Mediation Analysis Using Observational Data:
Correlation Still Does Not Imply Causation!

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Faculty/Presenter Disclosure

➢ Bruce Weaver
  • Relationships with commercial interests: NONE
  • Potential for conflict(s) of interest: NONE

Learning Objectives
At the end of this program, participants will be able to:
  • Describe statistical mediation.
  • Describe confounding.
  • Recognize that mediation and confounding are “identical statistically and can be distinguished only on conceptual grounds.”
  • Recognize that detection of a statistically significant indirect effect when analyzing observational data does not prove that mediation has occurred.

What is Statistical Mediation?

➢ This presentation has not undergone ethical review of any sort.
➢ Therefore, you listen at your own peril.
In order to keep things relatively straightforward, I'll stick to the simple 3-variable mediation model.

That's a relief. I was afraid things might get complicated.

The causal effect of X on Y may be mediated by variable M.

Path diagram for the mediated model looks like this:

\[ \text{Total Effect} = \text{direct effect} + \text{indirect effect} = c' + a \times b \]

Mediation analysis is concerned with estimating these effects, with most interest (typically) being on the indirect effect \((a \times b)\).

One can use regression methods (e.g., Hayes' PROCESS macro) or structural equation modeling (SEM).

General agreement that SEM is the best method.

Bootstrap CIs recommended for indirect effects.

Mediation analysis estimates:

- Direct effect of X on Y \((c')\)
- Indirect effect of X on Y \((a \times b)\)
- Total effect of X on Y \((c' + a \times b)\)

Confidence intervals are also computed.

- For the indirect effect \((a \times b)\), the usual asymptotic method of computing the CI is considered inappropriate.
- Therefore, bootstrap CIs are usually computed.
- If CI excludes value of 0, effect is statistically significant.

What is Confounding?
Unlike a mediator, a **confounder** is **not** on a (presumed) causal pathway between X and Y.

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Results of the Mediation Analysis

There was a significant indirect effect of conscientiousness on overall physical health through health-related behaviours, \( b = 0.21 \), BCa CI [0.15, 0.26]. The mediator could account for roughly half of the total effect, \( P^2 = .44 \)

\[
\frac{0.21}{0.21 + 0.26} = 0.447
\]

One Final Point about this Example

This was an observational study—there was no manipulation of variables, and no random allocation to groups.

Some More Examples

Example 1

- Multi-site longitudinal observational study of 928 drivers aged 70+

"We observed that specific attitudes towards driving (e.g., driving comfort, negative attitudes towards driving) mediate the relations between health symptoms \( X \) and self-regulatory driving behaviours \( Y \) at baseline and over time."

"Only negative attitudes towards driving fully mediated the relationships between changes in perceived health symptoms \( X \) and changes in driving behavior \( Y \)."

Example 2

- Observational study on the relationship between perfectionism \( X \) and psychological distress \( Y \) in university students
- Q. Are worry and rumination mediators?

"Worry and rumination mediated the relationship between socially prescribed perfectionism and negative affect; however, the mediating effect of rumination was absent in those high in mindfulness."

Two Points to Notice

- In all 3 of these examples, mediation analysis was performed using observational data
- In all 3 cases, the authors concluded that some variable \( M \) mediated the association between \( X \) and \( Y \)
Yes, **many** authors who detect **statistically significant indirect effects** in mediation analyses using **observational data** summarize their results with a statement something like this:

**M mediates** the relationship between **X** and **Y**.

* I'm being **very cautious** here—I think I could safely say **most**!

By definition, a mediator is on a **causal path** between **X** and **Y**.

Therefore, stating that **M mediates** the **X-Y association** is **equivalent** to saying that **X causes M**, and **M causes Y**.

How can one justify those claims when the analysis has been done using **observational data**?
Since when does correlation imply causation?

Before going any further, let’s view some scatter-plots

These plots were created using the same observational data we used for the first mediation analysis example.

X causes Y, right?

Pearson $r = .475$ (95% CI, .404 to .541)

No, you cannot say that! Correlation does not imply causation!

X causes Y, right?

Pearson $r = .533$ (95% CI, .466 to .593)

No, you cannot say that! Correlation does not imply causation!
Pearson r = .531 (95% CI: .464 to .592)

**X causes Y, right?**

Therefore, X causes M and M causes Y, right?

