# Mediation Analysis in the Two Condition Pretest–Posttest Design: Treatment as Moderator of Time Effects

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#### Abstract

A psychological intervention, such as a weight loss program or a form of psychotherapy, is perceived as effective by a person if he or she experiences some kind of change in thoughts, feelings, or behavior following the intervention. Intervention effects manifest themselves in people in the form of changes over time. In this paper, we provide an approach to mediation analysis in pretest—posttest designs that coincides with such within-person psychological experience of change. Our approach focuses on differences between conditions (i.e., between those who do versus do not receive the intervention) in the indirect and direct effects of the passage of time. We provide an example of the analysis and interpretation using data from a study examining the mediating role of abdominal adiposity (fat) in the effect of an exercise intervention on insulin sensitivity. CURRENT WORD COUNT IN BODY OF TEXT: About 7100

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# Mediation Analysis in the Two Condition Pretest–Posttest Design: Treatment as Moderator of Time Effects

In the day-to-day psychology of a person, the effect of an intervention, such as a weight loss program or a form of psychotherapy to treat an psychological ailment, is experienced in the form of a change over time in a behavior, thought, or physical or psychological state. When a person experiences a change, such as a reduction in his or her social anxiety, that change is often attributed to something that happened between an earlier and a later observation, such as beginning psychotherapy. But scientists studying the effects of interventions recognize that change from a prior state following the implementation of an intervention is not sufficient to claim that the intervention had an effect. Perhaps the person's anxiety would have changed anyway, even if he or she didn't start therapy. For this reason, scientists studying the effects of interventions prefer to simultaneously observe a group of people who don't experience the intervention. Evidence that the intervention had an effect is obtained by showing that change over time was different in some manner for those who experienced the intervention compared to those who did not experience it.

Scientists thinking ahead will collect data relevant to possible mechanisms by which an intervention may work. For example, if a form of psychotherapy reduces social anxiety because the therapy reduces the perceived threat of social interactions, it would be important to measure not only people's social anxiety before and after starting psychotherapy, but also how threatening they construe certain social situations. With such data, a mediation analysis can be used to examine if those who do versus those who do not receive therapy show differences over time in their threat construal which in turn reduces social anxiety.

The reasoning above describes treatment condition (i.e., receiving psychotherapy or not) as a moderator of a mediation process. A moderator is a variable that influences or is in some way related to the size of the effect of one variable on another. The mediation

process being examined is one where *time* influences the mediator (e.g., threat construals) and those changes in the mediator then influence the outcome (e.g., social anxiety). If change in the mediator variable differs between those who do and do not receive the intervention and change in the outcome corresponds to change in the mediator, then we deem the intervention as responsible for differences between groups over time as a result of the change in the mediator which in turn causes differences in the outcome.

In this article, we present an approach to mediation analysis in two condition pretest–posttest designs that treats interventions as moderators of *time* effects. Relying on a difference-score approach to mediation analysis first described by Judd, Kenny, and McClelland (2001), later modernized by Montoya and Hayes (2017), we show how difference between groups in change in an outcome variable over time breaks into differences between direct and indirect processes, and that a formal test of the difference in the size of the indirect effects of time in the two groups can be used as formal test of mediation. To facilitate adoption, we describe implementation of the method in the easy-to-use and freely-available MEMORE macro available for SPSS and SAS. We also provide comparable Mplus code that conducts the analysis in a structural equation modeling framework.

# The Vocabulary and Mechanics of Mediation Analysis

Mediation analysis is used to test a hypothesis about the mechanism by which some causal antecedent or agent X influences some outcome Y through a *mediator* variable M. A mediator is a variable causally located between X and Y, meaning that it is causally determined by X (at least in part) while also causally determining Y. Thus, X influences M, and M in turn influences Y.

Ordinary least squares regression analysis is the most popular approach to mediation analysis when M and Y are continuous measures and measured only once and participants are observed on or randomly assigned to X. This approach is represented in the form of a

path diagram in Figure 1. When using this approach, the *total effect* of X is estimated by regressing Y on X:

$$Y = i_Y + cX + e_Y \tag{1}$$

where  $e_Y$  is an error in estimation of a person's Y from his or her X. The weight for X, c, is the total effect of X and quantifies the difference in Y between two cases that differ by one unit on X. If X is dichotomous and the groups are coded such that they differ by one unit (e.g., 0 and 1, or -0.5 and 0.5), then c is the difference between the group means on Y.

The total effect of X breaks up algebraically into a direct effect and indirect effect of X. These are estimated by regressing M on X and Y on both M and X:

$$M = i_M + aX + e_M \tag{2}$$

$$Y = i_Y + c'X + bM + e_Y \tag{3}$$

The indirect effect of X on Y through M is the product of a and b and estimates the difference on Y between two cases that differ by one unit on X that is attributable to the joint effect of X on M and the effect of M on Y. The direct effect of X on Y is c'. It estimates the difference in Y between two cases that differ by one unit on X but who are equal on M. As such, it represents the component of X's effect on Y that operates independently of the  $X \to M \to Y$  causal sequence. When the indirect and direct effects are added together, they equal c, the total effect of X. That is c = c' + ab.

Historically, the causal steps approach popularized by Baron and Kenny (1986) or variants of it (e.g., Kraemer, Kiernan, Essex, & Kupfer, 2008) have been used to establish whether M is functioning as a mediator of the effect of X on Y. This approach requires establishing evidence of a nonzero total effect of X on Y (c in Figure 1) as well as statistically significant effects of X on M and M on Y (a and b in Figure 1). But since about the turn of the century, this approach has begun to out of favor. By 21st-cenutry thinking, evidence of total effect of X is no longer seen as a prerequisite to empirically examining how a causal effect of X on Y may operate (Cerin & MacKinnon, 2009; Hayes,

2009; Hayes & Rockwood, 2017; O'Rourke & MacKinnon, 2018; Rucker, Preacher, Tormala, & Petty, 2011; Shrout & Bolger, 2002). Furthermore, an indirect effect can exist even if it can't be established that a and b are both significantly different from zero (Hayes, 2018).

Modern approaches to mediation analysis focus on the indirect effect of X on Y through M quantified as ab. An inference that ab is not zero combined with signs of a and b that are consistent with the proposed process is sufficient to support a claim of mediation, even if a and/or b is not statistically significant. A vestige of 20th-century thought, some still use the Sobel test for inference about the indirect effect, which assumes the sampling distribution of the indirect effect is normal (Sobel, 1982). Modern thinking relies an inferential method that doesn't make assumptions about the shape of the sampling distribution of the indirect effect of X, as the Sobel test does. Of these methods, the bootstrap confidence interval has become most popular. For a discussion of bootstrap confidence intervals and other approaches to inference about an indirect effect, see Hayes (2018), MacKinnon, Lockwood, and Williams (2004), Preacher and Selig (2012), and Shrout and Bolger (2002).

