

Classical and causal inference approaches to statistical mediation analysis

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Abstract

Background: Although there is a broad consensus on the use of statistical procedures for mediation analysis in psychological research, the interpretation of the effect of mediation is highly controversial because of the potential violation of the assumptions required in application, most of which are ignored in practice. **Method:** This paper summarises two currently independent procedures for mediation analysis, the classical/SEM and causal inference/CI approaches, together with the statistical assumptions required to estimate unbiased mediation effects, in particular the existence of omitted variables or confounders. A simulation study was run to test whether violating the assumptions changes the estimation of mediating effects. **Results:** The simulation study showed a significant overestimation of mediation effects with latent confounders. **Conclusions:** We recommend expanding the classical with the causal inference approach, which generalises the results of the first approach to mediation using a common estimation method and incorporates new tools to evaluate the statistical assumptions. To achieve this goal, we compare the distinguishing features of recently developed software programs in R, SAS, SPSS, STATA and Mplus.

Keywords: Classical mediation approach, causal inference mediation approach, statistical mediation analysis, sensibility analysis.

Resumen

El enfoque clásico y el enfoque de la inferencia causal para el análisis de la mediación. Antecedentes: aunque existe un amplio consenso en el uso de los procedimientos estadísticos para el análisis de la mediación en la investigación psicológica, la interpretación del efecto de mediación resulta muy controvertida debido al potencial incumplimiento de los supuestos que requiere su aplicación, la mayoría de los cuales son ignorados en la práctica. **Método:** se resumen los procedimientos actualmente vigentes para el análisis de mediación desde los enfoques clásico y de la inferencia causal, junto con los supuestos estadísticos para estimar efectos de mediación no sesgados, en particular la existencia de variables omitidas o confundidores, y se utiliza un estudio de simulación para determinar si la violación de los supuestos puede cambiar la estimación del efecto de mediación. **Resultados:** el estudio de simulación mostró una sobreestimación importante del efecto de mediación en presencia de confundidores latentes. **Conclusiones:** se recomienda complementar el enfoque clásico con el enfoque de la inferencia causal, que generaliza los resultados del primer enfoque al análisis de la mediación e incorpora nuevas herramientas para evaluar sus supuestos estadísticos. Para alcanzar tal objetivo se comparan las características distintivas de los programas de software recientemente desarrollados en R, SAS, SPSS y Mplus.

Palabras clave: enfoque clásico para la mediación, enfoque de la inferencia causal para la mediación, análisis de la mediación estadística, análisis de la sensibilidad.

The mediation model is one of the most popular procedures for studying the role of third variables involved in the relationship between an independent variable and a response/outcome variable (Ato & Vallejo, 2010). There are two main approaches for mediation analysis. The classical approach is the standard in psychology and the social sciences. It was developed in the 1980s (Judd & Kenny, 1981; Baron & Kenny, 1986), but has a more remote history, and is connected with Campbell's causation theory. Mediation estimation and inference with classical approach use a structural equation model (SEM) framework, from regression models (e.g., Anderson & Hunter, 2012; Sánchez-Manzanares, Rico, Gil, & San Martín, 2006) to path analysis with latent variables (e.g., Cava, Musitu, &

Murgui, 2006). The causal inference (CI) approach is the standard in epidemiology and health sciences. It was developed in the 1990s (Robins & Greenland, 1992; Pearl, 2009) and it is connected with Rubin's causation theory (Shadish, 2010). Mediation estimation with causal inference approach is based on potential outcomes and contrafactuals.

Dissatisfaction with how mediation is analysed and interpreted with classical approach has grown alarmingly in recent years (Bullock, Green, & Ha, 2010; Pardo & Román, 2013; Spencer, Zanna, & Fong, 2005; Zhao, Lynch, & Chen, 2010). By far, the main problem is that applied psychological researchers have focused on the statistical model, ignoring the fact that a mediation model is essentially a causal model whose restrictive assumptions are not taken into account (Bullock & Ha, 2011; Roe, 2012).

In this paper, we compare the basic features of these approaches and we suggest complementing the classical with the causal inference approach. Although both produce similar equations when the variables are numeric, the second approach can be generalised to variables of any kind and to many more complicated scenarios.

Moreover, it also has more sophisticated diagnostic tools and can be applied with programs that have been developed for the most popular computing platforms (R/STATA, SAS/SPSS and Mplus).