Our mediation analysis example from earlier:

\[
\text{Indirect effect (a×b) = .2050 (BCa 95% CI: .1533, .2654)}
\]

Judging by the way mediation analysts typically summarize their results, the answer would **appear** to be **YES, X causes M and M causes Y.**

**Q.** When using observational data, can we **really** conclude, on the basis of a statistically significant indirect effect, that **mediation has occurred?**

**Q.** When using observational data, can we **really** conclude, on the basis of a statistically significant indirect effect, that **mediation has occurred?**
Because M, the suspected mediator, could be a confounder.

Suppression is another name for negative confounding.

Required Reading for Anyone Doing Mediation Analysis

*Equivalence of the Mediation, Confounding and Suppression Effect*

Authors: David P. MacKinnon, Jennifer L. Krull, Chandra M. Lockwood
This paper describes the statistical similarities among mediation, confounding, and suppression. Each is quantified by measuring the change in the relationship between an independent and a dependent variable after adding a third variable to the analysis. Mediation and confounding are identical statistically and can be distinguished only on conceptual grounds.

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Another Example:

Mediation analysis when the third variable is known to be a confounder

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Results of Mediation Analysis

<table>
<thead>
<tr>
<th>Observed Coef.</th>
<th>Bootstrap 95% CI (BCa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Effect</td>
<td>1.4781 1.3342 1.6367</td>
</tr>
<tr>
<td>Indirect Effect</td>
<td>0.3487 0.2896 0.4067</td>
</tr>
<tr>
<td>Total Effect</td>
<td>1.8268 1.6660 1.9825</td>
</tr>
</tbody>
</table>

- The indirect effect of BMI on Systolic BP through Age is statistically significant.
- This does not prove that Age is a mediator.
The “Truth” vs. The Statistical Result

<table>
<thead>
<tr>
<th>The “Truth” about the third variable</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediator</td>
<td>Correct</td>
<td>Type II error</td>
</tr>
<tr>
<td>Confounder</td>
<td>Correct</td>
<td>Type II error</td>
</tr>
<tr>
<td>Unrelated</td>
<td>Type I Error</td>
<td>Correct</td>
</tr>
</tbody>
</table>

No statistical means of distinguishing between the 3 possible “truths”.

Mediation and confounding are identical statistically and can be distinguished only on conceptual grounds.

When mediation analysis is done using observational data, and the indirect effect is statistically significant, researchers should not summarize by stating that the third variable (M) is a mediator. Rather, they should say that the results are consistent with the proposed mediation model, but do not rule out the possibility that M is merely a confounder, or that a Type I error has occurred.

1. What exactly do statisticians mean when they say that correlation does not imply causation?

2. Why have I been emphasizing the use of observational data?

Correlation does not imply causation!

- Correlation in a general sense—i.e., association
  - Not restricted to Pearson’s r (i.e., linear association)
  - Includes curvilinear relationships and associations between categorical variables
  - Really means statistical association on its own

- Logical implication
  - Not the more informal meaning of hinting at something
In logic, the technical use of the word "implies" means "to be a sufficient circumstance.

Indeed, \( p \) implies \( q \) has the technical meaning of logical implication: if \( p \) then \( q \) symbolized as \( p \implies q \).

That is "if circumstance \( p \) is true, then \( q \) necessarily follows."

In this sense, it is always correct to say "Correlation does not imply causation."

Source: [http://psychology.wikia.com/wiki/Correlation_does_not_imply_causation](http://psychology.wikia.com/wiki/Correlation_does_not_imply_causation)

**Q1**

What **exactly** do statisticians mean when they say that **correlation does not imply causation**?

**A1**

They mean that **statistical association, on its own, does not logically imply causation**.
Having gathered the data in this fashion, if one can establish that the experimentally manipulated variable is correlated with the dependent variable (and that correlation does not need to be linear), then one should be (somewhat) comfortable in making a causal inference.

That is, when the data have been gathered by experimental means and confounds have been eliminated, correlation does imply causation.

Source: http://core.ecu.edu/psyc/wuenschk/StatHelp/Correlation-Causation.htm

Why have I been emphasizing the use of observational data?