# Mediation Analysis in the Two-Instance Repeated Measures Design

The mediation model just described ssumes M and Y are measured only once and that X (i.e., intervention) is the causal agent of interest. When M and Y are measured at twice, once at pretest and again at posttest, there are many approaches to testing whether M can be deemed as serving a mediating role in the effect of X on Y while using information about the repeated measurements over time (MacKinnon, 2008; Valente & MacKinnon, 2017). These approaches all treat the intervention manipulation is the focal causal agent X and the data analysis focuses on estimating the indirect effect of the intervention on change in Y through change in M. Our approach is different though mathematically related. With our approach, we conceptualize time as X, with time affecting Y through the effect of time on M. Mediation is established by showing that the indirect effect of time on Y through M differs between the two groups. Thus, experimental

condition is construed as a moderator of the indirect effect of time on Y through the effect of time on M. In this section, we describe our approach by showing how to quantify the total, direct, and indirect effects of the passage of time on Y. Later we note some of the similarities and differences between our approach and others.

In our notation,  $Y_t$  and  $M_t$  refer to measurements on a dependent variable Y and mediator variable M at time t, where t = 1 denotes the first measurement occasion (e.g., pretest) and t = 2 refers to the second measurement (e.g., posttest). In the pretest-posttest design, the result is four variables containing the measurements of M and Y for each participant, two that occur at pretest  $(Y_1, M_1)$  and two at posttest  $(Y_2, M_2)$ . A fifth variable W codes group. The mathematics of our discussion below assumes groups are coded with values of 0 and 1. In our example, the control condition is group w = 0 and the exercise condition is w = 1.

# Working Example

We rely on data from a study of older (60 to 80 years) obese adults reported in Ko, Davidson, Brennan, Lam, and Ross (2016) and based on a randomized clinical trial described in Davidson et al. (2009). The study sought to identify mediators of the effect of an exercise intervention on insulin sensitivity. The inverse of insulin sensitivity, *insulin resistance*, is a precursor to various serious diseases and conditions such as diabetes and cardivascular health problems as well as general morbidity. Our analysis focuses on *abdominal adiposity* or, more simply, abdominal fat, as a mediator of the effect of exercise on insulin sensitivity. Adbominal fat produces hormones and other chemicals that can enhance the likelihood of health problems such as diabetes.

Fifty nine participants were randomly assigned to an exercise condition and 21 were randomly assigned to a no exercise control condition. Insulin sensitivity and abdominal fat were measured at randomization as well as 6 months after the exercise intervention or a comparable delay for those assigned to control. The data for this example are publicly available at

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0167734.

Descriptive statistics for each variable at each time as well as the difference over time can be found in Table 1.

Repeated-measures t-test shows that on average, those assigned to the exercise intervention showed improved insulin sensitivity,

23.503 - 19.315 = 4.188, t(58) = 6.215, p < .001, as well as reduced abdominal fat, 7.448 - 8.236 = -0.788, t(58) = 8.993, p < .001 over time. Similar though smaller changes (higher insulin sensitivity and less abdominal fat at posttest compared to at pretest) also occurred among control participants (21.922 - 21.678 = 0.244) for insulin sensitivity, 8.406 - 8.453 = -0.047 for abdominal fat), but neither of these changes is statistically significant, both |t| < 1, both p > .60. Finally, the change in insulin sensitivity over time between the two groups, 4.188 - 0.244 = 3.944, is statistically significant using a mixed ANOVA with time as a between factor and condition as a between factor, F(1,78) = 9.112, p = .003, as is the difference in change in abdominal fat, -0.788 - (-0.047) = -0.744, F(1,78) = 23.357, p < .001.

Although the analysis just described is not formal mediation analysis of the variety we discuss throughout the rest of this paper, the pattern of results suggests that the effect of exercise on insulin sensitivity may operate in part by reducing abdominal fat. Among those who exercised, abdominal fat was reduced and insulin sensitivity improved over time. But among those who did not exercise, there was no corresponding change in insulin sensitivity or abdominal fat during the same time period.

## Conditional Total, Direct, and Indirect Effects of Time

In a mediation analysis, an effect is decomposed into two components or "pathways of influence," indirect and direct. In a pretest-posttest design, the effect of interest is the change in Y over time, with something happening (or not) between the two measurements assumed to be responsible for any observed change. The average change in Y between measurements is the *total effect* of time. In an intervention, there are two total effects, one

for each group. Let  $c_w$  denote the average difference in Y over time using only the participants in group w:

$$c_w = \overline{\Delta Y} = \overline{Y}_2 - \overline{Y}_1 \tag{4}$$

where  $\Delta Y$  is the difference between a participant's Y at posttest relative to pretest (i.e,  $Y_2 - Y_1$ ). We call these *conditional total effects* of time. They are conditional because they apply to one of the groups. In the language of mediation analysis, they are *total* effects because they represent the effect of the passage of time on Y, not accounting for any effect the mediator (M) may have on Y.

In the insulin sensitivity study, from Table 1, the conditional total effects of time are

$$c_0 = 0.244 = 21.922 - 21.678 \tag{5}$$

in the control group (w=0) and

$$c_1 = 4.188 = 23.503 - 19.315 \tag{6}$$

in the exercise group (w = 1). Because the measurement at time 1 is subtracted from the measurement at time 2, a positive value reflects an increase in insulin sensitivity over time. So in both conditions, insulin sensitivity increased over time. Increases in insulin sensitivity are ultimately the goal of the exercise intervention, as low insulin sensitivity is predictive of later negative health outcomes.

An alternative approach to estimating the conditional total effect of time is to regress the difference in Y over time among on a constant—a "constant only regression"—as in

$$\Delta Y = c_w + e_Y \tag{7}$$

This equation is depicted visually at the top of Figure 2 panels A and B.

Building on the mathematics outlined in Judd et al. (2001), Montoya and Hayes (2017) describe a path-analytic approach to mediation analysis in the repeated measures design that breaks these total effects into direct and indirect effects. This is accomplished by estimating two regression models, one for the difference in M over time and one for the difference in Y over time. We depict the mathematics of this approach in visual form in

Figure 2, where the triangle is used to denote a regression constant, a square is used to denote a measured variable, and a circle denotes an error in estimation. Panel A is for group w = 0 (the control group) and Panel B is for group w = 1 (the exercise group).

These path diagrams depict two equations estimating the difference in Y and the difference in M using the data from participants in group w:

$$\Delta M = a_w + e_M \tag{8}$$

$$\Delta Y = c_w' + b_w \Delta M + d_w [(\Sigma M - \overline{\Sigma M})/2] + e_Y \tag{9}$$

where  $\Delta M = M_2 - M_1$ , the difference between a participant's measurements on M at preand posttest,  $\Sigma M$  is the sum of a participant's measurements of M over time,  $M_1 + M_2$ , and  $\overline{\Sigma M}$  is mean of the sum of mediator measurements for participants in group w. Thus,  $(\Sigma M - \overline{\Sigma M})/2$  is a participant's group mean-centered average mediator measurement.

In equation 8,  $a_w$  is the average change in M over time in group w. That is,

$$a_w = \overline{\Delta M} = \overline{M}_2 - \overline{M}_1$$

In equation 9,  $c'_w$  estimates the part of the effect of time on Y in group w not attributable to change in M in group w. In the lingo of mediation analysis,  $c'_w$  is the *direct effect* of time on Y in group w. But here it is a *conditional* direct effect, because it applies only to group w. And  $b_w$  in equation 9 estimates the effect of change in M on change in Y in group w.

