Published in final edited form as:
Res Soc Work Pract. 2011 November ; 21(6): 675–681. doi:10.1177/1049731511414148.

Integrating Mediators and Moderators in Research Design

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Abstract

The purpose of this article is to describe mediating variables and moderating variables and provide reasons for integrating them in outcome studies. Separate sections describe examples of moderating and mediating variables and the simplest statistical model for investigating each variable. The strengths and limitations of incorporating mediating and moderating variables in a research study are discussed as well as approaches to routinely including these variables in outcome research. The routine inclusion of mediating and moderating variables holds the promise of increasing the amount of information from outcome studies by generating practical information about interventions as well as testing theory. The primary focus is on mediating and moderating variables for intervention research but many issues apply to nonintervention research as well.

Keywords

methodology; methodological article; intervention; outcome

> It is sufficiently obvious that both analysis and synthesis is necessary in classification and that both splitting and lumping have a place, or, to the extent that the terms involve antithesis, that neither one is correct. It is desirable that all distinguishable groups should be distinguished (although it is not necessary that all enter into formal classification and receive names). It is also desirable that they should all be gathered into larger units of increasing magnitude with grades, each of which has practical value and which are numerous enough to suggest degrees of affinity that can be and need to be specified.
>
> (Simpson, 1945, p. 23)

Two common questions in intervention outcome research are "How does the intervention work?" and "For which groups does the intervention work?" The first question is a question about *mediating variables*—variables that describe the process by which the intervention achieves its effects. The second question is about *moderating variables*—variables for which the intervention has a different effect at different values of the moderating variable. More information can be extracted from research studies if measures of mediating and moderating variables are included in the study design and data-collection plan. Furthermore, including measures of moderating and mediating variables is inexpensive, given their potential for providing information about how interventions work and for whom interventions work.

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This article was previously presented at the Stockholm Conference on Outcome Studies of Social, Behavioral, and Educational Interventions, on February 7, 2011. It was invited and accepted at the discretion of the editor.

Declaration of Conflicting Interests
The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Mediating and moderating variables are important for nonintervention outcome research as well as intervention research. A mediating variable is relevant whenever a researcher wants to understand the process by which two variables are related, such that one variable causes a mediating variable which then causes a dependent variable. Moderating variables are important whenever a researcher wants to assess whether two variables have the same relation across groups.

Third-Variable Effects

Mediating and moderating variables are examples of third variables. Most research focuses on the relation between two variables—an independent variable X and an outcome variable Y. Example statistics for two-variable effects are the correlation coefficient, odds ratio, and regression coefficient. With two variables, there are a limited number of possible causal relations between them: X causes Y, Y causes X, both X and Y are reciprocally related. With three variables, the number of possible relations among the variables increases substantially: X may cause the third variable Z and Z may cause Y; Y may cause both X and Z, and the relation between X and Y may differ for each value of Z, along with others. Mediation and moderation are names given to two types of third-variable effects. If the third variable Z is intermediate in a causal sequence such that X causes Z and Z causes Y, then Z is a mediating variable; it is in a causal sequence $X \rightarrow Z \rightarrow Y$. If the relation between X and Y is different at different values of Z, then Z is a moderating variable. A primary distinction between mediating and moderating variables is that the mediating variable specifies a causal sequence in that a mediating variable transmits the causal effect of X to Y but the moderating variable does not specify a causal relation, only that the relation between X and Y differs across levels of Z. Diagrams for a mediating variable in Figure 1 and a moderating variable in Figure 2 demonstrate the difference between these two variables where the causal sequence is shown with directed arrows in Figure 1 to demonstrate a mediation relation. For moderation in Figure 2, there is not an indirect relation of X to Y but there is an interaction XZ that corresponds to a potentially different X to Y relation at values of Z.