The classical approach

Recent research states that a mediation model (see MacKinnon, 2007, 2012; Hayes, 2013) is basically an structural model with two equations: one for explaining a mediator M of a treatment or exposure X (i.e., $X \rightarrow M$) and another to explain the outcome Y of a treatment, given the mediator M (i.e., $X \rightarrow Y | M$). The model may incorporate one or more covariates. The resulting regression equations, assuming for simplicity a single covariate C with c_i values, are:

$$m_i = \gamma_0 + \gamma_1 x_i + \gamma_2 c_i + e_{i1} \tag{1}$$

$$y_i = \beta_0 + \beta_1 x_i + \beta_2 m_i + \beta_3 c_i + e_{i2} \tag{2}$$

where residuals e_{i1} and e_{i2} are assumed normally distributed with zero mean and variances σ_1^2 y σ_2^2 , uncorrelated to each other and with treatment. These equations represent the classical approach when regression models are used, where coefficient γ_1 is a, β_1 is c' and β_2 is b (Figure 1), or when structural equation models are used. A combined model is often used to express Equation (2) in terms of Equation (1) as follows:

$$y_i = \beta_0 + \beta_1 x_i + \beta_2 (\gamma_0 + \gamma_1 x_i + \gamma_2 c_i + e_{i1}) + \beta_3 c_i + e_{i2} \\ = \beta_0 + \beta_1 x_i + \beta_2 \gamma_0 + \beta_2 \gamma_1 x_i + \beta_2 \gamma_2 c_i + \beta_2 e_{i1} + \beta_3 c_i + e_{i2} \tag{3}$$

In Equation (3), the effect of mediation or indirect effect represents the changes which X produced on Y transmitted through M and is usually estimated by the product of the coefficients β_2 and γ_1 , while the direct effect is the effect of the treatment on the response at a fixed level of the mediator and is estimated by the coefficient β_1 . The inference is performed by dividing the indirect effect with a standard error using a formula proposed by Sobel (1982). The resulting Z test is very conservative because it assumes that the regression coefficients β_2 and γ_1 are independent and normally distributed, but it has been shown that the product distribution is highly skewed and leptokurtic (MacKinnon, Lockwood, & Williams, 2004). This is the procedure that is most commonly recommended in psychology.

To overcome some of the inferential problems posed by this procedure, several methods have been proposed to construct robust

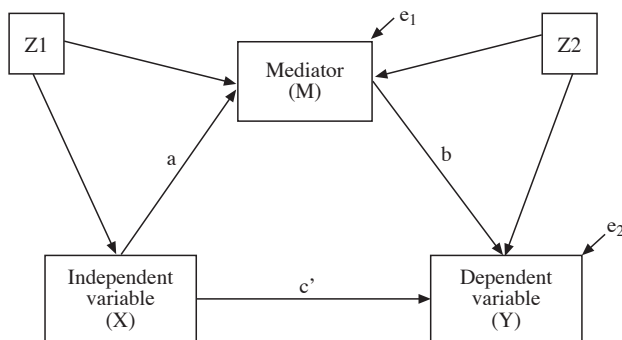


Figure 1. The classical approach to mediation analysis with confounders Z1 y Z2

confidence intervals around the product $\beta_2 \gamma_1$, in particular, the delta method, the product distribution, the Monte Carlo method, and various forms of bootstrap resampling. The Monte Carlo method appears to behave better (see Preacher & Selig, 2012), but some authors recommend the bias-corrected bootstrap method for these (Hayes & Scharkow, 2013) and other cases (Vallejo, Ato, Fernández, & Livacic, 2013). Various effect size measures have been proposed to assess the degree of mediation (see Preacher & Kelley, 2011) along with a power analysis for different mediation scenarios.

In addition to the linearity assumption (mediation analysis with the classical approach is not strictly applicable to models that include interactions or nonlinear terms), it is essential to consider three assumptions derived from the structural model, which represent situations where the error terms e_{i1} and e_{i2} covary.

Firstly, the mediation model should meet the assumption of temporal precedence of cause (X must precede in time to M and M to Y), a very complicated task with cross-sectional data (see Cole & Maxwell, 2003), and some have even suggested using the mediation model only with longitudinal data (see Maxwell & Cole, 2007; Maxwell, Cole, & Mitchell, 2011). If the treatment is a randomised variable, it is very unlikely to be caused by the mediator or the response. The mediator is rarely manipulated however, so the temporal precedence of the mediator on the outcome can only be justified measuring first the mediator and then the response or using appropriate control techniques, such as instrumental variables (Angrist, Imbens & Rubin, 1996) or propensity scores (Coffman, 2011; Jo, Stuart, MacKinnon, & Vinokur 2011).