The conditional indirect effect of time on Y in group w operating through change in M over time is  $a_w b_w$ . It estimates the change in Y over time attributable to change in M over time for people in group w. When  $a_w b_w$  is added to  $c'_w$ , the result is  $c_w$ , the conditional total effect of time on Y in group w from equation 4. That is,  $c_w = c'_w + a_w b_w$ .

Any regression analysis program can be used to estimate equations 8, 9, and 7. For example, assuming the mediators, outcome, and variable coding group are named y1, y2, m1, m2, and group, the SPSS code below conducts the analysis and produces the results described below and depicted in Figure 2 panels A and B.

```
/* construct difference scores */.
compute deltam=m2-m1.
compute deltay=y2-y1.
/* construct mean-centered means of mediators */.
if (group=0) summ=((m1+m2)-16.8602)/2.
if (group=1) summ=((m1+m2)-15.6851)/2.
/* generates c_g and a_g */.
sort cases by group.
split file by group.
descriptives variables=deltay deltam.
/* generates c'_w and b_w */.
regression/dep=deltay/method=enter deltam summ.
split file off.
```

Alternatively, the MEMORE macro for SPSS and SAS can be used (Montoya & Hayes, 2017). MEMORE automatically constructs differences scores and mean centers the mean of mediators with no additional input from the user, thereby minimizing the code the analyst has to write. The SPSS MEMORE code

```
memore y=y2 y1/m=m2 m1.
```

would be executed twice, once for cases in group w=0 and once for cases in group w=1.

Regardless of method used, as can be seen in Figure 2 panels A and B, among those in the exercise condition (w = 1), there was an average reduction in abdominal fat of slightly more than 3/4 kg ( $a_1 = -0.788$ ), and those who saw greater losses of abdominal fat saw greater increases in insulin sensitivity over time ( $b_1 = -2.508$ ). So in the exercise group, the conditional indirect effect of time on insulin sensitivity through change in abdominal fat is  $a_1b_1 = -0.788(-2.508) = 1.975$ . The conditional direct effect of time on insulin sensitivity, which is the component of change in insulin sensitivity over time not attributable to changes in abdominal fat, is  $c'_1 = 2.213$ . The sum of the conditional direct and conditional indirect effects of time in the exercise group is  $c_1$ , the conditional total effect of time from equations 4 and 6. That is,  $c_1 = c'_1 + a_1b_1 = 2.213 + 1.975 = 4.188$ 

A comparable analysis using the data from the control group reveals that  $a_0 = -0.047$ , meaning an average descrease in abdominal fat, and the greater the reduction

in abdominal fat over time, the greater the increases in insulin sensitivity over time,  $b_0 = -2.873$ . So among those in the control group, the indirect effect of time on insulin sensitivity through abdominal fat is positive,  $a_0b_0 = -0.047(-2.873) = 0.133$ . The direct effect of time in the control group is  $c'_0 = 0.111$ . When added to the indirect effect, the result is the total effect of time in the control group:

 $c_0 = c'_0 + a_0 b_0 = 0.111 + 0.133 = 0.244$ , from equations 4 and 5.

# Comparing Conditional Direct and Indirect Effects and a Formal Test of Mediation

We just showed that the  $c_1 = 4.188$  unit increase in insulin sensitivity observed among those who exercised can be broken into two components, one indirect through change in abdominal fat over time and one direct. The indirect effect of  $a_1b_1 = 1.975$  insulin sensitivity units results (or is assumed to result) from the  $a_1 = 0.788$  unit reduction in abdominal fat over time that then carried its effect onto change in insulin sensitivity  $b_1 = -2.508$ . The remaining increase over time in insulin sensitivity of  $c'_1 = 2.217$  units among those who exercised cannot be attributed to a change in abdominal fat following exercise.

These results are consistent with change in abdominal fat as the mechanism by which exercise can influence insulin sensitivity. However, at this point, we have merely described the pattern in the data. We have not yet discussed statistical inference. Furthermore, we have not acknowledged that a similar pattern of total, direct and indirect effects of time occurred among those who did not exercise, albeit to a much lesser degree. This may cast doubt on whether we can attribute the pattern of results observed among those who exercised to anything about the exercise itself.

In this section, we develop a formal test of mediation in a design of this sort. We do so by first showing how the direct, indirect, and total conditional effects estimated in the two sets of regression analyses just described can be estimated with one set of regression analyses using all of the data simultaneously. We then show how the difference between the

conditional total effects, which are of much substantive interest, breaks into the difference between the conditional indirect and the difference between conditional direct effects. We next show that mediation is supported if the conditional indirect effects of time differ between the two groups. We conclude this section by discussing implementation and inference using the MEMORE macro for SPSS and SAS. We also provide Mplus code that implements our approach using structural equation modeling.

# Estimation using Moderated Regression Analysis

It is not necessary to conduct two separate analyses, one in each group, to generate the conditional direct, indirect, and total effects of time. All of the regression coefficients estimated separately in each group in the prior analysis can be generated from one set of two regression models estimating the change in M over time and the change in Y over time, using all of the data simultaneously. The models are

$$\Delta M = a_0 + aW + e_M \tag{10}$$

$$\Delta Y = c_0' + c'W + b_0 \Delta M + d_0 [(\Sigma M - \overline{\Sigma M})/2] + b(\Delta M)W$$

$$+d[(\Sigma M - \overline{\Sigma M})/2]W + e_Y$$
(11)

where  $\Delta Y$ ,  $\Delta M$  and  $\Sigma M$  are defined as earlier and W is coded 0 for participants in group w=0 and 1 for participants in group w=1. In equation 11,  $(\Sigma M - \overline{\Sigma M})/2$  is a participant's within-group mean-centered sum of mediators. That is, the centering is done around the mean of the mediators calculated across all participants in his or her group.

Equations 10 and 11 can be estimated using any regression analysis program. Assuming  $\delta M$ ,  $\Delta Y$ , and  $(\Sigma M - \overline{\Sigma M})/2$  are constructed as in the earlier code and stored in variables named deltam, deltay, and summ, the SPSS code below does the work.

compute deltamw=deltam\*group.
compute summw=summ\*group.
regression/dep=deltam/method=enter group.
regression/dep=deltay/method=enter group deltam summ deltamw summw.

The resulting regression coefficients are found in Table 2 and Figure 2, panel C. However, additional computations, a structural equation modeling program, or the assistance of a computational tool we describe later is needed for some inferences and to formally test a mediation hypothesis.