Another important third variable is the confounding variable that causes both X and Y such that failure to adjust for the confounding variable will confound or lead to incorrect conclusions about the relation of X to Y. A confounding variable differs from a mediating variable in that the confounding variable is not in a causal sequence but the confounding variable is related to both X and Y. A confounder differs from a moderating variable because the relation of X to Y may not differ across values of the confounding variable. Mediating and moderating variables are the focus of this article. More on these different types of third-variable effects are described elsewhere (Greenland & Morgenstern, 2001; MacKinnon, 2008; MacKinnon, Krull, & Lockwood, 2000).

As you might expect, there are many more possible combinations of relations among four variables and as more variables are added, the number of possible relations among variables soon grows very complex. In this case with many variables, researchers typically often focus on third-variable effects such as moderating and mediating variables even in the most complex models. It is useful to remember that even though I focus on the simplest moderating and mediating model in this article, as the number of variables increases the number of possible models increases dramatically. Typically, the complexity of multivariable models is addressed with specific theoretical comparisons, specific types of variables, randomization, and specific tests based on prior research.

Mediating Variables

A single mediator model represents the addition of a third variable to an $X \rightarrow Y$ relation so that the causal sequence is modeled such that X causes the mediator, M, and M causes Y, that is, $X \rightarrow M \rightarrow Y$. Mediating variables are central to many fields because they are used to understand the process by which two variables are related. There are two overlapping ways in which mediating variables have been used in prior research: (a) mediation for design where interventions are designed to change a mediating variable and (b) mediation for explanation where mediators are selected after an effect of X to Y has been demonstrated to explain the mediating process by which X affects Y (MacKinnon, 2008, Chap. 2). The use of mediating variables for design is central to interventions designed to affect behavior. Intervention studies are based on theory for how the intervention is expected to change mediating variables and the change in the mediating variables is hypothesized to be what causes changes in an outcome variable. If the theory that the mediating constructs are causally related to the outcome is correct, then an intervention that changes the outcome will change the mediator. In an intervention to prevent sexually transmitted diseases, the intervention may be designed to change mediators of abstinence and condom use. In drug prevention research, mediating variables such as social norms, social competence skills, and expectations about drug use are targeted in order to change drug use. Many researchers have stressed the importance of assessing mediation in intervention research (Baranowski, Anderson, & Carmack, 1998; Fraser & Galinsky, 2010; Judd & Kenny, 1981a, 1981b; Kazdin, 2009; Kraemer, Wilson, Fairburn, & Agras, 2002; MacKinnon, 1994; Weiss, 1997).

The other major application of mediating variables is after an effect is observed and researchers investigate how this effect occurred. Mediation for explanation has a long history starting with the work of Lazarsfeld and others (Hyman, 1955; Lazarsfeld, 1955) whereby observed relations between two variables are elaborated by considering a third variable and one explanation of why the two variables are related is because of mediation. Evaluating mediation to explain an observed effect is probably more susceptible to chance findings than evaluating mediation by design because the mediators in the mediation for design studies are selected before the study and mediators for explanation are usually selected after the study. Most programs of research employ both mediation by design and mediation for explanation approaches (MacKinnon, 2008, Chap. 2).

Reasons for including mediating variables in a research study

There are many overlapping reasons for including mediating variables in a research study. Seven reasons are listed below for the case of an intervention study as described elsewhere (MacKinnon, 1994, 2008; MacKinnon & Luecken, 2011).

1. Manipulation check: Mediation analyses provide a check on whether the intervention produced a change in the mediating variables it was designed to change (e.g., if the intervention was designed to engender an antitobacco norm, then program effects on norms should be observed). If the program did not change the mediating variable, it is unlikely to have the desired effects on the targeted outcome. Failure to significantly change the mediator may occur because the intervention was unsuccessful, the measurement of the mediating variable was inadequate, or by chance statistical fluctuations.
2. Program improvement: Mediation analyses generate information to identify successful and unsuccessful intervention components. If an intervention component did not change the mediating variable, then the actions selected to change the mediating variable need improvement. For example, if no program effects on social norms are found, the intervention may need to reconsider the intervention components used to change norms. If the program increases norms but norms do not affect the outcome, the norms component of the program may be ineffective and/or unnecessary and new mediators may need to be included.