Because as Karl Wuensch says, we are in the strongest position to infer causation when we have experimental data, and have taken care to control for or eliminate potential confounders.

Even with experimental data, and with care taken to control or eliminate confounders, Wuensch was very cautious in his wording:
- “(somewhat) comfortable in making a causal inference”
- “...make causal inferences with reasonable confidence”

This falls short of logical implication, where causation would necessarily follow from correlation.

I think Wuensch was right to be cautious.

At the risk of sounding like a Bayesian:
- We should (probably) think of confidence (or comfort) in making a causal inference as a continuum (0% to 100%), not as a Yes/No dichotomy
- We should think about the various factors that affect where we fall on that continuum:
  - Study design
  - Control of confounders
  - Strength of association
  - Etc.

Probably the shortest true statement that can be made about causality and correlation is “Empirically observed covariation is a necessary but not sufficient condition for causality.” Or possibly “Correlation is not causality but it sure is a hint.” Or possibly this:

Source: https://www.edwardtufte.com/blogs-and-a-few-things/EdwardTufte-00003.png
So a strong correlation hints at causation?

A more conventional scatter-plot

Pearson $r = .947$ (95% CI, .786 to .988)

Q. Does this very strong correlation hint at a causal relationship?
Okay, are there any
conditions under which a
strong correlation does
hint at causation?

Sir Austin Bradford Hill

- Sir Austin Bradford Hill FRS
  (July 8, 1897 - April 18, 1991),
- English epidemiologist and
  statistician
- Pioneered the randomized
  clinical trial (RCT)
- With Richard Doll, was the first
to demonstrate the connection
between cigarette smoking and
lung cancer.

From https://en.wikipedia.org/wiki/Austin_Bradford_Hill
Classic Essay on Establishing Causation

- Hill wrote the classic essay on “criteria” for establishing a causal relationship.
- It can be read here: www.edwardtufte.com/tufte/hill
- Hill asks,
  - “What aspects of that association should we especially consider before deciding that the most likely interpretation of it is causation?”
- He then lists aspects of association that ought to be considered. Note that Hill never referred to his 9 points as criteria! Others started using that term.

Aspects of Association to be Considered

1. Strength of association
2. Consistency (upon repetition)
3. Specificity
4. Temporality
5. Biological gradient
6. Plausibility
7. Coherence
8. Experiment
9. Analogy

CAUTION!

- Hill’s “aspects of association” are often treated as a checklist, all of which must be present in order to establish causality.
- But that was never Hill’s intention.

“None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required sine qua non.”

Limitations of Hill’s Nine Viewpoints

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Description</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Strength</td>
<td>A strong effect size for an association</td>
<td>This reduces the chance of minor unmeasured confounding, but assumes that major confounding factors have been accounted for. Weak associations may also be causal.</td>
</tr>
<tr>
<td>2. Consistency</td>
<td>Repeated observations of an association in different populations/circumstances</td>
<td>This assumes that all necessary causal factors are evenly distributed between populations. If a risk factor-outcome association were present only in men, would this imply non-causality?</td>
</tr>
<tr>
<td>3. Specificity</td>
<td>A risk factor leads to a single outcome</td>
<td>There is no reason why a risk factor should be associated with a single disorder (e.g., multiple disorders associated with alcohol misuse).</td>
</tr>
<tr>
<td>4. Temporality</td>
<td>The cause should precede the effect</td>
<td>A study should ideally demonstrate this. However, the fact that one event follows another does not rule out the opposite direction of causation on other circumstances. For example, depression may cause physical ill-health but the opposite may also occur.</td>
</tr>
</tbody>
</table>

1. Has causation been established scientifically?
2. Should we act as if X causes Y?

The standard for taking action is lower than the standard for scientifically establishing causation.

"Finally, in passing from association to causation I believe in 'real life' we shall have to consider what flows from that decision."

"On scientific grounds we should do no such thing. The evidence is there to be judged on its merits and the judgment (in that sense) should be utterly independent of what hangs upon it – or who hangs because of it."

"But in another and more practical sense we may surely ask what is involved in our decision."

"In occupational medicine our object is usually to take action. If this be operative cause and that be deleterious effect, then we shall wish to intervene to abolish or reduce death or disease."
While that is a commendable ambition, it almost inevitably leads us to introduce differential standards before we convict.