When W is coded 0 and 1 for the two groups, equations 10 and 11 produce the conditional direct, indirect, and total effects of time in each group. In equation 11, the regression constant  $c'_0 = 0.244$  is the conditional direct effect in the control group (w = 0), and  $c'_0 + c' = 0.111 + 2.102 = 2.213$  is  $c'_1$ , the conditional direct effect in the exercise group (w = 1). It follows that the difference between the conditional direct effects is c' in equation 11:

$$c' = c'_1 - c'_0 = 2.213 - 0.111 = 2.102$$

Both conditional indirect effects as well as the difference between them are likewise generated by the regression coefficients in equations 10 and 11. In equation 10,  $a_0 = -0.047$  is the average change in M over time in the control group. The average change in M for those in the exercise group,  $a_1$ , is  $a_0 + a = -0.047 + (-0.741) = -0.788$  from equation 10. Therefore, a is the difference between the groups in change over time in M:

$$a = a_1 - a_0 = -0.788 - (-0.047) = -0.741$$

Likewise,  $b_0$  and  $b_1$ , the effect of change in M on change in Y, are generated from equation 11:  $b_0 = -2.873$  is the regression coefficient for  $\Delta M$  in equation 11 and  $b_1 = b_0 + b = -2.873 + 0.365 = -2.508$ . So b in equation 11 is the difference between the groups in the effect of change in M over time on the change in Y over time:

$$b = b_1 - b_0 = -2.508 - (-2.873) = 0.365$$

From earlier, the conditional indirect effect of time on change in Y through change in M in group 0 is  $a_0b_0$ , which can be computed from equations 10 and 11. The indirect effect in group 1 is  $a_1b_1$ , or  $(a_0 + a)(b_0 + b)$  in terms of equations 10 and 11. So the difference

between the two conditional indirect effects using only the regression coefficients in equations 10 and 11 is

$$a_1b_1 - a_0b_0 = (a_0 + a)(b_0 + b) - a_0b_0$$

$$= a_0b_0 + a_0b + ab_0 + ab - a_0b_0$$

$$= a_0b + ab_0 + ab$$

$$= a_0b + a(b_0 + b)$$

Indeed, observe from the insulin sensitivity study,

$$a_1b_1 - a_0b_0 = a_0b + a(b_0 + b)$$

$$1.975 - 0.133 = -0.047(0.365) + (-0.741)(-2.873 + 0.365)$$

$$1.842 = -0.017 + (-0.741)(-2.508)$$

$$1.842 = 1.842$$

The difference between the conditional total effects,  $c_1 - c_0$ , is typically of much substantive interest because this difference quantifies differential change between groups on dependent variable Y over time on average. The difference between the conditional total effects could be estimated by regressing the difference in Y over time on W, the variable coding experimental condition:

$$\Delta Y = c_0 + cW + e_Y \tag{12}$$

In this model, the regression constant  $c_0$  is average change in Y over time for participants in group w = 0 (the control group) and the difference in Y over time for those in group w = 1 (the exercise group) is  $c_1 = c_0 + c$ . So c is the mean difference in change over time in Y between the two conditions—the difference between the conditional total effects of time

$$c = c_1 - c_0 = 4.188 - 0.244 = 3.944$$

Estimation of equation 12 is not necessary, however, as this difference can be computed from the regression coefficients in equations 10 and 11 because it is equivalent to the sum

of the difference between the conditional direct effects and the difference between the conditional indirect effects. That is,

$$c = (c'_1 - c'_0) + (a_1b_1 - a_0b_0)$$
$$= c' + [a_0b + a(b_0 + b)]$$

Indeed, from the insulin sensitivity study,

$$3.944 = (2.213 - 0.111) + [-0.788(-2.508) - (-0.047)(-2.873)]$$

$$3.944 = (2.102) + [-0.047(0.365) + (-0.741)(-2.873 + 0.365)]$$

$$3.944 = 2.102 + [-0.017 + (-0.741)(-2.508)]$$

$$3.944 = 2.102 + 1.842$$

$$3.944 = 3.944$$

So the difference between the groups in change in insulin sensitivity over time (3.944) is the sum of the difference between the groups in the direct effect of time (2.102) and the difference between the groups in indirect effect of time through change in M over time (1.842).

#### A Statistical Test of Mediation

In our initial discussion of the mechanics of mediation analysis when X and Y are measured only once, we pointed out that the total effect of X (c in equation 1) breaks up into a indirect effect of X (ab from equations 2 and 3) and a direct effect of X (c' in equation 3). Furthermore, we said then that 21st-century thinking about mediation analysis stipulates that mediation is supported by the statistical evidence if the indirect effect of X is different from zero with the pattern of signs of a and b consistent with the logical or theoretical argument being made about the process at work. Gone is the 20th-century requirement or expectation that the total effect of X is statistically different from zero, or that both a and b are different from zero.

We now apply this modern logic to the two-group pretest-posttest design and our derivations. An intervention is deemed effective if those who receive the intervention change over time on Y in some desirable way and in a manner different those who don't experience the intervention. This is manifested statistically in the difference between conditional total effects of time,  $c_1 - c_0$ . We showed that this difference breaks into indirect and direct components or, more precisely, the difference between the conditional indirect effect of time on Y through changes in M over time  $(a_1b_1 - a_0b_0)$ , and the difference between the conditional direct effects of time,  $c'_1 - c'_0$ . Using the same argument now well accepted in ordinary mediation analysis, we propose that statistical evidence consistent with change in M over time as the mechanism by which an intervention operates on change in Y is found in evidence that the conditional indirect effects of time are different between the two groups. That is, does the magnitude of the change in Y over time attributable to change in M over time differ among those who receive the intervention relative to those who do not?

Of course, mere difference between groups in the indirect effects of time would not be sufficient to support a specific mediation hypothesis. The observed difference must be larger than can plausibly attributed to chance by a hypothesis testing standard or a confidence interval that does not include zero. Although several approaches to comparing two conditional indirect effects exist, we recommend the use of a bootstrap confidence interval, as the difference between conditional indirect effects involves the product of regression coefficients so its sampling distribution isn't likely to be normal or symmetrical in form. Bootstrapping also does not require an estimate of the standard error of the difference, the derivation of which would require certain assumptions being met. In addition, bootstrapping is already a well-accepted inferential approach in mediation analysis when the goal is to determine whether an indirect effect differs as a function of a moderator (Hayes, 2015).

But it is still not sufficient to merely establish by an inferential standard that two conditional indirect effects of time are different. Also important is that the pattern of change in M and Y in the two groups (e.g., the signs of change, and the relationship between change in M and change in Y) be logically consistent with the theory or hypothesis about how the intervention is presumed to operate in the presence of the intervention but not in its absence. Two conditional indirect effects could be different, but the pattern of change may be inconsistent with expectations given the predictions about change made by the hypothesis or theory.

Our approach is a test of mediation, but analytically, mediation is established by showing a pattern of results that can be interpreted instead as moderation—moderation of an indirect effect by condition. Affirmative evidence of moderation is often "probed" in order to be able to articulate under which conditions, situations, or for what types of people an effect exists or does not, or when the effect is large versus small. An analogous probing exercise after establishing that two conditional indirect effects differ would involve examining which of the causal paths differ between the two conditions (e.g., the effect of X on X; the effect of X on X; both?) as well as conducting an inference about the conditional indirect effect of time in each group. Is the conditional indirect effect statistically different from zero in one group but not another?<sup>1</sup>.

An important consequence of our approach is that even though often it is the difference between the conditional total effects of time that leads one to ask questions about how differential change operates, one not need to find a statistically significant difference between conditional total effects to test for mediation in a pretest-posttest design such as this. The difference between the conditional total effects carries no information about the difference between the conditional indirect effects. That is,  $c_1 - c_0$  does not determine or in any way influence the size of  $a_1b_1 - a_0b_0$ . It is the difference between conditional indirect effects that ultimately matters, not the difference between the

<sup>&</sup>lt;sup>1</sup>Note that differences in significance of the conditional indirect effects is not a requirement of mediation. What matters is whether the conditional indirect effects are statistically different from *each other*. Nevertheless, establishing evidence of mediation in one group but not another when combined with evidence that the two indirect effects differ from each other is a more elegant and potentially more convincing pattern of results

conditional total effects. So one can proceed with a mediation analysis even if one cannot definitively establish differential change between groups in Y over time. Groups may differ in indirect effects of time even if they don't appear to differ in the total effects of time.