3. Measurement improvement: A lack of an intervention effect on a mediator can suggest that the measures of the mediator were not reliable or valid enough to detect changes. If no program effects are found on norms, for example, it may be that the method used to measure norms is not reliable or valid.

4. Possibility of delayed program effects: If the intervention does not have the desired effect on the outcome variable but does significantly affect theorized mediating variables, it is possible that effects on outcomes will emerge later after the effects of the mediating variable have accumulated over time. For example, the effects of a norm change intervention to reduce smoking onset among young children may not be evident until the children are older and have more opportunities to smoke.

5. Evaluating the process of change: Mediation analysis provides information on the processes by which the intervention achieved its effects on an outcome measure. For example, it is possible to study whether the changes in mediators like norms or another mediator were responsible for intervention effects on smoking.

6. Building and refining theory: One of the greatest strengths of including mediating variables is the ability to test the theories upon which intervention programs were based. Many theories are based on results of cross-sectional relations with little or no randomized experimental manipulation. Mediation analysis in the randomized design is ideal for testing theories because it improves causal inference. Competing theories for smoking onset and addiction, for example, may suggest alternative mediating variables that can be tested in an experimental design.

7. Practical implications: The majority of intervention programs have limited resources to accomplish their goals. Intervention programs will cost less and provide greater benefits if the critical ingredients of interventions can be identified because critical components can be retained and ineffective components removed. Mediation analyses can help decide whether to discontinue an intervention approach or not by providing information about whether it was a failure of the intervention to change the mediator, called action theory or whether it was a failure of a significant relation of the mediator to the outcome, called conceptual theory, or both.

How to include mediating variables in a research study

There are two major aspects to adding mediating variables to a research study. First is during the planning stage where the theoretical framework of the study and testing theory is considered and often specified in a logic model. In many cases, the development of a logic model may take considerable time and resources because it forces researchers to carefully consider how the intervention components could be reasonably expected to change an outcome. In fact, the most important aspect of considering mediating variables in a research study may be that it forces researchers to think in a concrete manner about how the intervention could be expected to work both in terms of action theory for how the intervention affects the mediators and conceptual theory for which mediators are related to the outcome. The second aspect to adding mediating variables is deciding how to measure theoretical mediating variables. Typically, this requires adding measures to a questionnaire or some other measurement procedure. In many cases, there may not be existing measures of relevant mediating constructs and psychometric work must be done to develop measures of mediating variables. Furthermore, the addition of measures of mediating variables can add to the respondent burden on a questionnaire. Nevertheless, the addition of mediating variable measures may generate practical and theoretical information from a research study. It is important to measure mediating variables in both intervention and control conditions before and after the intervention to ascertain change in the measures and for statistical mediation analysis.

Mediation Regression Equations

The ideas regarding mediating variables can be translated into equations suitable for estimating mediated effects and conducting statistical tests as for the single mediator model for *X, M*, and *Y* shown in Figure 1 and defined in Equations 2 and 3 below. Equation 1 is also shown because it provides information for mediation relations and corresponds to the overall intervention effect:

$$Y = i_1 + c\,X + e_1, \tag{1}$$

$$Y = i_2 + c'\,X + b\,M + e_2, \tag{2}$$

$$M = i_3 + a\,X + e_3, \tag{3}$$

Where *X* is the independent variable, *Y* is the outcome variable, and *M* is the mediating variable; the parameters i_1, i_2, and i_3 are intercepts in each equation; and e_1, e_2, and e_3 are residuals. In Equation 1, the coefficient *c* represents the total effect, that is, the total effect that *X* can have on *Y*, the outcome variable. In Equation 2, the parameter *c'* denotes the relation between *X* and *Y* controlling for*M*, representing the direct effect—the effect of *X* on *Y* that is adjusted for *M*, the parameter *b* denotes the relation between *M* and *Y* adjusted for *X*. Finally, in Equation 3, the coefficient *a* denotes the relation between *X* and*M*. Equations 2 and 3 are represented in Figure 1, which shows how the total effect of *X* on *Y* is separated into a direct effect relating *X* to *Y* and a mediated effect by which *X* indirectly affects *Y* through *M*. Complete mediation is the case where the total effect is completely explained by the mediator, that is, there is no direct effect. In this case, the total effect is equal to the mediated effect (i.e., $c = ab$). Partial mediation is the case where the relation between the independent and the outcome variable is not completely accounted for by the mediating variable. There are alternative estimators of the mediated effect including difference in coefficients and product of coefficients, which are based on the regression equations. More on the different approaches to mediation analysis can be found elsewhere including standard errors, confidence limit estimation, multiple mediators, qualitative methods, experimental designs, limitations for causal inference, and categorical outcomes (MacKinnon, 2008).

Assumptions of the Single Mediator Model

Although statistical mediation analysis is straightforward under the assumption that the mediation equations above are correctly specified, the identification of true mediating variables is complicated by several testable and untestable assumptions (MacKinnon, 2008). New developments in mediation analysis address statistical and inferential assumptions of the mediation model. For the estimator of the mediated effect, simultaneous regression analysis assumptions are required, such as the residuals in Equations 2 and 3 are independent and that M and the residual in Equation 2 are independent (MacKinnon, 2008; McDonald, 1997). No XM interaction in Equation 2 is assumed, although this can be tested statistically. The temporal order of the variables in the model is also assumed to be correctly specified (see Cheong, MacKinnon, & Khoo, 2003; Cole & Maxwell, 2003; MacKinnon, 2008). The methods assume a self-contained model such that no variables related to the variables in the mediation equations are omitted from the estimated model and that coefficients estimate causal effects (Holland, 1988; Imai, Keele, & Tingley, 2010; Lynch, Cary, Gallop, & Ten Have, 2008; Ten Have et al., 2007; VanderWeele, 2010). It is also assumed that the model has minimal errors of measurement (James & Brett, 1984; McDonald, 1997).

Moderating Variables

The strength and form of a relation between two variables may depend on the value of a moderating variable. A moderator is a variable that modifies the form or strength of the relation between an independent and a dependent variable. The examination of moderator effects has a long and important history in a variety of research areas (Aguinis, 2004; Aiken & West, 1991). Moderator effects are also called interactions because the third variable interacts with the relation between two other variables. However, theoretically moderator effects differ slightly from interaction effects in that moderators refer to variables that alter an observed relation in the population while interaction effects refer to any situation in which the effect of one variable depends on the level of another variable. As mentioned earlier, the moderator is not part of a causal sequence but qualifies the relation between X and Y. For intervention research, moderator variables may reflect subgroups of persons for which the intervention is more or less effective than for other groups. In general, moderator variables are critical for understanding the generalizability of a research finding to subgroups.

The moderator variable can be a continuous or categorical variable, although interpretation of a categorical moderator is usually easier than a continuous moderator. A moderating variable may be a factor in a randomized manipulation, representing random assignment to levels of the factor. For example, participants may be randomly assigned to a moderator of treatment dosage in addition to type of treatment received in order to test the moderator effect of duration of treatment across the two treatments. Moderator variables can be stable aspects of individuals such as sex, race, age, ethnicity, genetic predispositions, and so on. Moderator variables may also be variables that may not change during the period of a research study, such as socioeconomic status, risk-taking tendency, prior health care utilization, impulsivity, and intelligence. Moderator variables may also be environmental contexts such as type of school and geographic location. Moderator variables may also be baseline measure of an outcome or mediating measure such that intervention effects depend on the starting point for each participant. The values of the moderating variable may be latent such as classes of individuals formed by analysis of repeated measures from participants. The important aspect is that the relation between two variables X and Y depends on the value of the moderator variable, although the type of moderator variable, randomized or not, stable characteristic, or changing characteristic often affects interpretation of a moderation analysis. Moderator variables may be specified before a study as a test of theory or they may be investigated after the study in an exploratory search for different relations across subgroups. Although single moderators are described here referring to the situation where the relation between two variables differs across the levels of a third variable, higher-way interactions involving more than one moderator are also possible.

