis                            Number of obs = 2,000
Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
arthritis (Yes vs No)	-1.71165	.1496673	-11.44	0.000	-2.004993	-1.418308
NIE1						
arthritis (Yes vs No)	-1.814969	.1817366	-9.99	0.000	-2.171166	-1.458772
NIE2						
arthritis (Yes vs No)	-1.252368	.2507925	-4.99	0.000	-1.743912	-.7608239
TE						
arthritis (Yes vs No)	-4.778988	.2912224	-16.41	0.000	-5.349773	-4.208202

The output shows estimates of the total effect (TE), the natural direct effect (NDE), and both natural indirect effects (NIE1 and NIE2). The total effect is the average treatment effect that is decomposed into direct and indirect effects. It follows the usual interpretation of average treatment effects: if everyone in the population had arthritis, health-related quality of life would on average be 4.8 points lower than if no one in the population had arthritis. The indirect effect NIE1 estimates the indirect effect of arthritis on hrqol through the physact mediator. That is, 1.8 points of the 4.8-point total expected decrease in hrqol are due to reduced physical activity. The NIE2 estimate captures the indirect effect through depress and is slightly smaller than the other indirect effect. A reduction of around 1.3 points in hrqol is due to depression. Finally, the natural direct effect (NDE) captures causal mechanisms other than the ones we observed with our two mediators. That is, from the 4.8-point average decrease in the outcome, 1.7 points are due to mechanisms other than physical activity and depression.

By default, mediate shows only the estimated treatment effects. However, we could also take a look at the parameter estimates from the individual equations by replaying the results with the aequations option:

```
. mediate, aequations

Causal mediation analysis                               Number of obs = 2,000

Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary

------------------------------------------------------------------------------
             |               Robust
       hrqol | Coefficient  std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
NDE          |
   arthritis |
 (Yes vs No) |   -1.71165   .1496673   -11.44   0.000    -2.004993   -1.418308
-------------+----------------------------------------------------------------
NIE1         |
   arthritis |
 (Yes vs No) |  -1.814969   .1817366    -9.99   0.000    -2.171166   -1.458772
-------------+----------------------------------------------------------------
NIE2         |
   arthritis |
 (Yes vs No) |  -1.252368   .2507925    -4.99   0.000    -1.743912   -.7608239
-------------+----------------------------------------------------------------
TE           |
   arthritis |
 (Yes vs No) |  -4.778988   .2912224   -16.41   0.000    -5.349773   -4.208202
-------------+----------------------------------------------------------------
hrqol        |
   arthritis |
        Yes  |   -1.71165   .1496673   -11.44   0.000    -2.004993   -1.418308
     physact |   .8053262   .0741201    10.87   0.000     .6600534     .950599
     depress |  -3.117997   .5559884    -5.61   0.000    -4.207714   -2.028279
       _cons |   47.15107    3.59214    13.13   0.000      40.1106    54.19154
-------------+----------------------------------------------------------------
depress      |
   arthritis |
        Yes  |   .4016579   .0255639    15.71   0.000     .3515536    .4517623
       _cons |   6.040968   .0236416   255.52   0.000     5.994632    6.087305
-------------+----------------------------------------------------------------
physact      |
   arthritis |
        Yes  |  -2.253707   .2307478    -9.77   0.000    -2.705964   -1.801449
       _cons |   3.386249   .2171971    15.59   0.000      2.96055    3.811947
------------------------------------------------------------------------------
```

These estimates are typically not of substantive interest. However, it is always a good idea to check these and see whether the coefficient estimates appear reasonable in light of given theoretical considerations.

Example 2: Treatment–mediator interactions

The previous example was somewhat simplistic because our model did not include any interactions. We have two options related to treatment and mediator interactions in the case of parallel mediation: we can include treatment–mediator interactions as well as mediator–mediator interactions in the outcome equation. This adds flexibility to the underlying model equations at the cost of additional estimand complexity.

Continuing with the current example, we can allow the effects of physical activity and depression on quality of life to differ between treatment groups. We include these treatment–mediator interactions in the outcome equation by specifying the `tinteraction` option:

```
. mediate (hrqol) (depress) (physact) (arthritis), tinteraction

Iteration 0:  EE criterion = 1.158e-25
Iteration 1:  EE criterion = 3.275e-28

Causal mediation analysis                           Number of obs = 2,000

Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
00	-1.863452	.1961826	-9.50	0.000	-2.247963	-1.478941
10	-2.7116	.3099477	-8.75	0.000	-3.319086	-2.104114
01	-.7317365	.3513065	-2.08	0.037	-1.420285	-.0431885
11	-1.579885	.1577089	-10.02	0.000	-1.888988	-1.270781
NIE1						
00	-1.582646	.1686346	-9.39	0.000	-1.913164	-1.252129
11	-2.430795	.3236353	-7.51	0.000	-3.065108	-1.796481
NIE2						
00	-1.616457	.2614895	-6.18	0.000	-2.128967	-1.103947
11	-.4847413	.2181954	-2.22	0.026	-.9123964	-.0570863
TE						
arthritis (Yes vs No)	-4.778988	.2912224	-16.41	0.000	-5.349773	-4.208202

```
Note: Outcome equation includes treatment-mediator interactions.
```

The interpretation of the total effect is the same as before. However, we now have four distinct natural direct-effect estimates and two distinct indirect-effect estimates for each mediator. Differences among these estimates are due to differences in corresponding potential-outcome means, as shown in table 4.

The natural direct effect labeled `00` is the estimated direct effect when both `physact` and `depress` are at their values associated with being untreated (`arthritis` = 0). Similarly, the natural direct effect labeled `10` is the estimated direct effect when `physact` is at its value associated with being treated and `depress` is at its value associated with being untreated. The other natural direct effects are interpreted similarly. Based on this specification, the natural direct effects range form −0.73 to −2.71.

Before discussing the effect estimates in more detail, we will explore options for limiting interactions and including other interactions. With the `tinteraction` option, interactions with the treatment variable are added for both mediators. However, we can specify that only one of these interactions should be included. For example, if we want to add an interaction term only for physical activity, we specify the `tinteraction()` option with the name of the mediator in parentheses:

```
. mediate (hrqol) (depress) (physact) (arthritis), tinteraction(physact)
Iteration 0:  EE criterion = 1.580e-27
Iteration 1:  EE criterion = 5.149e-29
Causal mediation analysis                             Number of obs = 2,000
Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
00	-1.562983	.2001687	-7.81	0.000	-1.955307	-1.17066
10	-1.735797	.148358	-11.70	0.000	-2.026574	-1.445021
01	-1.562983	.2001687	-7.81	0.000	-1.955307	-1.17066
11	-1.735797	.148358	-11.70	0.000	-2.026574	-1.445021
NIE1						
00	-1.799643	.175755	-10.24	0.000	-2.144116	-1.455169
11	-1.972457	.2491519	-7.92	0.000	-2.460785	-1.484128
NIE2						
00	-1.243548	.2369214	-5.25	0.000	-1.707905	-.7791903
11	-1.243548	.2369214	-5.25	0.000	-1.707905	-.7791903
TE						
arthritis (Yes vs No)	-4.778988	.2912224	-16.41	0.000	-5.349773	-4.208202

```
Note: Outcome equation includes treatment-mediator interactions.
```

Now the two estimates for the `NIE2` indirect effect are the same. Omitting the interaction of treatment with the `depress` mediator leads to a single `NIE2` effect (reported as `NIE2-00` = `NIE2-11`). For `NIE1`, we still have two distinct effect estimates due to the `arthritis` × `physact` interaction.