# Implementation and Inference in Computing Software

As already discussed, any regression analysis program can estimate equations 10 and 11, but inference for conditional indirect effects and the difference between them requires the integration of information across the two equations, something not available from canned regression analysis programs. A structural equation modeling program such as Mplus could be used, and we provide Mplus code in Appendix B that conducts this analysis. But most will find the MEMORE macro for SPSS and SAS much easier to use so we restrict our discussion to the interpretation of MEMORE output. Through originally designed for repeated-measures mediation analysis in two-instance single group designs (see Montoya & Hayes, 2017), features have recently been added to MEMORE to conduct tests of moderation (Montoya, 2019), including the moderation of conditional indirect effects estimated in two groups. In one line of code, MEMORE constructs the needed difference scores, group mean centers sums of mediators, estimates equations 10, 11, and 12, and provides point estimates as well as ordinary least squares standard errors and confidence intervals for most of the effects we have discussed, both within and between groups. For inference about indirect effects, it conducts our test of mediation by generating a bootstrap confidence interval for the difference between the conditional indirect effects, as well bootstrap confidence intervals for each of the conditional indirect effects.

Assuming that the variable coding group (exercise intervention or control), W in our notation above, is named group in the data, the SPSS version of the MEMORE command memore y=y2 y1/m=m2 m1/w=group/model=4.

estimates the model. The resulting MEMORE output can be found in Appendix A. In the right margins of the output we provide the symbols for various effects we have discussed

and that appear in Figure 2, with arrows pointing to the relevant row in the MEMORE output to ease following our discussion. But these symbols do not appear in the output itself.

Below the top section of the output, which provides information about the variables being used in the analysis and the names of difference scores and (mean centered) mediator sums as they appear in the output, can be found the model of the difference in Y over time from equation 12 that produces the total effect of time on insulin sensitivity in the control group  $c_0$  as well as the difference between the total conditional effects of time, c, which is equal to  $c_1 - c_0$ . The conditional total effects of time differ between the groups, c = 3.944, p < .001. These two conditional total effects can be found just below in the section labeled "Conditional effect of X on Y at values of the moderator(s)." As can be seen, in the control group (group=0), there is no statistically significant change in insulin sensitivity,  $c_0 = 0.244, p = 0.829$ , but insulin sensitivity is significantly higher at posttest among those who exercised (group=1),  $c_1 = 4.188, p < .001$ . But recall that as noted above, a statistically significant difference between the total conditional effects of time is not a requirement of mediation.

The next section of output contains the results of equation 10 that estimates change in the mediator from condition. The two regression coefficients here are the conditional effect of time on change in abdominal fat in the control condition  $(a_0)$  and the difference in change in abdominal fat between the groups (a). As can be seen, there was a significance difference in change in abdominal fat between those who exercise and those who did not, a = -0.741, p < .001. Below the regression model, in the section that reads "Conditional effect of X on M at values of moderator(s)" are the two conditional effects of time on change in abdominal fat. Among those who exercised (group=1), abdominal fat was significantly lower at posttest compared to at pretest,  $a_1 = -0.788, p < .001$ . There was no statistically significant difference over time in abdominal fat among those who did not exercise (group=0),  $a_0 = -0.047, p = .731$ .

The next section of output is the model of the difference in Y corresponding to equation 11. This model generates the conditional direct effect of time in the control group  $c_0$  as well as the difference between the conditional direct effects in the two groups (c), but we save a discussion of these until later, when and where they appear in the summary section of the MEMORE output. Also found here are  $b_0$ ,  $b_1$ , and b the conditional effect of the change in abdominal fat on change in insulin sensitivity in each group as well as the difference between the groups in this effect. As can be seen in the section labeled "Conditional effect of Mdiff on Ydiff at values of the moderator," among those who exercised, a reduction in abdominal fat was associated with a significant increase in insulin sensitivity,  $b_1 = -2.508$ , p = .011. Not so among those who did not exercise,  $b_0 = -2.873$ , p = .286. However, the regression coefficient for the product of the difference in M over time and group W is b = 0.364 and not statistically significant. So we cannot conclude that these conditional effects are different from each other.

The final section of output is a summary of the conditional direct, indirect, and total effects of time in the two groups as well as differences between them. Everything here is derived from the earlier model equations, and some of this output is redundant with sections of output that appear earlier and that we have already discussed, such as the conditional total effects. New information in this section includes the conditional direct effects of time, differences between the conditional direct effects, and, importantly, the conditional indirect effects and the test of mediation we developed throughout this paper based on the difference between the conditional indirect effects.

As can be seen in the section labelled "Conditional indirect effect of X on Y through M," the conditional indirect effect of time on change in insulin sensitivity through change in abdominal fat among those who did not exercise (group=0) is  $a_0b_0 = 0.133$ . This positive indirect effect is the result of the negative (though nonsignificant) reduction in abdominal fat among those who did not exercise, which translates to an increase (though nonsignificant) in insulin sensitivity. But among those who exercised (group=1), the

indirect effect is  $a_1b_1 = 1.976$ , resulting from the negative (and statistically significant) reduction in abdominal fat that translates into an increase (that is statistically significant) in insulin sensitivity. Importantly, these two conditional indirect effects are different from each other, as revealed in the section labeled "Test of moderation of the indirect effect." The difference between these conditional indirect effects is 1.842, and we can rule zero out as a plausible value of the difference, as a bootstrap confidence interval based on 5,000 bootstrap samples (the default in MEMORE) does not include zero (0.129 to 3.554). This is evidence of mediation of the effect of exercise on change (an increase) in insulin sensitivity resulting from a change (a reduction) in abdominal fat that, in turn, influences (by causal assumption) insulin sensitivity.

With evidence of mediation, manifested in the moderation of the indirect effects, we can probe this result by noticing that the conditional indirect effect of time on insulin sensitivity through abdominal fat is not definitively different from zero among those who exercised, as a bootstrap confidence interval for the indirect effect of 0.133 includes zero (-0.497 to 1.087). However, among those who exercised, the increase in insulin sensitivity over time due to the decrease in abdominal fat during this same period (1.986) is definitively different from zero, with a bootstrap confidence interval that is entirely above zero (0.498 to 3.578).

Causal effects can operate through mechanisms or other processes that are not part of the statistical model being used. These other processes at work manifest themselves in the form of direct effects. The conditional direct effects of time in each condition as well as a test of the difference between them can be found in the same summary section of the MEMORE output. As can be seen in the section titled "Conditional direct effect of X on Y" and "Tests of moderation of direct effect", the conditional direct effect of time among those who exercised is  $c'_1 = 2.213$ , p = .029, meaning an increase in insulin sensitivity over time not attributable to change in abdominal fat. No statistically significant direct effect is observed among those in the control condition  $c'_0 = 0.111$ , p = .919. However, difference in

significance does not mean statistically different. Complicating interpretation, from a formal test of the difference between these conditional direct effects, we cannot say they differ from each other, c' = 2.102, p = .158.