Reasons for including moderating variables in a research study

There are several overlapping reasons for including moderating variables in a research study.

1. Acknowledgment of the complexity of behavior: The investigation of moderating variables acknowledges the complexity of behavior, experiences, and relationships. Individuals are not the same. It would be unusual if there were no differences across individuals. This focus on individual versus group effects is more commonly known as the tendency for researchers to be either lumpers or splitters (Simpson,

1945). Lumpers seek to group individuals and focus on how persons are the same. Splitters, in contrast, look for differences among groups. By making this distinction, I guess I am a splitter. Generally, the search for moderators is a goal of splitters while lumpers would tend not to focus on moderator variables but on general results across all persons. Of course both approaches have problems with splitters yielding smaller and smaller groups until there is one person in each group. Lumpers will fail to observe real subgroups, including subgroups that may have iatrogenic effects or miss predictive relations because of opposite effects in subgroups.

2. Manipulation check: If there is an additional experimental factor picked so that an observed relation is differentially observed across subgroups, then the intervention effect is a test of the intervention theory. For example, if dose of an intervention is manipulated as well as intervention or control, then the additional dosages could be considered a moderator and if the intervention effect is successful, the size of the effect should differ across levels of dosage.

3. Generalizability of results: Moderation analysis provides a way to test whether an intervention has similar effects across groups. It would be important, for example, to demonstrate that intervention effects are obtained for males and females if the program would be disseminated to a whole group containing males and females. Similarly, the consistency of an intervention effect across subgroups demonstrates important information about the generalizability of an intervention.

4. Specificity of effects: In contrast to generalizability, it is important to identify groups for which an intervention has its greatest effects or no effects. This information could then be used to target groups for intervention thereby tailoring of an intervention.

5. Identification of iatrogenic effects in subgroups: Moderation analysis can be used to identify subgroups for which effects are counterproductive. It is possible that there will be subgroups for which the intervention causes more negative outcomes.

6. Investigation of lack of an intervention effect: If there are two groups that are affected by an intervention in opposite ways, the overall effect will be nonsignificant even if there is a statistically significant intervention effect in both groups, albeit opposite. Without investigation of moderating variables, these types of effects would not be observable. In addition, before abandoning an intervention or area of research it is useful to investigate subgroups for any intervention effect. Of course, this type of exploratory search must consider the possibility of multiplicity where by testing more effects will lead to finding effects by chance alone.

7. Moderators as a test of theory: There are situations where intervention effects may be theoretically expected in one group and not another. For example, there may be different social tobacco intervention effects for boys versus girls because reasons for smoking may differ across sex. In this way, mediation and moderation may be combined if it is expected that a theoretical mediating process would be present in one group but not in another group.

8. Measurement improvement: Lack of a moderating variable effect may be due to poor measurement of the moderator variable. Many moderator variables have reasonably good reliability such as age, sex, and ethnicity but others may have measurement limitations such as risk-taking propensity or impulsivity.

9. Practical implications: If moderator effects are found, then decisions about intervention delivery may depend on this information. If intervention effects are

positive at all levels of the moderator, then it is reasonable to deliver the whole program. If intervention effects are observed for one group and not another, it may be useful to deliver the program to the group where it had success and develop a new intervention for other groups. Of course, there are cases where the delivery of an intervention as a function of a moderating variable cannot be realistically or ethically used in the delivery of an intervention. For example, it may be realistic to deliver different programs to different ages and sexes but less realistic to deliver programs based on risk taking, impulsivity, or prior drug use, for example, because of labeling of individuals or practical issues in identifying groups. By grouping persons for intervention, there may also be iatrogenic effects, for example, grouping adolescent drug users together may have harmful effects by enhancing a social norm to take drugs in this group.