Example 3: Mediator–mediator interaction

In addition to treatment–mediator interactions, we can include a mediator–mediator interaction if we think that the effects of the mediators on the outcome depend on one another. To do so, we add the `minteraction` option:

```
. mediate (hrqol) (depress) (physact) (arthritis), tinteraction minteraction
Iteration 0:  EE criterion = 2.526e-26
Iteration 1:  EE criterion = 1.137e-28
Causal mediation analysis                            Number of obs = 2,000
Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
00	-1.745654	.1767601	-9.88	0.000	-2.092097	-1.39921
10	-1.449735	.2693148	-5.38	0.000	-1.977582	-.9218876
01	-1.804018	.2952766	-6.11	0.000	-2.38275	-1.225287
11	-1.638622	.139265	-11.77	0.000	-1.911576	-1.365667
NIE1						
00	-3.277243	.3619214	-9.06	0.000	-3.986596	-2.56789
10	-2.981325	.3508021	-8.50	0.000	-3.668884	-2.293765
01	-3.389729	.3789566	-8.94	0.000	-4.132471	-2.646988
11	-3.224333	.4005567	-8.05	0.000	-4.00941	-2.439256
NIE2						
00	-.174545	.1703176	-1.02	0.305	-.5083614	.1592713
10	-.2329098	.2139202	-1.09	0.276	-.6521856	.186366
01	-.2870311	.1642122	-1.75	0.080	-.6088811	.0348188
11	-.4759182	.2112993	-2.25	0.024	-.8900573	-.0617791
TE						
arthritis (Yes vs No)	-5.202896	.3531395	-14.73	0.000	-5.895037	-4.510756

```
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction.
```

We now have four distinct estimates each for natural direct and both natural indirect effects. That is, we have twelve distinct estimates plus the total effect. This is the maximum number of distinct estimates we can have under the parallel mediation design.

The four natural direct effects are interpreted in the same way as in example 1. The estimates of the natural indirect effects through `physact` are in the section labeled `NIE1`. The first one, labeled `00`, is the natural indirect effect via `physact` if no one was treated (`arthritis` $= 0$), and `depress` is set to the value associated with being untreated. Similarly, the value labeled `10` is the natural indirect effect via `physact` if everyone was treated (`arthritis` $= 1$), and `depress` is set to the value associated with being untreated. The other `NIE1` natural indirect effects are interpreted similarly. The `NIE2` section reports similar natural indirect effects through `depress` while setting values for `arthritis` and `physact`. Based on this model, indirect effects via `physact` range from -2.98 to -3.39, and indirect effects via `depress` range from -0.17 to -0.47.

There are six ways to decompose the total effect into sums of these natural direct and indirect effects as shown in table 5.

We can check the coefficient estimates for each of the included interaction terms by replaying the results with the aequations option:

```
. mediate, aequations

Causal mediation analysis                              Number of obs = 2,000

Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary

------------------------------------------------------------------------------
             |               Robust
       hrqol | Coefficient  std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
NDE          |
          00 |  -1.745654   .1767601    -9.88   0.000    -2.092097    -1.39921
          10 |  -1.449735   .2693148    -5.38   0.000    -1.977582   -.9218876
          01 |  -1.804018   .2952766    -6.11   0.000     -2.38275   -1.225287
          11 |  -1.638622    .139265   -11.77   0.000    -1.911576   -1.365667
-------------+----------------------------------------------------------------
NIE1         |
          00 |  -3.277243   .3619214    -9.06   0.000    -3.986596    -2.56789
          10 |  -2.981325   .3508021    -8.50   0.000    -3.668884   -2.293765
          01 |  -3.389729   .3789566    -8.94   0.000    -4.132471   -2.646988
          11 |  -3.224333   .4005567    -8.05   0.000     -4.00941   -2.439256
-------------+----------------------------------------------------------------
NIE2         |
          00 |   -.174545   .1703176    -1.02   0.305    -.5083614    .1592713
          10 |  -.2329098   .2139202    -1.09   0.276    -.6521856     .186366
          01 |  -.2870311   .1642122    -1.75   0.080    -.6088811    .0348188
          11 |  -.4759182   .2112993    -2.25   0.024    -.8900573   -.0617791
-------------+----------------------------------------------------------------
TE           |
   arthritis |
 (Yes vs No) |  -5.202896   .3531395   -14.73   0.000    -5.895037   -4.510756
------------------------------------------------------------------------------
```

hrqol						
arthritis						
Yes	2.526337	4.33281	0.58	0.560	-5.965815	11.01849
physact	.7034825	.0376614	18.68	0.000	.6296675	.7772976
depress	-.85535	.407575	-2.10	0.036	-1.654182	-.0565176
arthritis#						
c.physact						
Yes	-1.002342	.2613421	-3.84	0.000	-1.514564	-.4901213
arthritis#						
c.depress						
Yes	-.6335682	.6635123	-0.95	0.340	-1.934028	.666892
c.physact#						
c.depress	.1242639	.0077999	15.93	0.000	.1089765	.1395514
arthritis#						
c.physact#						
c.depress						
Yes	.1441887	.046566	3.10	0.002	.0529211	.2354563
_cons	31.88665	2.635727	12.10	0.000	26.72072	37.05258
depress						
arthritis						
Yes	.4016579	.0255639	15.71	0.000	.3515536	.4517623
_cons	6.040968	.0236416	255.52	0.000	5.994632	6.087305
physact						
arthritis						
Yes	-2.253707	.2307478	-9.77	0.000	-2.705964	-1.801449
_cons	3.386249	.2171971	15.59	0.000	2.96055	3.811947

```
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction.
```

Looking at the `hrqol` outcome equation, we see the coefficient estimates for these terms. Also notice that, with both the `tinteraction` and `minteraction` options specified, the outcome equation includes the three-way interaction of the two mediators and the treatment, which allows the mediator–mediator interaction to vary by treatment group.

Example 4: Accounting for confounding variables

For causal inference, we must evaluate the potential of confounding. Under the parallel mediation design, there are three types of confounders that we need to consider: treatment–outcome confounders, treatment–mediator confounders, and mediator–outcome confounders. For the sequential model, we must additionally consider mediator–mediator confounders. A treatment–outcome confounder, for example, is a variable that affects both the selection into treatment and the outcome. If confounders exist, we need to add them as covariates to the model to prevent biased results.

In this example, we consider age to be a treatment–outcome confounder and male to be a treatment–mediator confounder. Thus, we include age as a covariate in our outcome equation and male as a covariate in our mediator equations. We also specify the aequations option to inspect their coefficients:

```
. mediate (hrqol age) (depress i.male) (physact i.male) (arthritis),
> tinteraction minteraction aequations

Iteration 0:  EE criterion = 4.054e-26
Iteration 1:  EE criterion = 5.196e-30

Causal mediation analysis                            Number of obs = 2,000

Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf. interval]	
NDE						
00	-2.923315	.0983242	-29.73	0.000	-3.116027	-2.730603
10	-2.328291	.131225	-17.74	0.000	-2.585487	-2.071094
01	-3.024462	.15042	-20.11	0.000	-3.31928	-2.729645
11	-2.410038	.0614085	-39.25	0.000	-2.530397	-2.28968
NIE1						
00	-2.439151	.2229985	-10.94	0.000	-2.87622	-2.002082
10	-1.844127	.1837655	-10.04	0.000	-2.204301	-1.483953
01	-2.481129	.2301443	-10.78	0.000	-2.932204	-2.030054
11	-1.866705	.1901424	-9.82	0.000	-2.239377	-1.494033
NIE2						
00	-.589078	.0943036	-6.25	0.000	-.7739097	-.4042464
10	-.6902256	.1139496	-6.06	0.000	-.9135627	-.4668885
01	-.6310562	.0940434	-6.71	0.000	-.8153779	-.4467346
11	-.7128041	.1142426	-6.24	0.000	-.9367155	-.4888926
TE						
arthritis (Yes vs No)	-5.480245	.251458	-21.79	0.000	-5.973094	-4.987397