Secondly, it is assumed that the treatment and the mediator are measured without error. If there is not a high reliability in the measurement of the variables, the coefficients become biased and the mediating causal effect will be affected. The consequences of measurement error are documented in Valeri (2012) and VanderWeele, Valeri and Ogburn (2012). There are several procedures to correct the bias due to measurement error in the variables, the most effective being the use of latent variables instead of individual indicators of treatment and mediator.

Thirdly, it is assumed that there are no omitted variables (also called spurious or confounder variables in this context) in relationships $X \rightarrow M$ and $M \rightarrow Y$. Figure 1 shows a situation with two potential omitted variables (Z_1 and Z_2), the first acting as a confounder in $X \rightarrow M$ and the second acting as a confounder in $M \rightarrow Y$ relationships. Randomisation of the treatment (e.g., using an experimental design) assures that no omitted variables will bias the $X \rightarrow M$ relationship, but since it is not easy or not possible to randomise the mediator, the $M \rightarrow Y$ relationship can potentially be affected by the presence of confounders. This is the most problematic situation that can often arise. Some solutions have been proposed, but the most effective way to circumvent the problem of omitted variables is to measure all potential confounders and control their effects.

The causal inference approach

An independent alternative to the classical is the causal inference approach (Pearl, 2010). This new approach focuses on the concept of the counterfactual, considering what would happen to an individual if instead of observing one feature (e.g., belonging to the experimental group) it were observed together with another (e.g., belonging to the control group). CI approach uses the theory of potential outcomes (Holland, 1986; Rubin, 2005), which defines

a causal mechanism as a process by which a treatment (or exposure) causally affects an outcome given a mediator. Identifying a causal mechanism in this approach is formulated as a decomposition of the total causal effect into direct and indirect effects (Pearl, 2009).

Following Imai, Keele and Tingley (2010), Muthen (2011), Pearl (2012) and Valeri and VanderWeele (2013), let $Y_i(x)$ denote the potential outcome that would have been observed for i participant from a population ($i = 1, \dots, N$) had the treatment X_i been set at the value x . Note that $Y_i(x)$ is not an observed outcome so it may be counterfactual. Assuming a randomised binary treatment ($X_i = 0$, for participants assigned to the control group and $X_i = 1$, for those assigned to the experimental group), then for the participant i , the causal effect of the treatment would be $Y_i(1) - Y_i(0)$, but this result is not identified because participant i is observed for only one treatment. Nevertheless, for N participants of a large sample the average effect of treatment is identifiable and defined as the difference $E[Y_i(1) - Y_i(0)]$.

Let $Y_i(1)$ and $M_i(1)$ now be values of the outcome and the mediator that would have been obtained for participant i if treatment X_i were observed at level 1, and also let $Y_i(1, M_i(1))$ be the value of the outcome that would be obtained if both the treatment X_i and the mediator M_i were observed at level 1. Additionally, introducing a covariate C (there can be more than one) observed at level c , the causal inference approach defines the Average Total Effect (ATE) by comparing the outcome variable between the two treatment levels conditional on the value c of the covariate,

$$ATE = E[Y_i(1, M_i(1)) - E(Y_i(0, M_i(0)) | C_i = c)] \quad (4)$$

This equation has two components: firstly, the effect of Average Causal MEiation (ACME), which is the result of comparing the treatment at level 1 with level 0, fixing the mediator at level x , conditional on the level c of the covariate,

$$ACME = \delta_i(x) = E[Y_i(x, M_i(1)) - Y_i(x, M_i(0)) | C_i = c] \quad (5)$$

and secondly the Average Direct Effect (ADE) which is the result of comparing the treatment at level 1 with level 0, setting the mediator at level x , conditional on the level c of the covariate

$$ADE = \zeta_i(x) = E[Y_i(1, M_i(x)) - Y_i(0, M_i(x)) | C_i = c] \quad (6)$$

Equations (5) and (6) are average effects and assume that there is no interaction between treatment and mediator.

Identifying indirect (ACME) and direct (ADE) causal effects requires what is known as the Sequential Ignorability (SI) assumption (see Robins & Greenland, 1992; Pearl, 2009) which consists of two parts: (A) given one or more observed covariates, the treatment is ignorable, that is, independent of the potential values of the mediator and the outcome, and (B) given the treatment and one or more observed covariates, the mediator is ignorable, that is, independent of all potential values of outcome. More specifically, the SI assumption implies the following requirements: 1) there should be no latent confounders in the $X \rightarrow Y$ path (all of the variables that cause both X and Y must be included in the model), 2) there should be no latent confounders in the $M \rightarrow Y$ path (all the variables that cause both M and Y must be included in the model), 3) there should be no latent confounders in the $X \rightarrow M$ path, and 4) treatment cannot be a cause of any confounder of the $M \rightarrow Y$ path.