#### **Extensions and Alternatives**

In this paper, we have described an approach to mediation analysis in the two-condition pretest-posttest design that conceptualizes an experimental intervention as a moderator of the total, direct, and indirect effects of time. We showed that evidence of mediation of the effect of an experimental intervention can be found in differences between groups (intervention versus control) in the indirect effects of time on an outcome Y through a mediator M. This approach corresponds statistically with the psychology of intervention effects, as changes experienced in people over time, while providing information the scientist needs about how an intervention influences this change. We conclude by discussing some extensions of this method as well as some alternative analytical approaches.

#### More Than One Mediator

Throughout this article we have focused one a single mediator representing the sole mechanism by which an effect operates. But our method is easily extended to models with more than one mediator (see e.g., Hayes, 2018; Preacher & Hayes, 2008). Equations 10 and 11 can be generalized to multiple mediators in parallel or in serial. A thorough exposition of this generalization is beyond the scope of this article. Suffice it to say that MEMORE allows the user to specify more than one mediator. More information about multiple mediator models in pretest–posttest designs can be found in Montoya and Hayes (2017) and the MEMORE documentation at akmontoya.com.

### **Alternative Antecedents and Moderators**

Our focus has been on the effect of the passage of time on an outcome through a mediator and how this effect is moderated by an experimental manipulation in a two-condition pretest-posttest design. But this is not the only design for which our approach is appropriate. The causal antecedent variable X need not be time. For example,

in a related design, participants experience both versions of a stimulus that vary on some manipulated factor with the goal of examining how that manipulation affects a dependent variable. This is the very design that Judd et al. (2001) and Montoya and Hayes (2017) focused on in their treatment of mediation analysis that is the underpinning our method. In such repeated measures designs, order of stimulus is often randomized between participants to rule out order effects. Using our method, order could be used as the moderator to examine whether the indirect effect of the repeated measures manipulation on an outcome through a mediator depends on the order of stimulus presentation.

Indeed, our method can be used to examine any dichotomous variable as a moderator of the indirect effect of a variable manipulated within-person or measured over time. The moderator need not be an experimental manipulation. For example, a version of the insulin sensitivity study might seek to examine if the indirect effect of time on insulin sensitivity through abdominal fat among participants encouraged to exercise differs between Type I and Type II diabetics. In such a design, absent a no-exercise control condition, we would lose the ability to make claims about the effectiveness of exercise itself, but observing differences in the indirect effects of time consistent with predictions about how such groups should differ in the mechanisms at work can also be an approach to confirming whether that mechanism is indeed in operation.

#### A Simpler Difference Score Approach?

MacKinnon (2008) and Valente and MacKinnon (2017) describe an alternative difference score approach commonly used in the interventions literature. We call this alternative the treatment indirect effect (TIE) approach. In the TIE approach, the difference in M over time is first regressed on W, the variable coding condition, as in

$$\Delta M = a_0 + aW + e_M \tag{13}$$

When W is coded such that there is a one unit difference between the control and intervention condition (e.g., 0 and 1, or -0.5 and 0.5), a quantifies the difference in change

in M between the control and intervention conditions, just as does a from our approach (equation 10, which is the same as equation 13).

Next, the TIE approach requires estimation of the difference in the outcome Y using experimental condition W and the difference in the mediator over time as predictors:

$$\Delta Y = i_Y + c'W + b\Delta M + e_Y \tag{14}$$

Using the TIE approach, mediation is established by showing that the indirect effect of the intervention on the change in Y through the change in M, ab, is different from zero.

Although simpler than our approach to be sure, the TIE approach makes two assumptions that our method does not. First, it assumes that the relationship between M and Y at pretest is the same as the relationship between M and Y at posttest. When met, this assumption warrants the interpretation of b as an estimate of the effect of change in M on the change in Y. Second, it assumes, using our notation, that  $b_0 = b_1$ , meaning that the relationship between  $\Delta M$  and  $\Delta Y$  is the same in the control and intervention conditions. When both of these assumptions are met, our approach and the TIE approach are equivalent. In that case, ab from the TIE approach corresponds to the difference between the two conditional indirect effects from our approach. But our approach is more flexible, in that it is works under these same assumptions the TIE approach makes but does not require them.

#### Do Groups Need To Be The Same at Pretest?

Randomization to experimental conditions in a pretest-posttest design largely ensures that groups are equal at pretest on observed and unobserved variables and so any differences observed at posttest can be attributed to the manipulation rather than preexisting group differences. However, sometimes random assignment to conditions is not possible or ethical. Our method does not require that the groups be randomized to condition or be the same at pretest in order to be valid, though differences at pretest introduce some potential complexities in inference.

Our method is based on observed difference scores on Y and M over time. Systematic differences between the two groups at pretest open up regression to the mean as a possible explanation for differences between groups over time. Regression to the mean is a common phenomenon where extreme measurements earlier tend toward the population mean over time. Successful randomization results in the expectation that regression to the mean will influence both groups equally, rendering it less of a threat to the validity of inferences about the effect of an intervention. If the moderator (experimental condition in our method) is not randomized and there are difference between the groups at pretest, differences between the groups may occur due to regression to the mean but incorrectly interpreted as evidence of mediation. For instance, in our example, if the exercise group was systematically lower on insulin sensitivity and higher in abdominal fat than the control group at pretest, then we might see an increase in insulin sensitivity and a decrease in abdominal fat over time due to regression to the mean in the treatment group but not in the control group.

Floor and ceiling effects in measurement can also produce difficulties in inference when groups are not equal at pretest. If those in one group tend to be closer to a measurement scale boundary on average than in the other group, opportunities for change may differ across conditions. This can manifest itself in the form of differential change between groups, in total, directly, or indirectly.

Because randomization is not always possible and such effects often cannot be ruled out, alternatives have been advanced, such as including both  $M_1$  and  $Y_1$  on the right sides of the equations that define the TIE approach. This ANCOVA approach, as Valente and MacKinnon (2017) call it, helps deal with regression to the mean and artifacts attributable to floor and ceiling effects, but it still makes the same assumptions the TIE method makes that our approach does not. Valente and MacKinnon (2017) have studied the relative strength and weaknesses of the TIE and ANCOVA approaches and favor the ANCOVA approach. Research comparing the performance of the TIE and ANCOVA approaches to our proposed approach would be worthwhile.

#### References

- Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations.