hrqol						
arthritis						
Yes	-1.160197	1.875236	-0.62	0.536	-4.835591	2.515197
physact	.7273916	.0122129	59.56	0.000	.7034547	.7513284
depress	-1.372237	.174576	-7.86	0.000	-1.7144	-1.030074
arthritis#c.physact						
Yes	-.1328243	.0598191	-2.22	0.026	-.2500676	-.015581
arthritis#c.depress						
Yes	-.1585676	.2871678	-0.55	0.581	-.721406	.4042709
c.physact#c.depress	.0340505	.0037065	9.19	0.000	.0267859	.041315
arthritis#c.physact#c.depress						
Yes	-.015736	.0117052	-1.34	0.179	-.0386777	.0072057
age	-.307173	.0031765	-96.70	0.000	-.3133989	-.3009472
_cons	50.26891	1.147244	43.82	0.000	48.02036	52.51747
depress						
arthritis						
Yes	.4710086	.0273445	17.22	0.000	.4174144	.5246029
male						
Yes	-.2003285	.0271024	-7.39	0.000	-.2534482	-.1472087
_cons	6.104774	.0240335	254.01	0.000	6.057669	6.151878
physact						
arthritis						
Yes	-2.617407	.2337319	-11.20	0.000	-3.075514	-2.159301
male						
Yes	1.050597	.2306835	4.55	0.000	.5984654	1.502728
_cons	3.05163	.2330003	13.10	0.000	2.594958	3.508302

Note: Outcome equation includes treatment-mediator interactions and mediator-mediator interaction.

The `age` and `male` coefficients appear to have considerable size. Indeed, if we look at the effect estimates, we see substantial increases (in absolute value) in estimates of natural direct effect, decreases in estimates of natural indirect effects through physical activity (`NIE1`), and slight increases in natural indirect effects through depression (`NIE2`).

Example 5: Additional interactions

It is conceivable that the effect of age on quality of life may be moderated by one or both of the mediators. To include additional interactions of covariates and mediators, we simply add them by using factor-variable notation:

```
. mediate (hrqol age c.depress#c.age c.physact#c.age)
>         (depress i.male)
>         (physact i.male)
>         (arthritis), tinteraction minteraction
Iteration 0:  EE criterion = 1.762e-25
Iteration 1:  EE criterion = 8.149e-30
Causal mediation analysis                              Number of obs = 2,000
Mediation type: Parallel
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
00	-2.93327	.0986156	-29.74	0.000	-3.126553	-2.739987
10	-2.2664	.1321111	-17.16	0.000	-2.525333	-2.007467
01	-3.13574	.1548724	-20.25	0.000	-3.439284	-2.832196
11	-2.441183	.0633247	-38.55	0.000	-2.565297	-2.317068
NIE1						
00	-2.559244	.2330217	-10.98	0.000	-3.015958	-2.102529
10	-1.892373	.1842448	-10.27	0.000	-2.253486	-1.53126
01	-2.596165	.2396821	-10.83	0.000	-3.065933	-2.126396
11	-1.901607	.1889659	-10.06	0.000	-2.271974	-1.531241
NIE2						
00	-.4994956	.0965284	-5.17	0.000	-.6886879	-.3103033
10	-.7019653	.1137533	-6.17	0.000	-.9249177	-.4790128
01	-.5364167	.0960709	-5.58	0.000	-.7247123	-.3481211
11	-.7111994	.1138654	-6.25	0.000	-.9343716	-.4880273
TE						
arthritis (Yes vs No)	-5.536843	.2526692	-21.91	0.000	-6.032065	-5.04162

```
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction.
```

Here we included interactions of both mediators with age. Had we used the aequations option, we would see that the coefficients on these interaction terms are both close to 0. Consequently, the above results do not change in any meaningful way compared with those of the previously fitted model.

Example 6: Sequential causal mediation model

We now move on to a sequential mediation model, that is, a causal mediation model with two causally ordered mediators. In this case, the total causal effect is decomposed into four path-specific effects: the natural direct effect that goes through neither of the mediators (NDE), a natural indirect effect through only the first mediator (NIE1), a natural indirect effect through only the second mediator (NIE2), and a natural indirect effect through both of the mediators (NIE12).

We start with a model without interactions and without covariates, in which case we will have only a single estimand per effect. The syntax of the `mediate` command is similar to that for the parallel mediation model, but we will have to be cognizant about the causal order between mediators. The specification follows the causal sequence from right to left, where the causal sequence is $Y \leftarrow M_2 \leftarrow M_1 \leftarrow T$. Thus, if we distinguish between the first and second mediator such that the first mediator is a predictor of the second, then we specify the first mediator right next to the treatment and the second mediator next to the outcome.

In the following example, we hypothesize that the causal sequence is arthritis affects physical activity, which in turn affects depressive symptoms. Thus, we specify `physact` as our first mediator right next to the treatment `arthritis`, and we specify `depress` as our second mediator next to the outcome `hrqol`. We also specify the `sequential` option to fit a sequential model:

```
. mediate (hrqol) (depress) (physact) (arthritis), sequential
Iteration 0:  EE criterion = 1.539e-27
Iteration 1:  EE criterion = 5.798e-29
Causal mediation analysis                               Number of obs = 2,000
Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
arthritis (Yes vs No)	-1.71165	.1496673	-11.44	0.000	-2.004993	-1.418308
NIE1						
arthritis (Yes vs No)	-1.814969	.1817366	-9.99	0.000	-2.171166	-1.458772
NIE2						
arthritis (Yes vs No)	-.5203296	.1197562	-4.34	0.000	-.7550474	-.2856118
NIE12						
arthritis (Yes vs No)	-.7320385	.1400059	-5.23	0.000	-1.006445	-.457632
TE						
arthritis (Yes vs No)	-4.778988	.2912224	-16.41	0.000	-5.349773	-4.208202

The output provides estimates of all four path-specific effects as well as the total effect. The total effect of −4.78 decomposes into the natural direct effect of −1.71, an indirect effect through `physact` alone of −1.81, an indirect effect through `depress` alone of −0.52, and an indirect effect through both `physact` and `depress` of −0.73. The interpretation of these effects is the same as before.

Example 7: Sequential model with treatment–mediator interactions

We now include interactions of both mediator variables with the treatment. While this is often a reasonable thing to do, it comes at the expense of increased complexity with respect to the number of estimands. To fit the model including these interactions, we specify the `tinteraction` option:

```
. mediate (hrqol) (depress) (physact) (arthritis), sequential
> tinteraction
Iteration 0:  EE criterion = 1.158e-25
Iteration 1:  EE criterion = 5.666e-28
Causal mediation analysis                              Number of obs = 2,000
Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
------------------------------------------------------------------------------
             |               Robust
       hrqol | Coefficient  std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
NDE          |
         000 |  -1.863452   .1961826    -9.50   0.000    -2.247963   -1.478941
         100 |    -2.7116   .3099477    -8.75   0.000    -3.319086   -2.104114
         010 |  -1.393251   .2242743    -6.21   0.000     -1.83282   -.9536811
         001 |  -1.201938   .2449106    -4.91   0.000    -1.681954   -.7219218
         110 |  -2.241399    .203996   -10.99   0.000    -2.641224   -1.841574
         101 |  -2.050086   .1664379   -12.32   0.000    -2.376298   -1.723873
         011 |  -.7317365   .3513065    -2.08   0.037    -1.420285   -.0431885
         111 |  -1.579885   .1577089   -10.02   0.000    -1.888988   -1.270781
-------------+----------------------------------------------------------------
NIE1         |
         000 |  -1.582646   .1686346    -9.39   0.000    -1.913164   -1.252129
         111 |  -2.430795   .3236353    -7.51   0.000    -3.065108   -1.796481
-------------+----------------------------------------------------------------
NIE2         |
         000 |  -.6715998    .129398    -5.19   0.000    -.9252152   -.4179843
         111 |  -.2013986   .0907096    -2.22   0.026    -.3791862   -.0236111
-------------+----------------------------------------------------------------
NIE12        |
         000 |  -.9448568   .1463968    -6.45   0.000    -1.231789   -.6579242
         111 |  -.2833427   .1292444    -2.19   0.028     -.536657   -.0300283
-------------+----------------------------------------------------------------
TE           |
   arthritis |
  (Yes vs No)|  -4.778988   .2912224   -16.41   0.000    -5.349773   -4.208202
------------------------------------------------------------------------------
Note: Outcome equation includes treatment-mediator interactions.
```

We now estimate eight natural direct effects and two distinct indirect effects each for `NIE1`, `NIE2`, and `NIE12`. For each of the indirect effects, we have one labeled `000`, which is the indirect-effect estimate evaluated as if no one in the population has arthritis, and the one labeled `111` is the indirect effect evaluated as if everyone in the population has arthritis. For example, the estimated natural direct effects via only `physact` are NIE1-000 $= -1.58$ and NIE1-111 $= -2.43$. Here the effects NIE1-000 can be interpreted analogously to a pure natural indirect effect, with everything set to values corresponding to no treatment. Similarly, NIE1-000 is analogous to a total natural indirect effect with everything set to values corresponding to treatment. If we had a good theoretical or even practical argument for focusing on either pure or total natural effects, we could pick estimates of interest accordingly.