The first part of the sequential ignorability assumption (requirements 1 and 3) is satisfied if experimental designs or rigorous effective controls with non-experimental designs are used. But the second part of the sequential ignorability assumption (requirements 2 and 4) is not satisfied because it is virtually impossible to exclude the existence of omitted variables that confound the relationship between the mediator and the outcome. Under this assumption, Imai, Keele and Yamamoto (2010) proved that the effects of causal mediation are nonparametrically identified (i.e., they can be estimated without requiring a functional form and a known distribution), irrespective of the statistical model, of which the regression models of the classical approach are one particular case.

Then with the sequential ignorability assumption verified, the product of coefficients $\beta_2 \gamma_1$ of the classical approach (equations 1 and 2, which must meet the assumptions of linearity and non-interaction) and the indirect effect of causal inference approach (Equation 5, assuming sequential ignorability) provide a valid estimate of the causal mediation effect if mediator and outcome are normally distributed variables. The main advantage of the causal inference over the classical approach is that the formulas for mediation (Pearl, 2012) can easily be generalised to a variety of models that do not require the assumptions of linearity and interaction to be met. Moreover, within the causal inference approach there are sophisticated procedures to assess the degree of compliance with the sequential ignorability assumption and the measurement error bias in the variables (Valeri, 2012). Additionally, Imai, Keele and Yamamoto (2013) have proposed specific experimental designs that can easily be implemented to facilitate the identification of causal mechanisms.

Sensitivity analysis

Even if the sequential ignorability assumption is not verified, it is possible to determine to what extent the estimates may be affected by the presence of confounders. Figure 2 shows a scenario where a latent confounder Z_2 (see Figure 1) is not included in the model creating a residual covariance between e_1 and e_2 whose magnitude depends on the mediation effect. Although the inclusion of a non-null covariance would render the model unidentifiable, Muthen (2011) proved that the removal of the $M \rightarrow Y$ path does not affect the estimate of the causal effects and makes the model with a residual covariance included identifiable, as shown in Figure 3.

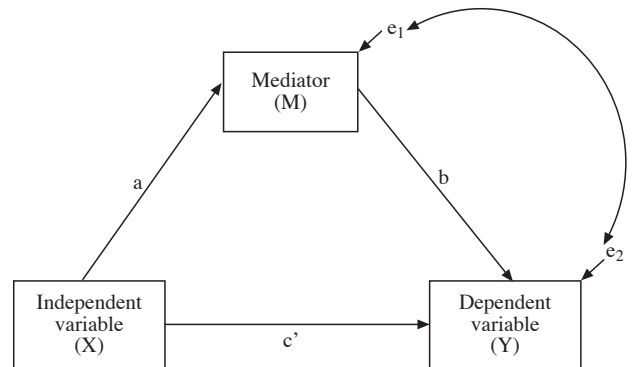


Figure 2. Mediation with covariance between errors of mediator and response

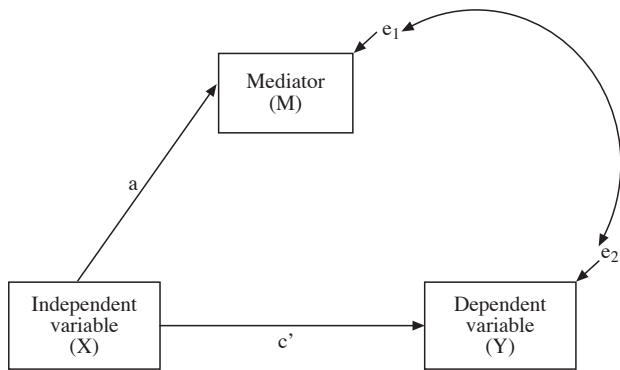


Figure 3. Mediation with covariance between errors of mediator and response (with path *b* deleted)

Imai, Keele and Yamamoto (2010) proposed to assess the presence of confounders through an analysis of sensitivity where the causal effects are calculated presetting values for the correlation between the residuals of equations (4) and (5). This procedure is useful in analysing existing data, because it allows us to assess the potential presence of confounders, but it is also used in planning new studies, because it allows us to estimate optimal sample sizes and the magnitude of the indirect effect so that the confidence bands do not include zero given a certain degree of confounding in the $M \rightarrow Y$ path.

