

## Chapter 2: Applications

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Two overlapping reasons for mediation analysis: (1) Mediation for design and (2) Mediation for Explanation  
Studies designed to manipulate a mediator but do not measure the mediator  
Lots of Applications

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## Mediation for Explanation

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- Observed relation and try to explain it.
- Elaboration method described by Lazarsfeld and colleagues (1955; Hyman, 1955) where third variables are included in an analysis to see if/how the observed relation changes.
- Replication (Covariate)
- Explanation (Confounder)
- Intervening variable (Mediator)
- Specification (Moderator)

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## Mediation by Design

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- Select mediating variables that are causally related to an outcome variable.
- Manipulations are designed to change these mediators.
- If mediators are causally related to the outcome, then a manipulation that changes the mediator will change the outcome.
- Common in applied research like prevention and treatment.

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## Example experiment to change a mediator without measuring the mediator

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- Theory is that feeling good leads to helping behavior.
- Gave some participants cookies, that got them in a good mood which increased helping behavior (Isen & Levin, 1972).
- Set up a situation where persons found a dime (It was a long time ago) in a telephone coin return and they were then in a situation where they could help a person. If they found the dime they were more likely to help. (Levin & Isen, 1975).

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## Manipulations to change mediators

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Manipulation designed to change the mediator of feeling good. Feeling good was not measured so there was not a measure of the mediator.

Many experimental studies manipulate the mediator but do not measure it.

Mediation analysis is a method that incorporates measures of the mediator in a statistical analysis.

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## Prevention

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- Mediators selected for change because they are thought to be causally related to the dependent variable. Often the relation that prevention researchers are most confident about is the M to Y relation.
- Many large scale prevention efforts, alcohol, tobacco, drug use, AIDS/HIV prevention, obesity, poverty....
- Mediation model is the basis of all of them.

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## Mediation in Intervention Research Theory

- Mediation is important for intervention science. Practical implications include reduced cost and more effective interventions if the mediators of programs are identified. Mediation analysis is an ideal way to test theory.
- A theory based approach focuses on the processes underlying interventions. Mediators play a primary role. **Action theory** corresponds to how the program will affect mediators. **Conceptual Theory** focuses on how the mediators are related to the dependent variables (Chen, 1990, Lipsey, 1993; MacKinnon, 2008).

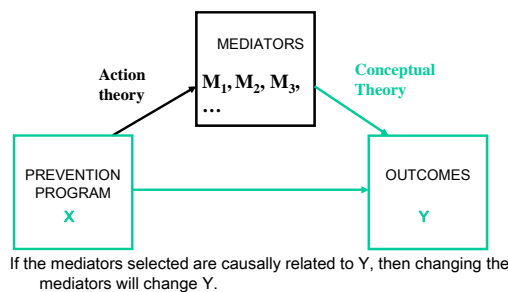
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## Questions about mediators selected for an intervention program

- Are these the right mediators? Are they causally related to the dependent variable. Is knowledge causally related to drug use? **Conceptual Theory**
- Can these mediators be changed? Can personality be changed? **Action Theory**
- Will the change in these mediators that we can muster with our intervention program be sufficient to lead to desired change in the dependent variable? Do we have the resources to change self-esteem in a two-week program? **Both Action and Conceptual Theory**.

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## Intervention Mediation Model



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## Reasons for mediation analysis in intervention research.

1. Manipulation check. Did the program change the mediators it was designed to change?
2. Program Improvement. What do the program effects on mediators suggest about program improvements?
3. Measurement Improvement. Is a lack of program effects due to poor measurement?
4. Delayed effects. Will program effects on the dependent variable emerge later?
5. Test the process of mediation. Was the theory-based prediction of mediation correct?
6. Practical implications. Can the program be redesigned to cost less and be more efficient?

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## Theory of Social Influence Drug Prevention Programs

Social Learning Theory (Bandura, 1977), Problem Behavior Theory (Jessor & Jessor, 1980), and Theory of Reasoned Action (Ajzen & Fishbein, 1980) provide much of the background of drug prevention. These theories predict that social norms, social skills, and beliefs play important roles in the initiation and progression of drug use.

Twelve major program components in drug prevention programs: information, decision making, pledges, values clarification, goal-setting, stress management, self-esteem, resistance skills, life skills, norm-setting, assistance, and alternatives (Hansen, 1992).

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## Three example drug prevention program components

In the correction of normative expectations, students respond whether they use drugs or not and they estimate the percentage of persons who use drugs. Students always predict that more persons are using drugs than report using drugs. This correction of their expectations is commonly used in prevention programs.