How to include moderators in a research study

Moderators such as age, sex, and race are often routinely included in surveys. Demographic characteristics are also often measured including family income, marital status, number of siblings, and so on. Other measures of potential moderators have the same measurement and time demand issues as for mediating variables described earlier; that is, additional measures may increase respondent burden.

Moderation Regression Equations

The single moderating variable effect model is shown in Figure 2 and summarized in Equation 4.

$$Y = i_1 + c_1 X + c_2 Z + c_3 XZ + e_1, \tag{4}$$

Where Y is the dependent variable, X is the independent variable, Z is the moderator variable, and XZ is the interaction of the moderator and the independent variable; e_1 is a residual, and c_1, c_2, and c_3 represent the relation between the dependent variable and the independent variable, moderator variable, and moderator by independent variable interaction, respectively. The moderating variable XZ is the product of X and Z where X and Z are often centered (centered means that the average is subtracted from each observed value of the variable). If the XZ interaction is statistically significant, the source of the significant interaction is often explored by examining conditional effects with contrasts and plots. More on interaction effects including procedures to plot interactions and test contrasts can be found in Aguinis (2004), Aiken and West (1991), Keppel and Wickens (2004), and Rothman, Greenland, and Lash (2008).

Assumptions of Moderation Analysis

There are several challenges to accurate identification of moderator effects. For example, interactions are often scale dependent so that changing the measurement scale can remove an interaction effect. The range of values of the moderator may affect whether a moderator effect can be detected. The number of moderators tested may increase the chance of finding a Type I error and the splitting of the total sample into subgroups limits power to detect moderator effects. Several types of interaction effects are possible that reflect different conclusions, for example, an intervention effect may be statistically significant and beneficial in each group but the effect may differ, an intervention effect may be statistically significant in one group but not another, and so on. More on these issues can be found in Aiken and West (1991) and Rothman et al. (2008) and a special issue on subgroup analysis in a forthcoming issue of the journal *Prevention Science*.

Moderation and Mediation in the Same Analysis

Both moderating and mediating variables can be investigated in the same research project but the interpretation of mediation in the presence of moderation can be complex statistically and conceptually (Baron & Kenny, 1986; Edwards & Lambert, 2007; Fairchild & MacKinnon, 2009; Hayduk & Wonnacott, 1980; James & Brett, 1984; Preacher, Rucker, & Hayes, 2007). There are two major types of effects that combine moderation and mediation as described in the literature (Baron & Kenny, 1986; Fairchild & MacKinnon, 2009): (a) *moderation of a mediation effect*, where the mediated effect is different at different values of a moderator and (b) *mediation of a moderation effect*, where the effect of an interaction on a dependent variable is mediated.

An example of moderation of a mediation effect is a case where a mediation process differs for males and females. For example, a program may affect social norms equally for both males and females but social norms only significantly reduce subsequent tobacco use for females not for males. These types of analyses can be used to test homogeneity of action theory across groups and homogeneity of conceptual theory across groups (MacKinnon, 2008). An example of moderation of a mediated effect is a case where social norms mediate the effect of an intervention on drug use but the size of the mediated effect differs as a function of risk-taking propensity. An example of mediation of a moderator effect would occur if the effect of an intervention depends on baseline risk-taking propensity such that the interaction is due to a mediating variable of social norms, which then affects drug use. These types of effects are important because they help specify types of subgroups for whom mediational processes differ and help quantify more complicated hypotheses about mediation and moderation relations. Despite the potential for moderation of a mediation effect and mediation of a moderation effect, few research studies include both mediation and moderation, at least in part because of the difficulty of specifying and interpreting these models. General models that include mediation and moderation have been described that include the single mediator model as a special case and the single moderator model as special cases (Fairchild & MacKinnon, 2009; MacKinnon, 2008).