Sensitivity analysis is interpreted in terms of a range, and has a high degree of subjectivity, but it may be useful in assessing the degree to which the bias due to the inclusion of confounders may affect the interpretation of the effects (Imai, Keele, Tingley, & Yamamoto, 2011). The example in the next section illustrates this point.

An example with simulated data

Using a code previously proposed by Muthen (2011, pp. 35-37), we conducted a study with a binary categorical randomised treatment (V3), a numeric mediator (V2) and a numerical outcome variable (V1) simulating 200 observations and 1000 repetitions. We used the model in Figure 2 as the population model, setting an indirect effect of 0.09 and an direct effect of 0.50, and as the analysis model we used the model in Figure 3, with three different fixed values of the correlation between residuals (ρ): 0, 0.25 and 0.50. The remaining parameters were set to the appropriate values to produce the desired causal effects. For each value of ρ , the population values and the mean estimates of 1,000 repetitions were practically the same (with a maximum bias of .005 units), revealing that the indirect and direct causal effects were estimated correctly in the three cases. Then we randomly selected one of the 1,000 replicates registered for each value of ρ , and these data were analysed with the R-mediation package (4.2.4 version, see Tingley, Yamamoto, Hirose, Keele, & Imai, 2013). We follow the suggestions of García, Pascual, Frías, Van Krunkelsven and Murgui (2008) for interpretation of power and confidence intervals.

The first part of the Output 1 (Table 1) shows the R code used and the estimates of the causal effects with quasi-Bayesian Monte Carlo confidence intervals, assuming that the correlation between residuals is $\rho = 0$. The two equations were estimated with the R-lm function, the mediation effects with the R-mediate function and the sensitivity analysis with the R-medsens function of the mediation package. For the random replicate used, we found a non-significant indirect effect (ACME = 0.0755, $p = .08$)

and a mediated proportion of 0.115 ($p = 0.08$), so the presence of a mediating effect was discarded. The second part of Output 1 (Table 1) is a sensitivity analysis with the medsens function, which reveals that the confidence interval of indirect effects includes zero in the entire spectrum of the sensitivity parameter ρ (from - 0.9 to + 0.9). In fact, sensitivity analysis is not required when the indirect effect is not significant. Figure 4 is a plot of sensitivity analysis and shows, together with the axes of indirect effect and Q , the observed

Table 1
Output 1: R-mediation program for simulated data with $\rho = 0$

```

> m1=lm(V2~V3,data=sim1)
> m2=lm(V1~V2+V3,data=sim1)
> med1=mediate(m1,m2,treat="V3",mediator="V2")
> summary(med1)

Causal mediation analysis
Quasi-Bayesian confidence intervals

```

	Estimate 95%	CI Lower 95%	CI Upper	p-value
ACME	0.0755	-0.00732	0.15906	0.08
ADE	0.5317	0.33333	0.73964	0.00
Total effect	0.6023	0.37395	0.82127	0.00
Prop. mediated	0.1147	-0.01425	0.25828	0.08

Sample size used: 200
Simulations: 1000

```

> asens1=medsens(med1,rho.by=.1,effect.type="indirect")
> summary(asens1)

Mediation sensitivity analysis for average causal mediation effect
Sensitivity region

```

Rho	ACME 95%	CI Lower 95%	CI Upper	R ² _M *R ² _{Y*}	R ² _M -R ² _{Y~}
[1,] -0.9	0.4599	-0.0424	0.9623	0.81	0.6161
[2,] -0.8	0.3214	-0.0302	0.6730	0.64	0.4868
[3,] -0.7	0.2545	-0.0244	0.5334	0.49	0.3727
[4,] -0.6	0.2109	-0.0206	0.4424	0.36	0.2738
[5,] -0.5	0.1782	-0.0180	0.3743	0.25	0.1902
[6,] -0.4	0.1515	-0.0158	0.3189	0.16	0.1217
[7,] -0.3	0.1284	-0.0141	0.2709	0.09	0.0685
[8,] -0.2	0.1075	-0.0127	0.2277	0.04	0.0304
[9,] -0.1	0.0879	-0.0115	0.1873	0.01	0.0076
[10,] 0.0	0.0688	-0.0107	0.1484	0.00	0.0000
[11,] 0.1	0.0498	-0.0106	0.1101	0.01	0.0076
[12,] 0.2	0.0302	-0.0120	0.0723	0.04	0.0304
[13,] 0.3	0.0093	-0.0189	0.0374	0.09	0.0685
[14,] 0.4	-0.0138	-0.0442	0.0165	0.16	0.1217
[15,] 0.5	-0.0405	-0.0920	0.0109	0.25	0.1902
[16,] 0.6	-0.0732	-0.1574	0.0109	0.36	0.2738
[17,] 0.7	-0.1168	-0.2470	0.0133	0.49	0.3727
[18,] 0.8	-0.1837	-0.3859	0.0184	0.64	0.4868
[19,] 0.9	-0.3223	-0.6747	0.0302	0.81	0.6161