  \*Journal of Personality and Social Psychology, 51, 1173–1182.
- Cerin, E., & MacKinnon, D. P. (2009). A commentary on current practice in mediating variable analyses in behavioural nutrition and physical activity. *Public Health Nutrition*, 12, 1182–1188.
- Davidson, L. E., Hudson, R., Kilpatrick, K., Kuk, J., McMillan, K., Janiszewski, P. M., ... Ross, R. (2009). Effects of exercise modality on insulin resistance and functional limitation in older adults: a randomized controlled trial. *Archives of Internal Medicine*, 169(2), 122–131.
- Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs*, 76, 408–420.
- Hayes, A. F. (2015). An index and test of linear moderated mediation. *Multivariate Behavioral Research*, 50, 1–22.
- Hayes, A. F. (2018). Introduction to mediation, moderation, and conditional process analysis: A regression-based approach (2nd ed.). New York: The Guilford Press.
- Hayes, A. F., & Rockwood, N. J. (2017). Regression-based statistical mediation and moderation analysis: Observations, recommendations, and implementation. Behaviour Research and Therapy, 98, 39–57.
- Judd, C. M., Kenny, D. A., & McClelland, G. H. (2001). Estimating and testing mediation and moderation in within-subject designs. *Psychological Methods*, 6, 115–134.
- Ko, G., Davidson, L. E., Brennan, A. M., Lam, M., & Ross, R. (2016). Abdominal adiposity, not cardiorespiratory fitness, mediates the exercise-induced change in insulin sensitivity in older adults. *PLoS ONE*, 11(12), e0167734.
- Kraemer, H. C., Kiernan, M., Essex, M., & Kupfer, D. J. (2008). How and why criteria defining moderators and mediators differ between the Baron and Kenny and

- MacArthur approaches. Health Psychology, 27, S101–S108.
- MacKinnon, D. P. (2008). *Introduction to statistical mediation analysis*. New York: Lawrence Erlbaum Associates.
- MacKinnon, D. P., Lockwood, C. M., & Williams, J. (2004). Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate Behavioral Research*, 39, 99–128.
- Montoya, A. K. (2019). Moderation analysis in two-instance repeated measures designs:

  Probing methods and multiple moderator models. *Behavior Research Methods*, 51, 61–82.
- Montoya, A. K., & Hayes, A. F. (2017). Two condition within-participant statistical mediation analysis: A path-analytic framework. *Psychological Methods*, 22, 6–27.
- O'Rourke, H. P., & MacKinnon, D. P. (2018). Reasons for testing mediation in the absence of an intervention effect: A research imperative in prevention and intervention research. *Journal of Studies on Alcohol and Drugs*, 79, 171–181.
- Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, 40, 879–891.
- Preacher, K. J., & Selig, J. P. (2012). Advantages of Monte Carlo confidence intervals for indirect effects. *Communication Methods and Measures*, 6, 77–98.
- Rucker, D. D., Preacher, K. J., Tormala, Z. L., & Petty, R. E. (2011). Mediation analysis in social psychology: Current practice and new recommendations. *Personality and Social Psychology Compass*, 5/6, 359–371.
- Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: New procedures and recommendations. *Psychological Methods*, 7, 422–445.
- Sobel, M. E. (1982). Asymptotic confidence intervals for indirect effects in structural equation models. In S. Leinhart (Ed.), *Sociological methodology* (pp. 290–312). San Francisco, CA: Jossey-Bass.

Valente, M. J., & MacKinnon, D. P. (2017). Comparing models of change to estimate the mediated effect in the pretest-posttest control group design. Structural Equation Modeling: A Multidisciplinary Journal, 23, 428 – 450.

Table 1 Descriptive statistics from a randomized controlled trial examining the effect of a exercise treatment on change in abdominal adiposity  $(\Delta M)$  and insulin sensitivity  $(\Delta Y)$ .

		Abdo	minal Adip	posity $(M)$	
		$M_1$	$M_2$	$\frac{\Delta M}{(M_2 - M_1)}$	_
Control $(w=0)$		8.453 1.697	8.406 1.675	-0.047 $0.414$	$\leftarrow a_0$
Exercise $(w=1)$	$ Mean \\ SD$	8.236 2.223	7.448 2.252	-0.788 $0.673$	$\leftarrow a_1$
Difference	between group means			-0.741	$\leftarrow a$
		Ins			
		<i>Y</i> <sub>1</sub>	$Y_2$	$\frac{\Delta Y}{(Y_2 - Y_1)}$	_
Control $(w=0)$		21.678 8.038	21.922 7.452	0.244 5.041	$\leftarrow c_0$
Exercise $(w=1)$		19.315 9.179	23.503 9.669	4.188 5.176	$\leftarrow c_1$
Difference	between group means			3.944	$\leftarrow c$

Table 2
Regression coefficients (standard errors in parentheses) from a two-instance repeated
measures mediation analysis with exercise intervention condition as moderator of all paths.

	Equation 10	Equation 11	Equation 12	
	Abdominal Adiposity $(\Delta M)$	Insulin Sensitivity $(\Delta Y)$	Insulin Sensitivity $(\Delta Y)$	
Constant	$a_0 \to -0.047$ $(0.135)$	$c_0' \to 0.111$ (1.086)	$c_0 \to 0.244$ $(1.122)$	
W	$a \to -0.741$ $(0.157)$		$c \rightarrow 3.944 $ (1.307)	
$\Delta M$		$b_0 \to -2.873$ (2.673)		
$(M_2 + M_1)^+$		$d_0 \to -0.969$ (0.662)		
$(\Delta M)W$		$b \rightarrow 0.365$ $(2.842)$		
$(M_2 + M_1)^+ W$		$d \to 0.795$ $(0.724)$		
$R^2$	.223	.215	.105	

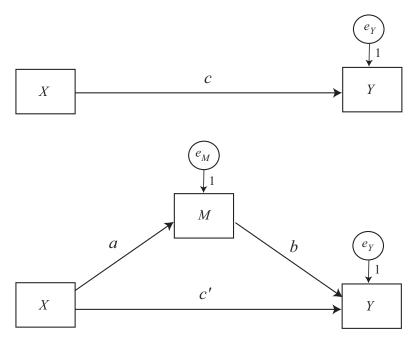


Figure 1. A simple mediation model in path diagram form.

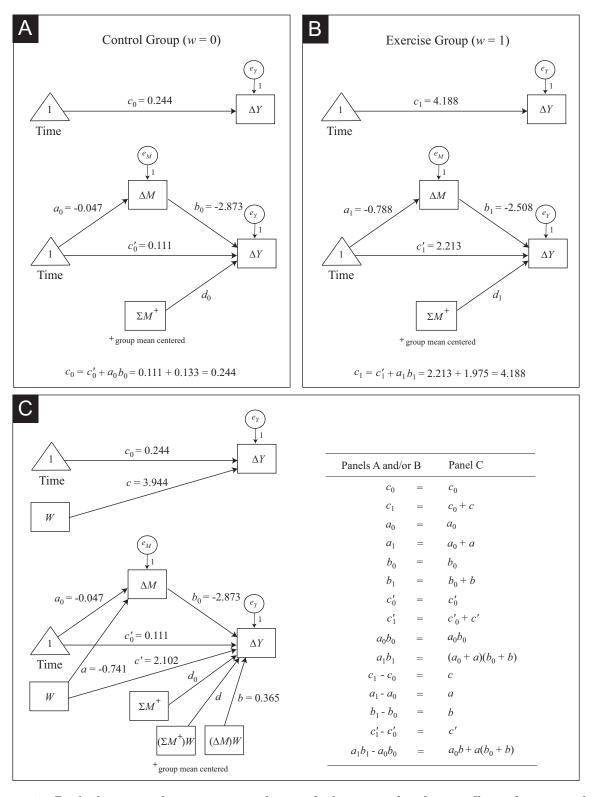


Figure 2. Path diagrams for estimating the total, direct, and indirect effect of time in the control group (A) and the experimental group (B). The path diagram in Panel C estimates all the effects in Panels A and B as well as moderation of these effects by group.