Example 8: Including the mediator–mediator interaction

Including the mediator–mediator interaction allows for additional flexibility in that the effect of one mediator on the outcome depends on the other mediator and vice versa. However, adding the mediator–mediator interaction increases complexity further. To include the interaction, we add the `minteraction` option:

```
. mediate (hrqol) (depress) (physact) (arthritis), sequential
> tinteraction minteraction
Iteration 0:  EE criterion = 6.373e-21
Iteration 1:  EE criterion = 2.803e-28
Causal mediation analysis                            Number of obs = 2,000
Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
000	-2.138797	.1763549	-12.13	0.000	-2.484447	-1.793148
100	-1.842878	.2916825	-6.32	0.000	-2.414566	-1.271191
010	-2.163046	.178523	-12.12	0.000	-2.512945	-1.813148
001	-2.172913	.1984872	-10.95	0.000	-2.561941	-1.783885
110	-1.921357	.2153885	-8.92	0.000	-2.34351	-1.499203
101	-1.953287	.194975	-10.02	0.000	-2.335431	-1.571144
011	-2.197162	.2759688	-7.96	0.000	-2.738051	-1.656273
111	-2.031766	.1850413	-10.98	0.000	-2.39444	-1.669091
NIE1						
000	-3.277243	.3619214	-9.06	0.000	-3.986596	-2.56789
100	-2.981325	.3508021	-8.50	0.000	-3.668884	-2.293765
010	-3.323979	.3679973	-9.03	0.000	-4.04524	-2.602717
001	-3.342994	.3728914	-8.97	0.000	-4.073848	-2.61214
110	-3.082289	.3685075	-8.36	0.000	-3.80455	-2.360028
101	-3.123369	.3820944	-8.17	0.000	-3.87226	-2.374478
011	-3.389729	.3789566	-8.94	0.000	-4.132471	-2.646988
111	-3.224333	.4005567	-8.05	0.000	-4.00941	-2.439256
NIE2						
000	-.0725194	.0703347	-1.03	0.303	-.2103728	.065334
101	-.0967685	.0893702	-1.08	0.279	-.2719309	.0783938
011	-.1192547	.0672674	-1.77	0.076	-.2510964	.012587
111	-.1977329	.0879458	-2.25	0.025	-.3701034	-.0253623
NIE12						
000	-.1020257	.100273	-1.02	0.309	-.2985572	.0945059
101	-.1361412	.1249654	-1.09	0.276	-.3810689	.1087865
011	-.1677764	.0977465	-1.72	0.086	-.3593561	.0238032
111	-.2781854	.125105	-2.22	0.026	-.5233866	-.0329842
TE						
arthritis (Yes vs No)	-5.59604	.4280766	-13.07	0.000	-6.435055	-4.757025

```
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction.
```

Notice that, when tinteraction is specified to include treatment–mediator interactions, adding minteraction will also add the three-way interaction of both mediators and the treatment. Therefore, we actually add two interaction terms in this case. We see that the indirect effects related to the second mediator depress (NIE2 and NIE12) become quite small and fairly close to zero. Perhaps the somewhat larger results that we obtained before (for example, NIE2 equals −0.52 in the model without interactions) were rather spurious and the result of nonflexible specifications of the structural equations.

Example 9: Complete set of interactions

Finally, we add an interaction of the treatment and first mediator to the equation of the second mediator by specifying the meqtinteraction option. We now estimate all 32 defined-effect estimands that are shown in table 1 (plus the total effect, of course).

```
. mediate (hrqol) (depress) (physact) (arthritis), sequential
> tinteraction minteraction meqtinteraction

Iteration 0:  EE criterion = 6.373e-21
Iteration 1:  EE criterion = 5.935e-28

Causal mediation analysis                          Number of obs = 2,000

Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
000	-2.137034	.1755708	-12.17	0.000	-2.481146	-1.792921
100	-1.841115	.2914441	-6.32	0.000	-2.412335	-1.269895
010	-2.175025	.1867005	-11.65	0.000	-2.540951	-1.809098
001	-2.170996	.1970605	-11.02	0.000	-2.557228	-1.784765
110	-1.93079	.2240868	-8.62	0.000	-2.369992	-1.491587
101	-1.951029	.1944125	-10.04	0.000	-2.33207	-1.569987
011	-2.210278	.284549	-7.77	0.000	-2.767984	-1.652573
111	-2.044882	.1971614	-10.37	0.000	-2.431311	-1.658453
NIE1						
000	-3.277243	.3619214	-9.06	0.000	-3.986596	-2.56789
100	-2.981325	.3508021	-8.50	0.000	-3.668884	-2.293765
010	-3.321785	.3659441	-9.08	0.000	-4.039022	-2.604548
001	-3.342699	.3726794	-8.97	0.000	-4.073137	-2.612261
110	-3.07755	.3644594	-8.44	0.000	-3.791877	-2.363223
101	-3.122732	.3817002	-8.18	0.000	-3.87085	-2.374613
011	-3.389729	.3789566	-8.94	0.000	-4.132471	-2.646988
111	-3.224333	.4005567	-8.05	0.000	-4.00941	-2.439256
NIE2						
000	-.0819393	.0646655	-1.27	0.205	-.2086815	.0448028
100	-.1199303	.0962299	-1.25	0.213	-.3085375	.0686768
010	-.126481	.0623618	-2.03	0.043	-.2487078	-.0042542
001	-.0858009	.068813	-1.25	0.212	-.2206718	.04907
110	-.2161557	.0956439	-2.26	0.024	-.4036142	-.0286971
101	-.1250831	.104926	-1.19	0.233	-.3307343	.0805681
011	-.1328312	.0670555	-1.98	0.048	-.2642576	-.0014048
111	-.2266847	.1099928	-2.06	0.039	-.4422665	-.0111028

```
NIE12        |
         000 |  -.101568    .100049   -1.02   0.310   -.2976605    .0945245
         100 | -.1355305   .1244552   -1.09   0.276   -.3794582    .1083972
         010 | -.1670238   .0977036   -1.71   0.087   -.3585193    .0244717
         001 | -.1054296   .1019476   -1.03   0.301   -.3052432    .0943841
         110 | -.2769374   .1246697   -2.22   0.026   -.5212856   -.0325893
         101 | -.1406833   .1288855   -1.09   0.275   -.3932943    .1119277
         011 | -.1733739   .0984035   -1.76   0.078   -.3662413    .0194934
         111 | -.2874664   .1298441   -2.21   0.027   -.5419561   -.0329768
-------------+----------------------------------------------------------------
TE           |
   arthritis |
(Yes vs No)  |  -5.62198    .452873  -12.41   0.000   -6.509595   -4.734365
------------------------------------------------------------------------------
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction, and mediator 2 equation includes
      treatment-mediator interaction.
```

The estimates of NIE_2 and NIE_{12} remain close to zero, and the NDE and NIE_1 estimates do not seem to change in a meaningful way either. Here we could conclude that the effect of arthritis on health-related quality of life is largely due to its effect on physical activity (NIE_1) as well as other causal mechanisms (NDE) but not so much due to the pathway through depression.