Summary

Both mediating variables and moderating variables are ideally specified before the study is conducted. Describing mediation and moderation theory clarifies the purpose of the intervention and forces consideration of alternative interpretations of the results of the study leading to better research design and more information gleaned from the study. Stable characteristic moderator variables such as age and sex are often routinely included in research studies. Often existing studies include some measures of moderating and mediating variables so that mediation and moderation analysis of many existing data sets can be conducted. More information can be obtained from these studies if mediation and moderation analyses are conducted.

There are some limitations of including moderating and mediating variables. First, there is the cost and time spent developing mediation and moderation theory prior to a study. It is likely that consideration of these variables may alter the entire design of a study possibly delaying an important research project. However, it is likely that interventions will be more successful if based on theory and prior research and the application of these analyses inform the next intervention study. Second, there are substantial conceptual and statistical challenges to identifying true moderating and mediating variables that require a program of research. The identification of true mediating processes, for example, requires a program of research with information from many sources. Third, the questions added to a survey to measure mediating and moderating variables must be balanced with the quality of data collected. A longer survey that bores participants or renders some or all of their data inaccurate will not help a research project. Nevertheless, the addition of mediating and moderating variables to any research program reflects the maturation of scientific research to addressing the specifics of how and for whom interventions achieve their effects.

Acknowledgments

Funding

The author disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported in part by Public Health Service Grant DA0957.

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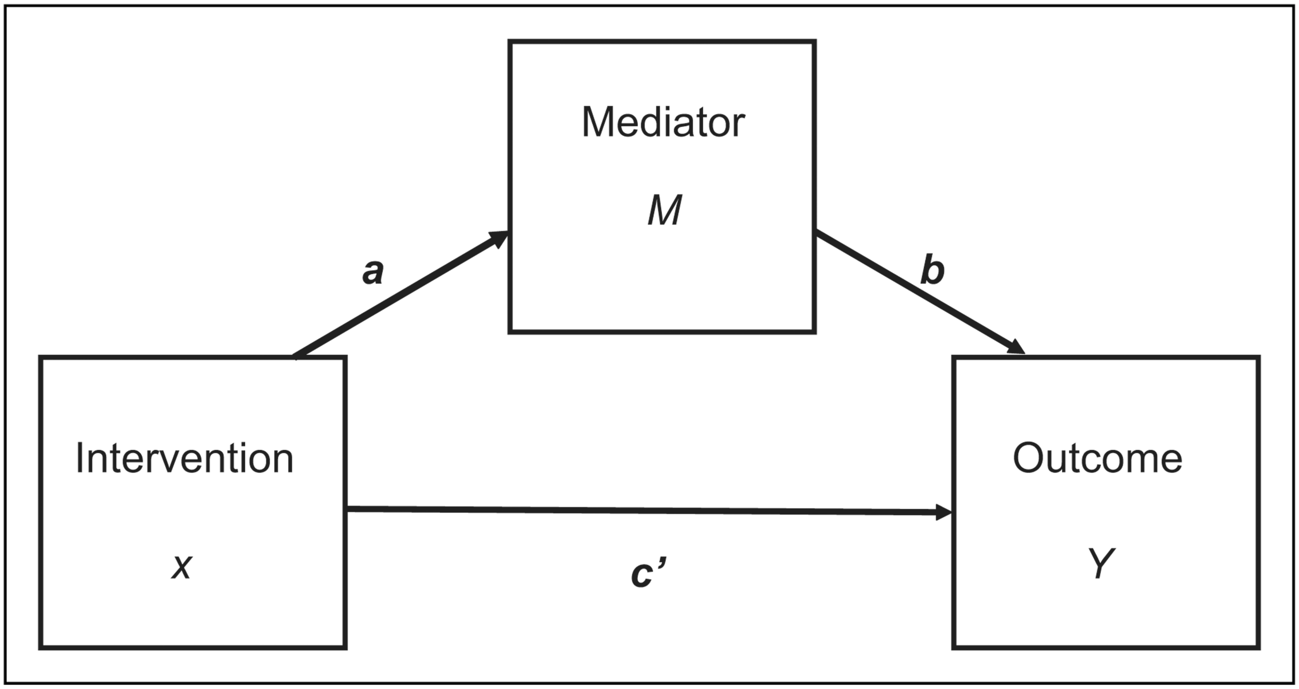

Figure 1.
Single mediator model.