## Appendix A

# Output from the MEMORE Macro

This output was generated by the SPSS version of the MEMORE macro when the command

MEMORE y=y2 y1/m=m2 m1/w=group/model=4.

was applied to the data from the insulin sensitivity study.

Written by Amanda Montoya

Documentation available at akmontoya.com

\*

Model:

4

Variables:

Y = Y2 Y1

M = M2 M1

W = GROUP

Computed Variables:

Ydiff = Y2 - Y1

Mdiff = M2 - M1

Mavg = (M2 + M1)/2 Group-Mean Centered

Mdiff\*W = Mdiff\*Group
Mavg\*W = Mavg\*Group

Sample Size:

80

Outcome: Ydiff = Y2 - Y1

Equation 12

Model Summary

R R-sq MSE F df1 df2 p
.3234 .1046 26.4391 9.1124 1.0000 78.0000 .0034

Model

ULCI Effect SE LLCI t р constant .2442 1.1221 .2177 .8282 -1.9896 2.4781  $c_0$ 3.9441 1.3066 .0034 1.3429 6.5453 group 3.0187

Degrees of freedom for all regression coefficient estimates: 78

Conditional effect of 'X' on Y at values of moderator(s)

		ULCI	LLCI	р	t	SE	Effect	group
$c_0$	$\leftarrow$	2.4781	-1.9896	.8287	.2177	1.1221	. 2442	.0000
$c_1$	$\leftarrow$	5.5211	2.8556	.0000	6.2567	.6694	4.1883	1.0000

Degrees of freedom for all conditional effects:

Model Summary

R R-sq MSE F df1 df2 p .4720 .2228 .3805 22.3568 1.0000 78.0000 .0000

Model

Effect SE LLCI ULCI t р -.0465 .2215 constant .1346 -.3453 .7308 -.3145  $\leftarrow a_0$ -.7411 .1567 -4.7283.0000 -1.0532 -.4291 group

Degrees of freedom for all regression coefficient estimates:

Conditional effect of 'X' on M at values of moderator(s)

Effect SE р LLCI ULCI group t -.0465 -.3453 .7308 .0000 .1346 -.3145 .2215  $a_0$ -9.8074 1.0000 -.7876 .0803 .0000 -.9475 -.6277  $a_1$ 

Degrees of freedom for all conditional effects:  $78\,$ 

Outcome: Ydiff = y2 у1 Equation 11 Model Summary R MSE df1 df2 R-sq F p .4636 .2149 24.4354 4.0511 5.0000 74.0000 .0026 Model Effect SE t LLCI ULCI р , х, .1107 1.0858 .1020 .9191 -2.0529 2.2743  $c'_0$ Mdiff -2.8727 2.6729 -1.0747.2860 -8.1986 2.4533  $b_0$ MavgC -.9694 .6615 -1.4654.1470 -2.2875 .3487  $d_0$ c'5.0384 2.1020 1.4264 .1580 -.8343 1.4737 bMdiff\*W .3643 2.8420 .1282 .8983 -5.5286 6.0272 MavgC\*W .7949 .7238 1.0982 .2757 -.6473 2.2370 d

Degrees of freedom for all regression coefficient estimates: 74

Conditional e	ffect of Md	iff on Ydif	f at values	of moderat	or(s)			
group	Effect	SE	t	р	LLCI	ULCI		
.0000	-2.8727	2.6729	-1.0747	. 2860	-8.1986	2.4533	$\leftarrow$	$b_0$
1.0000	-2.5084			.0113	-4.4321	-0.5841	$\leftarrow$	$b_1$
*******	*****	** TOTAL, D	IRECT, AND	INDIRECT EF	FECTS ****	*****	*****	***
G 1 1	m							
Conditional								
group	Effect	SE	t	р	LLCI	ULCI		
.0000	. 2442		.2177	.8282	1.9896	2.4781	$\leftarrow$	$c_0$
1.0000	4.1883	.6694	6.2567	.0000	2.8556	5.5211	$\leftarrow$	$c_1$
T+ -£		-+-7 -££+						
Test of mode					TTOT	III OT		
	coeff	SE	t	p	LLCI	ULCI		
group	3.9441	1.3066	3.0187	.0034	1.3429	6.5453	$\leftarrow$	c
Conditional	direct effe	ct of X on	Y					
group	Effect	SE	t	р	LLCI	ULCI		
.0000	.1107	1.0858	.1020	.9191	-2.0529	2.2743	$\leftarrow$	$c'_0$
1.0000	2.2127	.9963	2.2108	.0294	.2275	4.1980	$\leftarrow$	$c_1'$
Test of mode	ration of d	irect effec	+					
rest or mode	coeff	SE	t	n	LLCI	ULCI		
group	2.1020	1.4737	1.4264	р .1580	8343	5.0384	<b>←</b>	c'
group	2.1020	1.4/5/	1.4204	.1000	.0343	3.0304	<u></u>	C
Conditional			_	. М				
group	Effect	LLCI	ULCI					
.0000	. 1335	4966	1.0872		$a_0 b_0$			
1.0000	1.9756	.4984	3.5770	← (	$a_1b_1$			
Tost of mode	ration of i	ndiroct off	oct					

\* ANALYSIS NOTES AND WARNINGS \*

 $\leftarrow a_1b_1 - a_0b_0$ 

Level of confidence for all confidence intervals in output: 95.00

Index LLCI ULCI 1.8421 .1292 3.5538

### Appendix B

# Mplus Code for Insulin Sensitivity Analysis

Execute twice, first as is, and then after removal of exclamation points in the ANALYSIS and OUTPUT sections to generate bootstrap confidence intervals for indirect effects.

```
DATA:
file is 'c:\mplus\insulin.csv';
names are id group m1 m2 m1 m2;
usevariables are exercise mdiff ydiff summ summg mdiffg;
DEFINE:
ydiff=y2-y1;
mdiff=m2-m1;
if group==0 then summ=((m1+m2)-16.8602)/2;
if group==1 then summ=((y1+y2)-15.6851)/2;
summg=summ*group;
mdiffg=mdiff*group;
ANALYSIS:
 !bootstrap=10000;
MODEL:
mdiff on group (a);
ydiff on group (cp)
          summ (d0)
          mdiff (b0)
          mdiffg (b)
          summg (d);
 [mdiff] (a0);
 [ydiff] (cp0);
MODEL CONSTRAINT:
new a1 b1 a0b0 a1b1 cp1 c0 c1
     adiff bdiff cdiff cpdiff indiff;
a1=a0+a;
b1=b0+b;
 !indirect, direct, and total effects;
a0b0=a0*b0;
a1b1=(a0+a)*(b0+b);
 cp1=cp0+cp;
 c0=cp0+a0b0;
 c1=cp1+a1b1;
 !difference between effects;
 adiff=a1-a0;
bdiff=b1-b0;
 cdiff=c1-c0;
 cpdiff=cp1-cp0;
 inddiff=a1b1-a0b0;
OUTPUT:
 !cinterval (bootstrap);
```