There are 24 ways we can decompose the total effect into direct and indirect effects reported in the output above; see table 2.

Example 10: Estimating mediator-specific natural effects

A potential way of reducing the estimand complexity is to obtain a coarser decomposition. This can be done by focusing on the indirect effect of one mediator variable while combining the effect through the other mediator with the indirect effect that runs through both mediators. We refer to the resulting effects as mediator-specific effects.

To estimate mediator-specific effects, we first determine which mediator we wish to focus on. Focusing on the first mediator in the causal sequence, `physact` in this case, results in type-1 mediator-specific effects. Choosing the second mediator (`depress`) yields type-2 mediator-specific effects. To estimate type-1 effects, we use the `mseffects(physact)` option:

```
. mediate (hrqol age) (depress i.male) (physact i.male) (arthritis),
> sequential mseffects(physact)
Iteration 0:   EE criterion = 1.339e-27
Iteration 1:   EE criterion = 2.898e-29
Causal mediation analysis                                Number of obs = 2,000
Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
MS effects:     Type 1
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
MS-NDE						
arthritis						
(Yes vs No)	-2.48409	.0594904	-41.76	0.000	-2.600689	-2.367491
MS-NIE1						
arthritis						
(Yes vs No)	-1.938463	.1639594	-11.82	0.000	-2.259817	-1.617108
MS-NIE2						
arthritis						
(Yes vs No)	-.9174464	.1036528	-8.85	0.000	-1.120602	-.7142907
TE						
arthritis						
(Yes vs No)	-5.339999	.2326946	-22.95	0.000	-5.796072	-4.883926

We no longer have an effect that captures the pathway through both mediators because this is subsumed in the MS-NIE$_2$ effect now. Here we did not include any interactions, which is why we have only a single estimate per effect. However, even if we had included all interactions as we did in the previous example, we would have to deal with a total of only 12 estimands rather than 32, as described in the top half of table 3.

Example 11: Adding interactions of covariates with mediators and treatment

In some of the previous examples, we added treatment–mediator and mediator–mediator interactions to allow for model flexibility. However, if our model contains covariates, we can make it even more flexible by adding interactions of the covariates with both the treatment and the mediators. To do so, we use factor-variable notation and add the desired interactions to the equations of interest:

```
. mediate (hrqol age i.male i.male#c.(depress physact) i.male#i.arthritis)
>         (depress i.male i.male#(c.physact i.arthritis))
>         (physact i.male i.male#i.arthritis)
>         (arthritis), sequential tinteraction minteraction meqtinteraction
Iteration 0:  EE criterion = 7.489e-21
Iteration 1:  EE criterion = 1.034e-28

Causal mediation analysis                           Number of obs = 2,000

Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf. interval]	
NDE						
000	-2.861964	.0939964	-30.45	0.000	-3.046194	-2.677735
100	-2.217973	.1583486	-14.01	0.000	-2.52833	-1.907615
010	-2.949311	.0976019	-30.22	0.000	-3.140608	-2.758015
001	-2.972083	.1109218	-26.79	0.000	-3.189485	-2.75468
110	-2.297695	.0963058	-23.86	0.000	-2.486451	-2.108939
101	-2.317705	.0815672	-28.41	0.000	-2.477574	-2.157837
011	-3.047135	.1569048	-19.42	0.000	-3.354663	-2.739607
111	-2.386283	.0686456	-34.76	0.000	-2.520826	-2.25174
NIE1						
000	-2.465474	.2288064	-10.78	0.000	-2.913926	-2.017022
100	-1.821483	.1850826	-9.84	0.000	-2.184238	-1.458728
010	-2.484133	.2312894	-10.74	0.000	-2.937452	-2.030815
001	-2.490889	.233858	-10.65	0.000	-2.949243	-2.032536
110	-1.832517	.1875503	-9.77	0.000	-2.200109	-1.464925
101	-1.836512	.1893983	-9.70	0.000	-2.207726	-1.465298
011	-2.506735	.2357752	-10.63	0.000	-2.968846	-2.044624
111	-1.845883	.191579	-9.64	0.000	-2.22137	-1.470395
NIE2						
000	-.2491834	.045908	-5.43	0.000	-.3391614	-.1592055
100	-.3365307	.0588508	-5.72	0.000	-.4518762	-.2211853
010	-.2678428	.0454731	-5.89	0.000	-.3569683	-.1787172
001	-.2119778	.0394603	-5.37	0.000	-.2893185	-.1346371
110	-.347565	.0585846	-5.93	0.000	-.4623886	-.2327414
101	-.2870304	.0513105	-5.59	0.000	-.3875972	-.1864636
011	-.2278234	.0390462	-5.83	0.000	-.3043525	-.1512942
111	-.2964007	.051029	-5.81	0.000	-.3964157	-.1963858

NIE12						
000	-.328122	.0694224	-4.73	0.000	-.4641874	-.1920565
100	-.4382404	.0793344	-5.52	0.000	-.5937329	-.2827478
010	-.3535372	.0704798	-5.02	0.000	-.4916751	-.2153993
001	-.2909163	.0618135	-4.71	0.000	-.4120686	-.1697641
110	-.4532698	.0803072	-5.64	0.000	-.6106689	-.2958706
101	-.38874	.0704634	-5.52	0.000	-.5268457	-.2506343
011	-.3135178	.0627361	-5.00	0.000	-.4364783	-.1905573
111	-.4021055	.0713222	-5.64	0.000	-.5418943	-.2623166
TE						
arthritis (Yes vs No)	-5.433117	.2491783	-21.80	0.000	-5.921498	-4.944737

Note: Outcome equation includes treatment-mediator interactions and mediator-mediator interaction, and mediator 2 equation includes treatment-mediator interaction.

Here we include covariates age and male in our outcome equation and covariate male in both mediator equations. We also added the interaction term male × arthritis to the equation of the first mediator (physact), added male × arthritis and male × physact to the equation of the second mediator (depress), and added terms male × arthritis, male × depress, and male × physact to the outcome equation.

Example 12: Sensitivity analysis

In *Modeling and estimation*, we discussed performing sensitivity analysis on the unobserved correlation parameter related to the conditional covariance of $M_1(0)$ and $M_1(1)$. We can use the `estat smsensitivity` postestimation command to perform the analysis. By default, `mediate` assumes that the error terms related to $M_1(0)$ and $M_1(1)$ are identical and thus perfectly correlated (that is, $\rho = 1$). By varying the value of ρ, we can find out how sensitive our results are to the assumed correlation. By default, `estat smsensitivity` evaluates the effect estimates at values of $\rho = 0$ and $\rho = 0.5$ and compares them to the estimates we obtained from `mediate` using $\rho = 1$. We could evaluate other values of ρ by specifying them using the `rho()` option. Here, however, we use the default values:

```
. estat smsensitivity
Sequential mediation sensitivity analysis
Number of obs = 2,000

Correlation assumed in fitted model: rho = 1

Evaluating effects at rho = 0.0  ...
                      rho = 0.5  ...

--------------------------------------------------
                    rho=0.00 rho=0.50 rho=1.00
--------------------------------------------------
NDE
  000                 -2.900   -2.881   -2.862
                     (0.108)  (0.100)  (0.094)
  100                 -2.256   -2.237   -2.218
                     (0.156)  (0.156)  (0.158)
  010                 -2.983   -2.966   -2.949
                     (0.113)  (0.104)  (0.098)
  001                 -3.010   -2.991   -2.972
                     (0.126)  (0.118)  (0.111)
  110                 -2.331   -2.315   -2.298
                     (0.094)  (0.094)  (0.096)
  101                 -2.356   -2.337   -2.318
                     (0.078)  (0.078)  (0.082)
  011                 -3.081   -3.064   -3.047
                     (0.169)  (0.162)  (0.157)
  111                 -2.420   -2.403   -2.386
                     (0.066)  (0.066)  (0.069)
NIE1
  000                 -2.465   -2.465   -2.465
                     (0.229)  (0.229)  (0.229)
  100                 -1.821   -1.821   -1.821
                     (0.185)  (0.185)  (0.185)
  010                 -2.484   -2.484   -2.484
                     (0.231)  (0.231)  (0.231)
  001                 -2.491   -2.491   -2.491
                     (0.234)  (0.234)  (0.234)
  110                 -1.833   -1.833   -1.833
                     (0.188)  (0.188)  (0.188)
  101                 -1.837   -1.837   -1.837
                     (0.189)  (0.189)  (0.189)
  011                 -2.507   -2.507   -2.507
                     (0.236)  (0.236)  (0.236)
  111                 -1.846   -1.846   -1.846
                     (0.192)  (0.192)  (0.192)
```