In another normative manipulation in groups, students stand under one of two signs. For example, one sign says it is "OK to get drunk" and the other sign says "Not OK to get drunk". Students must decide which sign to stand under. Almost all stand under the not OK sign.

At the end of the program and at other times, students make a public commitment to avoid drugs.

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## Mediators of Drug Prevention Programs

Social Norms, especially norms among friends, seem to be an important mediator of successful gateway drug prevention programs. In MacKinnon et al. (1991) this mediator was measured by asking students, "How friendly would your friends be if you smoked cigarettes?" Descriptive norms, such as perceptions about how many persons use cigarettes was a less important mediator.

Resistance skills often not an important mediator.

Knowledge was not a substantial mediator probably because most young people already know the risks of drug use. Knowledge is important for other outcomes.

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## Mediators in Smoking Cessation

Nicotine Replacement Therapy (X) affects craving (M) and craving (M) is associated with relapse risk (Y) (Shiffman et al., 2008, SRNT)

Wellbutrin (X) (a.k.a. Bupropion) reduces withdrawal (M) and craving (M) which supports cessation (Y). (Piper et al., 2008, SRNT)

Wellbutrin increases subject's willingness to quit (M) and self-efficacy (M) which were associated with one month abstinence (Y) (McCarthy et al., 2008, SRNT)

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## Developmental Psychology Examples

- Influence of childhood experiences on later behavior.
- Neglect/Abuse in childhood (X) to impaired threat appraisal (M) to aggressive behavior in adolescence (Y).
- Positive Parenting (X) of an infant predicts self-esteem (M) which predicts positive parenting as an adult (Y).
- Equifinality (different start same end) and Multifinality (same start different end) (Cicchetti & Rogosch, 1996)

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## Surrogate Endpoints

- Intermediate or surrogate variables from epidemiology.
- Surrogate variables are variables that can be used in place of the ultimate outcome variable.
- Specific to medicine/epidemiology where it can take a long time for disease to occur and there are often only a few cases making it difficult to investigate the ultimate endpoint.
- Polyps as a surrogate endpoint for colon cancer.
- Premature ventricular contractions (PVCs) as a surrogate for cardiac deaths. But drugs to prevent PVCs actually increased death rates (Echt et al., 1991).
- Table of surrogate and ultimate endpoints on page 33 in MacKinnon (2008).

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## Surrogate Endpoints

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Table 2.1 Examples of Surrogates and Ultimate Endpoints

Disease	Surrogate
Death due to cardiovascular disease	Elevated lipid levels, congestive heart failure, arrhythmia, elevated blood pressure (Fleming & DeMets, 1996).
Death from breast cancer	Tumor size, malignancy, and invasion of lymph nodes by cancer cells (Day & Duffy, 1996)
Prostate cancer symptoms	Prostate biopsy (Fleming & DeMets, 1996)
HIV infection	CD4 <sup>+</sup> lymphocyte viral load (Choi et al., 1993)
Osteoporosis	Bone mineral density (Fleming & DeMets, 1996)
Ophthalmic conditions	Partial loss of vision (Buyse & Molenberghs, 1998)

## Mediators in your research.

Small group activity:

Describe a single mediator model in your research.

X is ?

M is ?

Y is ?

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### **Data for examples in the workshop I**

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- ATLAS (Adolescents Training and Learning to Avoid Steroids): Randomized (High school football teams) study of a steroid prevention program (X) to changes mediators such as knowledge of steroids (M) to reduce intentions to use steroids (Y) (**Linn Goldberg (Principal Investigator)**, Elliot, Clark, MacKinnon, et al., 1996, *Journal of the American Medical Association*: National Institute on Drug Abuse).

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### **Data for examples in the workshop II**

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- PHLAME (Promoting Healthy Lifestyles: Alternative Models' Effects): Randomized (Stations of firefighters) study of a health promotion program (X) to change mediators such as Knowledge of diet (M) to the change fruit and vegetable consumption (Y) (**Diane Elliot (Principal Investigator)**, Goldberg, Kuehl, et al., 2007, *Journal of Occupational and Environmental Medicine*: National Cancer Institute, National Institute on Arthritis and Musculoskeletal and Skin Diseases)

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### **Data for examples in the workshop III**

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- WORD: Randomized (Students in a class) experiment of primary (repeat word over and over) versus secondary (make images of words) rehearsal (X) on images created (M) on recall of 20 words (Y).
- Book data sets from simulated data and some real data.

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- Few things are harder to put up with than the annoyance of a good example.

*Mark Twain, Pudd'nhead Wilson*

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