Thus on relatively slight evidence we might decide to restrict the use of a drug for early-morning sickness in pregnant women.

If we are wrong in deducing causation from association no great harm will be done. The good lady and the pharmaceutical industry will doubtless survive.

On fair evidence we might take action on what appears to be an occupational hazard, e.g. we might change from a probably carcinogenic oil to a non-carcinogenic oil in a limited environment and without too much injustice if we are wrong.

But we should need very strong evidence before we made people burn a fuel in their homes that they do not like or stop smoking the cigarettes and eating the fats and sugar that they do like.

In asking for very strong evidence I would, however, repeat emphatically that this does not imply crossing every ‘t’, and swords with every critic, before we act.
All scientific work is incomplete – whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge.

That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time.

Back to the main issue...

Q. When using observational data, can we really conclude, on the basis of a statistically significant indirect effect, that mediation has occurred?

NO

The Take-Home Message

- “Mediation and confounding are identical statistically and can be distinguished only on conceptual grounds” (MacKinnon et al., 2002)
- When mediation analysis is performed using observational data, detection of a significant indirect effect does not prove that M is a mediator
  - M could be a confounder; a Type I error may have occurred
- When analyzing observational data, authors ought to say that a significant indirect effect is consistent with the proposed mediation model, but does not rule out the possibility that M is a confounder, or that a Type I error has occurred

Okay…it’s over!

Time to wake up!

Any Questions?
**Summary of Astrocat’s Key Points**

- **By definition, a mediator is on a causal path between X and Y**
- Therefore, claiming that M mediates the X-Y relationship is equivalent to saying that:
  - X causes M, and
  - M causes Y
- How can one justify those claims when the analysis has been done using observational data?

In other words, finding an indirect effect of X on Y through M does not prove that M is a mediator. The same result can occur when M is a confounder!

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**The Cutting Room Floor**

**Canadians need to eat more chocolate!**

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**Annual per capita chocolate consumption (kg)**

- **Action (or non-action) congruent with reality in cells a and f**
- **Action (or non-action) incongruent with reality in cells c and d**  
  - Acting when relationship is not causal (c)  
  - Failing to act when relationship is causal (d)  
- **Uncertain error status in cells b and e**
- When deciding whether to act, we must weigh the costs & benefits of all courses of action under all states of nature
Two Possible Logical Arguments

- A claim of mediation, I think, would have to be based on one of the following logical arguments:
  1. If M mediates the X-Y relationship, then mediation analysis will show an indirect effect of X on Y through M.
  2. If mediation analysis shows an indirect effect of X on Y through M, then M mediates the X-Y relationship.
- In either case, if a statistically significant indirect effect is observed, it is concluded that M mediates the relationship between X and Y.

A closer look at argument 1

- Symbolically, Argument 1 looks like this:
  - Let P = M is a mediator
  - Let Q = Indirect effect is significant
  - If P then Q.
  - Q.
  - Therefore P.
- This is classic example of the logical fallacy, *affirming the consequent*—it is not a valid form of argument.

Another (possibly clearer) example

- P = I ate some pizza recently
- Q = I will not be hungry
  - If I ate some pizza recently then I will not be hungry.
  - I am not hungry.
  - Therefore I ate some pizza recently.
- This is *not a valid argument*.
- There are many possible reasons for my lack of hunger
  - E.g., perhaps I ate something else; perhaps I am ill

Back to the original context

- P = M is a mediator
- Q = indirect effect is significant
  - If M is a mediator then the indirect effect will be significant.
  - The indirect effect is significant.
  - Therefore M is a mediator.
- Changing the content of P and Q changes nothing—structurally, this is *still not a valid argument*.
- M could be a confounder—i.e., associated with both X and Y but not on a causal pathway between them.

Two Possible Logical Arguments

- Argument 2 is *not valid*.
  - Argument 2 is not valid because the *if P then Q* statement (i.e., the *premise*) is *false*.
  - The statement, “If mediation analysis shows a significant indirect effect, then M is a mediator” is *not correct*.
  - The observation of an indirect effect could signal the presence of *confounding* rather than *mediation* (MacKinnon et al., 2000).
Love means never having to say you're sorry.
(Erich Segal)

izquotes.com