Rho at which ACME = 0: 0.3
R²_M*R²_{Y*} at which ACME = 0: 0.09
R²_M-R²_{Y~} at which ACME = 0: 0.0685

```

> plot(asens1) - see Figure 4 -

```

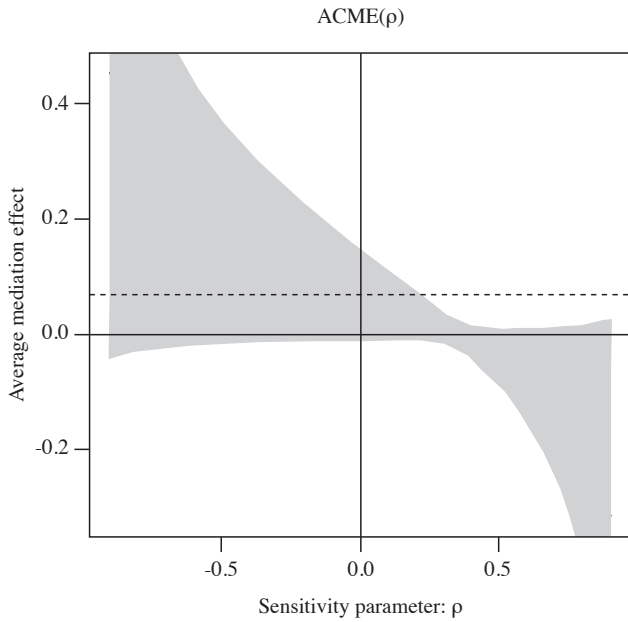


Figure 4. Sensitivity plot for simulated data with $\rho = 0$

mediating effect (dashed line) and the values that the indirect effect would reach varying the sensitivity parameter (solid curved line) along its range in steps of .10. Note that the confidence interval (limits represented with a grey background) always includes zero for the indirect effect whatever the value of ρ is. This result is expected as a consequence of imposing a zero correlation between the residuals of Equations (1) and (2).

In contrast, the estimators of the causal effects assuming $\rho = 0.25$ showed a moderate overestimation of the indirect effect, of $0.163 - 0.076 = 0.087$ units (see Output 2 on Table 2). The indirect effect was now significant ($ACME = .163; p = .04$) and the proportion mediated jumped from 0.11 to 0.25. The sensitivity analysis shown

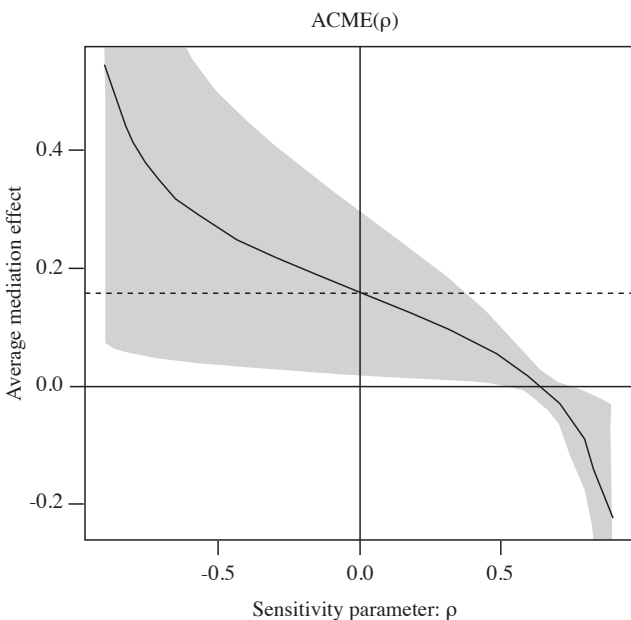


Figure 5. Sensitivity plot for simulated data with $\rho = 0.25$

in the textual output and the complementary plot of Figure 4 allow us to conclude that for the indirect effect to be zero, the correlation between the residuals of the regression models for mediator and outcome variables should be $\rho = .60$ (the confidence interval in Figure 5 ranges from about 0.55 to 0.75). An algebraically equivalent form of sensitivity analysis is to use the product of the determination coefficients of both regression models. It is shown in the penultimate line of Output 2 and indicates that the indirect effect will be zero when the confounders of the mediator-response relationship together explain 36% or more of the residual variance (i.e., $0.60 \times 0.60 = .36$). The last line of the output refers to the total variance instead of the residual variance and indicates that the indirect effect will be zero when the total variance explained by confounding is greater than 17% (i.e., $0.40 \times 0.43 = .17$). In rigorously applied research where no important confounders are unchecked, the researcher should conclude that a correlation as high as that required for the ACME zero is unlikely and therefore he or she should interpret the causal mediation effect found with confidence, when in fact, the simulated data assume a correlation of $\rho = .25$ and a causal effect was overestimated.