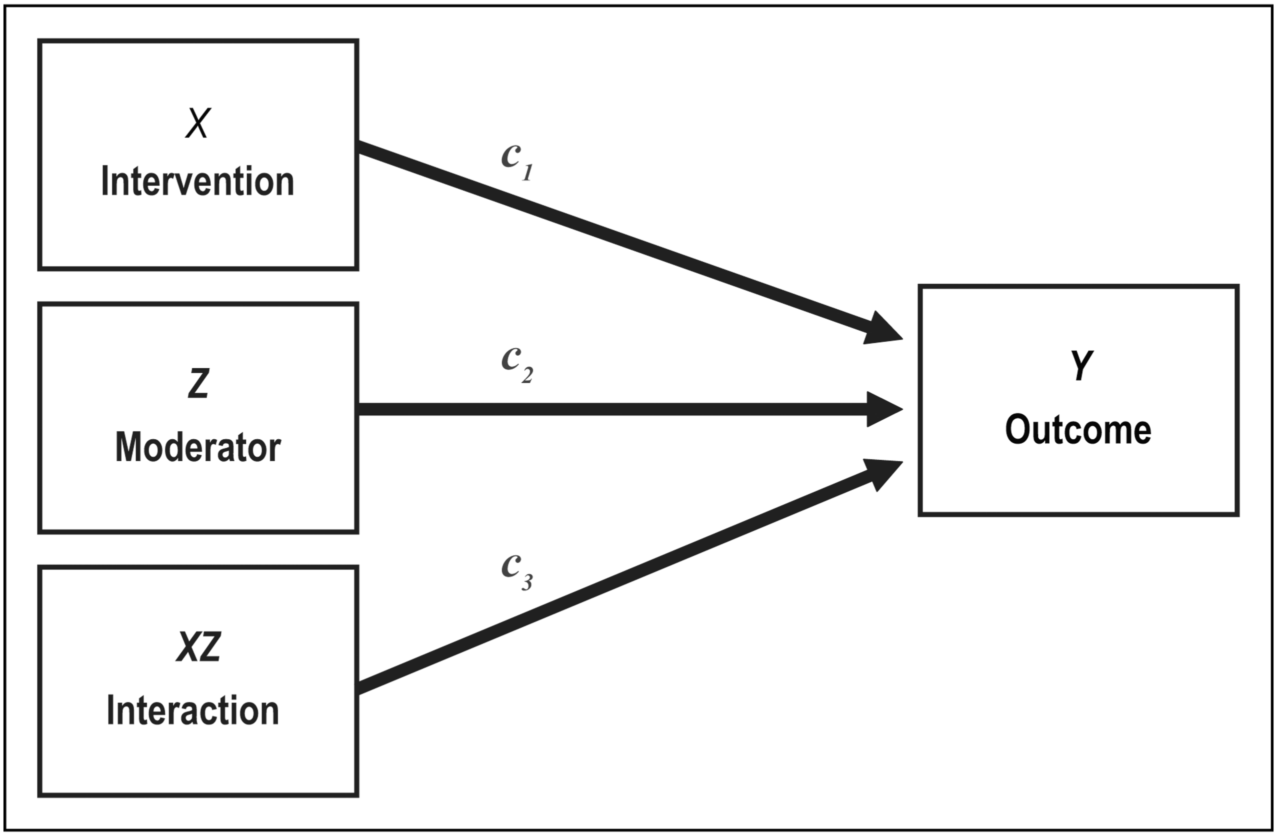

Figure 2.
Single moderator model.