NIE2			
000	-0.260	-0.254	-0.249
	(0.046)	(0.046)	(0.046)
100	-0.343	-0.340	-0.337
	(0.059)	(0.059)	(0.059)
010	-0.278	-0.273	-0.268
	(0.046)	(0.046)	(0.045)
001	-0.222	-0.217	-0.212
	(0.039)	(0.039)	(0.039)
110	-0.354	-0.351	-0.348
	(0.059)	(0.059)	(0.059)
101	-0.293	-0.290	-0.287
	(0.051)	(0.051)	(0.051)
011	-0.238	-0.233	-0.228
	(0.039)	(0.039)	(0.039)
111	-0.303	-0.300	-0.296
	(0.051)	(0.051)	(0.051)
NIE12			
000	-0.328	-0.328	-0.328
	(0.069)	(0.069)	(0.069)
100	-0.438	-0.438	-0.438
	(0.079)	(0.079)	(0.079)
010	-0.354	-0.354	-0.354
	(0.070)	(0.070)	(0.070)
001	-0.291	-0.291	-0.291
	(0.062)	(0.062)	(0.062)
110	-0.453	-0.453	-0.453
	(0.080)	(0.080)	(0.080)
101	-0.389	-0.389	-0.389
	(0.070)	(0.070)	(0.070)
011	-0.314	-0.314	-0.314
	(0.063)	(0.063)	(0.063)
111	-0.402	-0.402	-0.402
	(0.071)	(0.071)	(0.071)
TE			
Arthritis			
(Yes vs No)	-5.477	-5.455	-5.433
	(0.254)	(0.251)	(0.249)

The results do not change in a meaningful way over the different values of ρ. The assumption of perfect correlation is inconsequential in this case.

See [CAUSAL] **mediate multiple postestimation** for further information about `estat smsensitivity`.

Example 13: Estimating controlled direct effects

Controlled direct effects (CDEs) are different from the other estimands we have discussed so far. Here, rather than having potential outcomes of the form $Y_i[t, M_{1i}(t'), M_{2i}\{t'', M_{1i}(t''')\}]$, we have potential outcomes $Y_i(t|M_{1i} = m_{1i}, M_{2i} = m_{2i})$. That is, we have potential outcomes for each treatment level that are evaluated at set values of the mediators. Thus, CDEs use only the results of the outcome equation. Assuming a binary treatment, the CDE for values m_1 and m_2 of the two mediators is $\text{CDE}(\mathbf{m}) = Y_i(1|M_{1i} = m_1, M_{2i} = m_2) - Y_i(0|M_{1i} = m_1, M_{2i} = m_2)$. CDEs can be estimated using the `estat cde` postestimation command.

To demonstrate, we begin by fitting the following sequential mediation model:

```
. mediate (hrqol) (depress) (physact) (arthritis), sequential
> tinteraction minteraction
Iteration 0:  EE criterion = 6.373e-21
Iteration 1:  EE criterion = 2.803e-28
Causal mediation analysis                              Number of obs = 2,000
Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Binary

------------------------------------------------------------------------------
             |               Robust
       hrqol | Coefficient  std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
NDE          |
         000 |  -2.138797   .1763549   -12.13   0.000    -2.484447   -1.793148
         100 |  -1.842878   .2916825    -6.32   0.000    -2.414566   -1.271191
         010 |  -2.163046    .178523   -12.12   0.000    -2.512945   -1.813148
         001 |  -2.172913   .1984872   -10.95   0.000    -2.561941   -1.783885
         110 |  -1.921357   .2153885    -8.92   0.000     -2.34351   -1.499203
         101 |  -1.953287    .194975   -10.02   0.000    -2.335431   -1.571144
         011 |  -2.197162   .2759688    -7.96   0.000    -2.738051   -1.656273
         111 |  -2.031766   .1850413   -10.98   0.000     -2.39444   -1.669091
-------------+----------------------------------------------------------------
NIE1         |
         000 |  -3.277243   .3619214    -9.06   0.000    -3.986596    -2.56789
         100 |  -2.981325   .3508021    -8.50   0.000    -3.668884   -2.293765
         010 |  -3.323979   .3679973    -9.03   0.000     -4.04524   -2.602717
         001 |  -3.342994   .3728914    -8.97   0.000    -4.073848    -2.61214
         110 |  -3.082289   .3685075    -8.36   0.000     -3.80455   -2.360028
         101 |  -3.123369   .3820944    -8.17   0.000     -3.87226   -2.374478
         011 |  -3.389729   .3789566    -8.94   0.000    -4.132471   -2.646988
         111 |  -3.224333   .4005567    -8.05   0.000     -4.00941   -2.439256
-------------+----------------------------------------------------------------
NIE2         |
         000 |  -.0725194   .0703347    -1.03   0.303    -.2103728     .065334
         101 |  -.0967685   .0893702    -1.08   0.279    -.2719309    .0783938
         011 |  -.1192547   .0672674    -1.77   0.076    -.2510964     .012587
         111 |  -.1977329   .0879458    -2.25   0.025    -.3701034   -.0253623
-------------+----------------------------------------------------------------
NIE12        |
         000 |  -.1020257    .100273    -1.02   0.309    -.2985572    .0945059
         101 |  -.1361412   .1249654    -1.09   0.276    -.3810689    .1087865
         011 |  -.1677764   .0977465    -1.72   0.086    -.3593561    .0238032
         111 |  -.2781854    .125105    -2.22   0.026    -.5233866   -.0329842
-------------+----------------------------------------------------------------
TE           |
   arthritis |
 (Yes vs No) |   -5.59604   .4280766   -13.07   0.000    -6.435055   -4.757025
------------------------------------------------------------------------------
Note: Outcome equation includes treatment-mediator interactions and
      mediator-mediator interaction.
```

We now use `estat cde` to estimate CDEs. We specify at least one value of interest for each mediator in the `mvalue()` option. Here we evaluate the CDE at `physact` = 0 and `depress` = 7:

```
. estat cde, mvalue(physact=0 depress=7)

Controlled direct effect                              Number of obs = 2,000

Mediator variables: physact depress
Mediator values:
  physact = 0
  depress = 7

------------------------------------------------------------------------------
             |              Delta-method
             |        CDE    std. err.      z    P>|z|     [95% conf. interval]
-------------+----------------------------------------------------------------
   arthritis |
(Yes vs No)  |  -1.908641    .3501075    -5.45   0.000    -2.594839   -1.222443
------------------------------------------------------------------------------
```

The estimated effect is −1.9, which means that, if everyone in the population had a physical activity score of 0 and a depression score of 7, we would expect a difference in quality of life of 1.9 points as a direct consequence of arthritis.