Finally, with $\rho = 0.5$, the indirect effect estimator provided an important overestimation with respect to $\rho = 0$, of $0.208 - 0.076 = 0.132$ units (see Output 3 on Table 3), which was also significant ($ACME = 0.208; p = .03$), and the proportion mediated jumped in this case from 0.11 to 0.33. The textual output of the sensitivity

Table 2
Output 2: R-mediation program for simulated data with $\rho = 0.25$

```

> m3=lm(V2~V3,data=sim2)
> m4=lm(V1~V2+V3,data=sim2)
> med2=mediate(m3,m4,treat="V3",mediator="V2")
> summary(med2)
    
```

Causal mediation analysis
Quasi-Bayesian confidence intervals

	Estimate	95 % CI Lower	95 % CI Upper	p-value
ACME	0.1625	0.0156	0.3036	0.04
ADE	0.4821	0.3276	0.6472	0.00
Total effect	0.6446	0.4213	0.8641	0.00
Prop. mediated	0.2508	0.0332	0.4210	0.04

Sample size used: 200
Simulations: 1000

```

> asens2=medsens(med2,rho.by=.1,effect.type="indirect")
> summary(asens2)
    
```

Mediation sensitivity analysis for average causal mediation effect
Sensitivity region

Rho	ACME 95%	CI Lower 95%	CI Upper	R ² _M *R ² _{Y*}	R ² _M -R ² _{Y*}
[1.] 0.5	0.0513	-0.0004	0.1030	0.25	0.1206
[2.] 0.6	0.0190	-0.0118	0.0498	0.36	0.1736
[3.] 0.7	-0.0241	-0.0575	0.0093	0.49	0.2363

Rho at which ACME = 0: 0.6
R²_M*R²_{Y*} at which ACME = 0: 0.36
R²_M-R²_{Y*} at which ACME = 0: 0.1736

```

> plot(asens2) - see Figure 5 -
    
```

Table 3
Output 3: R-mediation program for simulated data with $\rho = 0.50$

```

> m5=lm(V2~V3,data=sim3)
> m6=lm(V1~V2+V3,data=sim3)
> med3=mediate(m3,m4,treat="V3",mediator="V2")
> summary(med3)

```

Causal mediation analysis
Quasi-Bayesian confidence intervals

	Estimate	95% CI Lower	95% CI Upper	p-value
ACME	0.2080	0.0327	0.3921	0.03
ADE	0.4306	0.2788	0.5769	0.00
Total effect	0.6386	0.3978	0.8738	0.00
Prop. mediated	0.3269	0.0696	0.5179	0.03

Sample size used: 200
Simulations: 1000

```

> asens3=medsens(med3,rho.by=.1,effect.type="indirect")
> summary(asens3)

```

Mediation sensitivity analysis for average causal mediation effect
Sensitivity region

Rho	ACME 95%	CI Lower 95%	CI Upper	R ² _M *R ² _{Y*}	R ² _M ~R ² _{Y~}
[1.] 0.7	0.0412	-0.0010	0.0833	0.49	0.1669
[2.] 0.8	-0.0201	-0.0496	0.0093	0.64	0.2181

Rho at which ACME = 0: 0.8
R²_M*R²_{Y*} at which ACME = 0: 0.64
R²_M~R²_{Y~} at which ACME = 0: 0.2181

```

> plot(asens3) - Figure 6-

```

analysis and Figure 6 show that the effect will be zero when the indirect effect is $\rho = 0.80$ or greater, or when the confounders in the