Rather than evaluating CDEs at single points, we could also provide lists of evaluation points. For example, we might be interested in the CDE for which we fix one mediator at a single value but fix the other mediator at a range of values. In the following example, we fix physact at 0 and let the values for depress range from 0 to 10:

```
. estat cde, mvalue(physact=0 depress=(0(1)10))
Controlled direct effect                             Number of obs = 2,000

Mediator variables: physact depress
Mediator values:
  1._at:  physact =  0
          depress =  0
  2._at:  physact =  0
          depress =  1
  3._at:  physact =  0
          depress =  2
  4._at:  physact =  0
          depress =  3
  5._at:  physact =  0
          depress =  4
  6._at:  physact =  0
          depress =  5
  7._at:  physact =  0
          depress =  6
  8._at:  physact =  0
          depress =  7
  9._at:  physact =  0
          depress =  8
  10._at: physact =  0
          depress =  9
  11._at: physact =  0
          depress = 10
```

	CDE	Delta-method std. err.	z	P>|z|	[95% conf.	interval]
arthritis@ _at						
(Yes vs No) 1	2.526337	4.33281	0.58	0.560	-5.965815	11.01849
(Yes vs No) 2	1.892769	3.669792	0.52	0.606	-5.299891	9.085429
(Yes vs No) 3	1.259201	3.006991	0.42	0.675	-4.634394	7.152795
(Yes vs No) 4	.6256324	2.344593	0.27	0.790	-3.969686	5.220951
(Yes vs No) 5	-.0079359	1.683074	-0.00	0.996	-3.306699	3.290828
(Yes vs No) 6	-.6415041	1.024135	-0.63	0.531	-2.648772	1.365764
(Yes vs No) 7	-1.275072	.3813991	-3.34	0.001	-2.022601	-.5275439
(Yes vs No) 8	-1.908641	.3501075	-5.45	0.000	-2.594839	-1.222443
(Yes vs No) 9	-2.542209	.9900416	-2.57	0.010	-4.482655	-.6017629
(Yes vs No) 10	-3.175777	1.648723	-1.93	0.054	-6.407214	.0556602
(Yes vs No) 11	-3.809345	2.310171	-1.65	0.099	-8.337196	.7185059

We can see that our specification expands to pairs of values at which the CDE is evaluated. That is, the CDE is evaluated at pairs ($\texttt{physact} = 0, \texttt{depress} = 0$), ($\texttt{physact} = 0, \texttt{depress} = 1$), ($\texttt{physact} = 0, \texttt{depress} = 2$), and so on.

See [CAUSAL] **mediate multiple postestimation** for further information about `estat cde`.

Example 14: Continuous treatment

Instead of a binary treatment, we can use a continuous treatment variable. With continuous treatments, we have to specify evaluation points of the treatment variable at which to evaluate the effects. The potential-outcome mean notation extends straightforwardly to this case where we simply replace the zeros and ones from the binary case with the evaluation points of interest from the continuous treatment variable. With continuous treatments, we have to specify two values, one to be taken as the treatment level and another to be taken as the control level.

Here we are using variable `arth_cont` as our treatment variable, which can be thought of as a measure of severity of arthritis. We wish to estimate natural direct and indirect effects related to contrasts in potential outcomes that are defined by the set control and treatment levels of the continuous variable. Here we set 0 as our control level (that is, no arthritis) and 10 as our level of treatment (that is, moderately severe arthritis) using the `continuous()` option:

```
. mediate (hrqol) (depress) (physact) (arth_cont, continuous(0 10)), sequential

Iteration 0:  EE criterion = 1.219e-27
Iteration 1:  EE criterion = 2.897e-29

Causal mediation analysis                                Number of obs = 2,000

Mediation type: Sequential
Mediator 1:     physact
Mediator 2:     depress
Treatment type: Continuous

Continuous treatment levels:
  0: arth_cont =  0 (control)
  1: arth_cont = 10
```

hrqol	Coefficient	Robust std. err.	z	P>|z|	[95% conf.	interval]
NDE						
arth_cont (1 vs 0)	-1.350019	.3748461	-3.60	0.000	-2.084703	-.6153338
NIE1						
arth_cont (1 vs 0)	-1.091863	.3515679	-3.11	0.002	-1.780923	-.4028024
NIE2						
arth_cont (1 vs 0)	-.5607094	.1522004	-3.68	0.000	-.8590167	-.2624022
NIE12						
arth_cont (1 vs 0)	-.7201396	.2306259	-3.12	0.002	-1.172158	-.2681211
TE						
arth_cont (1 vs 0)	-3.72273	.9267735	-4.02	0.000	-5.539173	-1.906288

The results are interpreted the same way as in the binary treatment case. For example, the total effect here is around −3.7. If everyone in the population had arth_cont = 0 versus everyone had arth_cont = 10, we would expect an average decrease in health-related quality of life by 3.7 points. This total effect decomposes into direct and indirect effects that are interpreted similarly.

Stored results

mediate stores the following in e():

Scalars

e(N)	number of observations
e(N_clust)	number of clusters
e(k_eq)	number of equations in e(b)
e(k_levels)	number of levels in treatment variable
e(mstype)	type of mediator-specific effects
e(tinteraction)	1 if treatment–mediator interactions included, 0 otherwise
e(minteraction)	1 if mediator–mediator interaction included, 0 otherwise
e(meqtinteraction)	1 if treatment–mediator interaction in mediator equation, 0 otherwise
e(rank)	rank of e(V)
e(converged)	1 if converged, 0 otherwise

Macros

e(cmd)	mediate
e(cmdline)	command as typed
e(depvar)	name of outcome variable
e(mvar1)	name of first mediator variable
e(mvar2)	name of second mediator variable
e(tvar)	name of treatment variable
e(med_type)	parallel or sequential
e(wtype)	weight type
e(wexp)	weight expression
e(title)	title in estimation output
e(clustvar)	name of cluster variable
e(tlevels)	levels of treatment variable
e(tvartype)	binary or continuous
e(control)	control level
e(vce)	*vcetype* specified in vce()
e(vcetype)	title used to label Std. err.
e(properties)	b V
e(estat_cmd)	program used to implement estat
e(predict)	program used to implement predict
e(marginsnotok)	predictions disallowed by margins

Matrices

e(b)	coefficient vector
e(V)	variance–covariance matrix of the estimators

Functions

e(sample)	marks estimation sample

In addition to the above, the following is stored in r():

Matrices

r(table)	matrix containing the coefficients with their standard errors, test statistics, *p*-values, and confidence intervals

Note that results stored in r() are updated when the command is replayed and will be replaced when any r-class command is run after the estimation command.

Methods and formulas

Two-mediator case

The two-mediator version of `mediate` fits causal mediation models with two mediators that can be causally ordered and provides the finest possible decomposition into all path-specific effects. Coarser decompositions are also available in form of mediator-specific effects. We follow the derivations and definitions discussed in Daniel et al. (2015).

With the potential-outcomes framework, the estimated treatment effects are the result of contrasts between potential-outcome means. Without loss of generality, let T_i be a binary treatment, $t \in \{0, 1\}$, for observations $i = 1, \dots, N$, and let Y_i be the outcome, $M_{i,1}$ the first mediator variable, and $M_{i,2}$ the second mediator variable. The potential-outcome means for models with causally ordered mediators take on the form

$$E(Y_i[t, M_{i,1}(t'), M_{i,2}\{t'', M_{i,1}(t''')\}])$$

The potential-outcome means are defined as the result of an integral of the conditional expectation of the outcome with respect to conditional distributions of mediators and covariates. This integral can be written as

$$\begin{aligned} E\left(Y[t, M_1(t'), M_2\{t'', M_1(t''')\}]\right) = \int_x \int_{m_1} \int_{m_1'} \int_{m_2} & E(Y \mid X = x, T = t, M_1 = m_1, M_2 = m_2) \\ & \times p(m_2 \mid x, t'', m_1') \times p(m_1' \mid x, m_1, t'') \times p(m_1 \mid x, t') \\ & \times p(x)\, dm_2\, dm_1'\, dm_1\, dx \end{aligned}$$

where $p(\cdot)$ denotes conditional densities. For models without causally ordered mediators, the potential-outcome means simplify to

$$E[Y_i\{t, M_{i,1}(t'), M_{i,2}(t'')\}]$$

Consequently, the integral from above simplifies to

$$\begin{aligned} E\left[Y\{t, M_1(t'), M_2(t'')\}\right] = \int_x \int_{m_1} \int_{m_2} & E[Y \mid X = x, T = t, M_1 = m_1, M_2 = m_2] \\ & \times p(m_2 \mid x, t'') \times p(m_1 \mid x, t') \times p(x)\, dm_2\, dm_1\, dx \end{aligned}$$

`mediate` uses a system of linear equations to approximate these integrals and estimate the potential-outcome means. For example, the general case of causal mediation with two causally ordered mediators and all possible treatment–mediator and mediator–mediator interactions (ignoring covariates here for simplicity) yields the following system of equations:

$$\begin{aligned} Y_i =& \beta_0 + \beta_1 T_i + \beta_2 M_{i,1} + \beta_3 M_{i,2} + \beta_4 T_i M_{i,1} + \beta_5 T_i M_{i,2} + \beta_6 M_{i,1} M_{i,2} + \\ & \beta_7 T_i M_{i,1} M_{i,2} + \epsilon_{Y_i} \\ M_{i,2} =& \gamma_0 + \gamma_1 T_i + \gamma_2 M_{i,1} + \gamma_3 T_i M_{i,1} + \epsilon_{M_{i,2}} \\ M_{i,1} =& \alpha_0 + \alpha_1 T_i + \epsilon_{M_{i,1}} \end{aligned}$$

Error terms ϵ_Y, ϵ_{M_1}, and ϵ_{M_2} are assumed independent with zero mean and variances σ^2_Y, $\sigma^2_{M_1}$, and $\sigma^2_{M_2}$. Plugging the M_1 and M_2 equations into the outcome equation yields the expectation

$$\begin{aligned}E(Y[t, M_1(t'), M_2\{t'', M_1(t''')\}]) =& \beta_0 + \beta_1 t + (\beta_2 + \beta_4 t)(\alpha_0 + \alpha_1 t')+\\ &(\beta_3 + \beta_5 t)(\gamma_0 + \gamma_1 t'' + (\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t'''))+\\ &(\beta_6 + \beta_7 t)[(\alpha_0 + \alpha_1 t')\{\gamma_0 + \gamma_1 t''+\\ &(\gamma_2 + \gamma_3 t'')(\alpha_0 + \alpha_1 t''')\}]+\\ &(\beta_6 + \beta_7 t)(\gamma_2 + \gamma_3 t'')E(\epsilon^{t'}_{M_1}\epsilon^{t'''}_{M_1})\end{aligned} \tag{2}$$

Using estimates of $\boldsymbol{\beta}$, $\boldsymbol{\gamma}$, and $\boldsymbol{\alpha}$, obtained by OLS, the estimated potential-outcome mean is the sample average

$$\widehat{\text{POM}}_{t,t',t'',t'''} = \frac{1}{N}\sum_{i=1}^{N} Y_i[t, M_{i,1}(t'), M_{i,2}\{t'', M_{i,1}(t''')\}] \,|\, \mathbf{X}_i = \mathbf{x}$$

Estimates of direct, indirect, and total effects can then be obtained by taking differences between potential-outcome means. The effect definitions and corresponding decompositions are shown in tables 1, 2, 4, and 5.

`mediate` uses a method of moments estimator, also known as an estimating equations estimator, to estimate all auxiliary and effect parameters as well as their variance–covariance matrix. For more information about the underlying `gmm` command, see [R] **gmm**.

Sequential mediation sensitivity analysis

The reduced form in (2) contains the expected value of the product of error terms $\epsilon^{t'}_{M_1}$ and $\epsilon^{t'''}_{M_1}$ that is to be computed for sequential models that contain treatment–mediator as well as mediator–mediator interactions. Following Daniel et al. (2015), the error terms can be thought of as arising from the fact that $M_1(t)$ can be evaluated at different t when $t' \neq t'''$. If we set $t' = 0$ and $t''' = 1$, for example, potential outcomes for mediator M_1 are

$$\begin{aligned}M_1(t') &= M_1(0) = \alpha_0 + \epsilon^{t'}_{M_1}\\ M_1(t''') &= M_1(1) = \alpha_0 + \alpha_1 + \epsilon^{t'''}_{M_1}\end{aligned}$$

Information about the residual covariance, which would be needed to compute the error product, is not available from the data. Therefore, this conditional correlation between $M_1(0)$ and $M_1(1)$ has to be set by assumption. We can write the expected value of the error product as $E(\epsilon^{t'}_{M_1}\epsilon^{t'''}_{M_1}) = E(\epsilon^{t'}_{M_1})E(\epsilon^{t'''}_{M_1}) + \rho_{M_1^{t'}M_1^{t'''}}\sigma_{M_1^{t'}}\sigma_{M_1^{t'''}}$, where $\rho_{M_1^{t'}M_1^{t'''}}$ is the correlation and $\sigma_{M_1^{t'}}$ and $\sigma_{M_1^{t'''}}$ are standard deviations. By assumption, we have that $\sigma_{M_1^{t'}} = \sigma_{M_1^{t'''}}$ and $E(\epsilon^{t'}_{M_1}) = E(\epsilon^{t'''}_{M_1}) = 0$. Thus, if we were to assume perfect correlation, that is, $\rho_{M_1^{t'}M_1^{t'''}} = 1$, we are left with $\sigma_{M_1^{t'}}\sigma_{M_1^{t'''}} = \sigma^2_{M_1}$. At the other extreme, assuming independence implies that $\rho_{M_1^{t'}M_1^{t'''}} = 0$ and thus that $E(\epsilon^{t'}_{M_1}\epsilon^{t'''}_{M_1}) = 0$. `mediate` assumes $\rho_{M_1^{t'}M_1^{t'''}} = 1$ and replaces $E(\epsilon^{t'}_{M_1}\epsilon^{t'''}_{M_1})$ with $\sigma^2_{M_1}$. The `estat smsensitivity` postestimation command can be used to perform a sensitivity analysis where the value of $\rho_{M_1^{t'}M_1^{t'''}}$ can be varied between 0 and 1.

CDEs

CDEs are differences in potential-outcome means between treatments where the mediators are fixed at certain values of interest. The potential outcomes in this case are $Y_i(t|M_{1i} = m_{1i}, M_{2i} = m_{2i})$ and require use of only the outcome equation. With binary treatment $T \in \{0, 1\}$, the CDEs for values $\mathbf{m} \equiv \{m_1, m_2\}$ of the two mediators are $\text{CDE}(\mathbf{m}) = Y_i(1|M_{1i} = m_1, M_{2i} = m_2) - Y_i(0|M_{1i} = m_1, M_{2i} = m_2)$. The potential outcomes $Y_i(t|M_{1i} = m_1, M_{2i} = m_2)$ reflect the conditional expectation $E(Y_i|T = t, M_{1i} = m_1, M_{2i} = m_2)$, which is computed by taking the linear prediction of the outcome equation while fixing T at 0 and 1 and the mediator values at m_1 and m_2.

Reference

Daniel, R. M., B. L. De Stavola, S. N. Cousens, and S. Vansteelandt. 2015. Causal mediation analysis with multiple mediators. *Biometrics* 71: 1–14. https://doi.org/10.1111/biom.12248.

Also see

[CAUSAL] **mediate multiple postestimation** — Postestimation tools for mediate+

[CAUSAL] **mediate intro** — Introduction to causal mediation analysis

[CAUSAL] **mediate** — Causal mediation analysis (one mediator)

[SEM] **sem** — Structural equation model estimation command

[U] 20 Estimation and postestimation commands

For suggested citations, see the FAQ on citing Stata documentation.