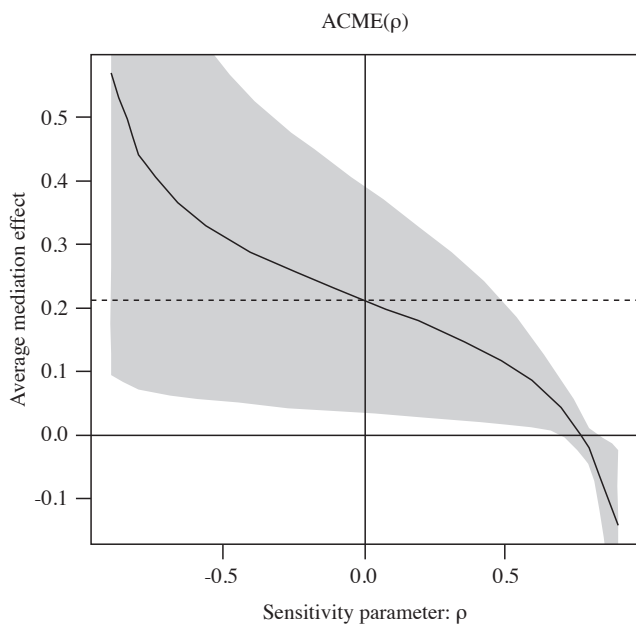


Figure 6. Sensitivity plot for simulated data with $\rho = 0.50$

response-mediator relationship explain at least 64% of the residual variance (e.g., $0.8 \times 0.8 = .64$), which would lead the researcher to conclude with absolute confidence on the relevance of the indirect effect if important confounders are not present.

This example with simulated data illustrates the overestimation of the indirect effect in the presence of confounders of the mediator-response relationship, from a non-significant indirect effect with $\rho = 0$ to significant effects with $\rho = .25$ and $\rho = .50$ using numerical variables with mediator and response. Unfortunately the existence of confounders is a fairly common situation in psychological research that results in an overestimation of the effects and frequently changes in the inference. The limited control of confounders in usual practice justifies the high degree of dissatisfaction with the mediation analysis applications within the classical approach and the need to supplement it with causal inference approach, where a better control on interaction mediator-response is available, the options to use non-interval variables for mediator and response and powerful diagnostic tools and its generalisation to more complicated research scenarios.

Software for mediation analysis with the causal inference approach

Four major programs of professional statistical computing (R, SAS, SPSS and STATA) can now be used to perform a mediation analysis with the causal inference approach. The main characteristics of these programs are summarised in Table 4 (see Valeri & VanderWeele, 2013). Firstly, the R-mediation package

Table 4
Comparative features of programs for mediation analysis with the causal inference approach

	Mediation (R/STATA)	Mediation (SAS/SPSS)	MPLUS
Estimates all causal effects	NO ^a	YES	YES
Interactions:			
Treatment-Mediator	YES	YES	YES
Mediator-Covariate/s	NO	NO	YES
Available models:			
Linear	YES (lm)	YES	YES
Generalised linear	YES (glm)	YES	YES
Non linear	YES	NO	YES
Works with latent variables	NO	NO	YES ^b
Research designs:			
Cross-sectional	YES	YES	YES
Cohort	YES	YES	YES
Case-control	YES	YES	NO
Standard errors:			
Bootstrap	YES	YES	YES
Delta	YES	YES	YES
Bayesian Monte Carlo	YES (default)	(default)	YES
Sensitivity analysis	YES	NO	NO ^c
Moderated mediation	YES	YES	YES
Multiple mediators	YES/NO ^d	NO	YES
Generalisation to multilevel analysis	YES/NO ^d	NO	NO ^c

^a: Natural causal effects only; ^b: Not available yet; ^c: Not available, but it may be programmable; ^d: Is available with R but not with STATA

(Tingley et al., 2013), which was used in the previous section, is an easy to implement but powerful alternative. Among its main features, we emphasize the availability of linear and nonlinear models (including R functions such as *lm* for linear models, *glm* for generalised linear models and *glmer* for mixed models), the sensitivity analysis tools, the option to use multiple mediators and the generalisation to multilevel models. However, it does not work with latent variables. There is a similar program, albeit more modest, for STATA (Hicks & Tingley, 2011), which analyses linear and nonlinear models and also includes sensitivity analysis, but not multilevel models or multiple mediators.

Second, the macro *mediation* developed under SAS 9.2 and SPSS 19.0 versions (Valeri & VanderWeele, 2013) is an important alternative with many interesting options, but it does not include sensitivity analysis, latent variables or multilevel models.

And finally, in an unpublished document (Muthen, 2011), a Mplus code (version 6.2) is presented for mediation analysis within the causal inference approach, inspired by macros developed for SAS/SPSS (Valeri & VanderWeele, 2013). This code shows the versatility of the program and its potential to include interactive terms, nonlinear models, multilevel and multiple mediators, latent variables and even the option to program a sophisticated sensitivity analysis if desired.

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