Multivariate thinking and the introductory (bio)statistics course: preparing students to make sense of a world of observational data

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Harvard TH Chan SPH, October 19, 2017

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- Steve Lagakos for his many contributions to the profession
- my parents and family





Nicholas J. Horton

multivariate thinking and confounding



BIO 231cd: Statistical Inference I Spring 1995

Meeting Times: Lectures on Monday and Wednesday, 1:30

Lab: time to be determined

Instructor: Stephen Lagakos

Kresge Room 624, 432-2815

Office Hours: Monday and Wednesday, 3:

TA: Joe Hogan

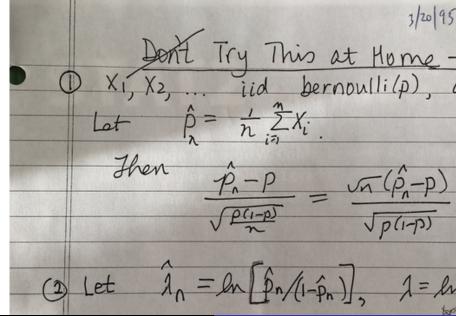
Kresge Room 612, 432-1056

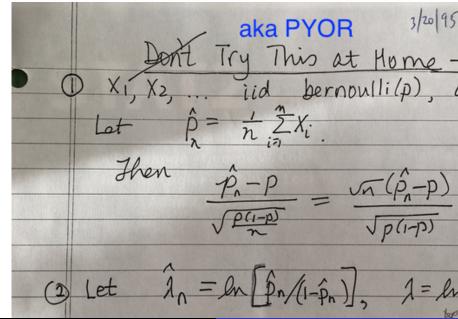
Office Hours: to be determined

Texts: Statistical Inference, by Casella and

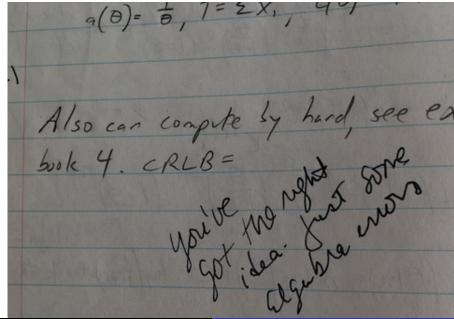
BIO 231 Supplementary Course Notes, by Available in Biostatistics Department not taking the course for credit or P/H

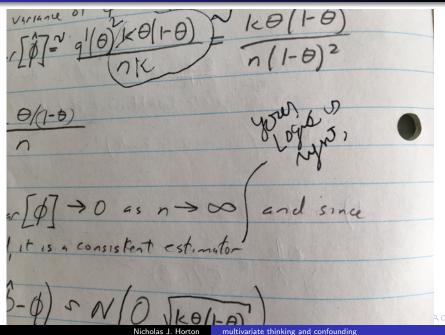
Biostatistics Department for these not





steadily or is relatively flat for intermediate exposure levels is probably beyond the information provided these data. 2] Because age (w) was only partially controlled for in the matching. the would be some variation in the ages of persons within a match set. Thus, the possibility exists to assess the association between W and Y, yet because the age rang within any set is small, only very strong associations might be detectable. One could assess whether W modified the X-Y association

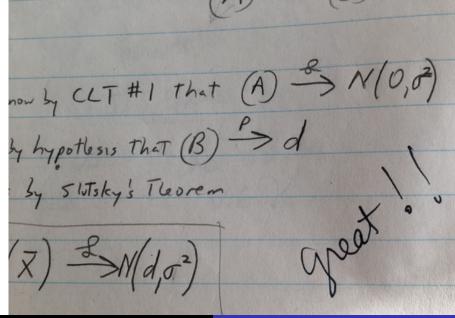




d) If an estimator sused on a complete & sufficient statistic exists with finite variance, it is umvuE for its expected valve. 1 null, this is The traction wis unbiased,

Souls (85, T) is winvill.

E(WIT) is winvill.



Motivation

Are we teaching what we should be teaching in our introductory statistics and biostatistics courses?

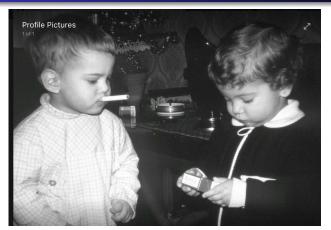
Motivation

OR do students leave our intro courses with a form of observational data paralysis?

Motivation

OR are we hiding the power of statistics behind our bushel basket?

Important assumption (Source: causal inference FB)



- While clinical trials are wonderful, we live in a world of 'found' data.
- "It is not that i believe an experiment is the only proper setting for discussing causality, but I do feel that it is the simplest such setting" - Holland (1986)

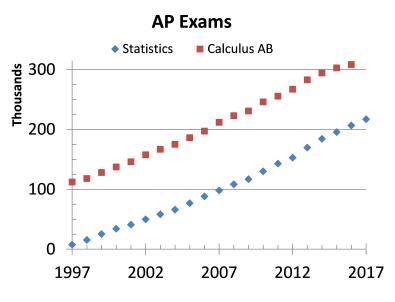
Do we teach multivariate thinking?

As we begin the 21st century, the introductory statistics course appears healthy, with its emphasis on real examples, data production, and graphics for exploration and assumption-checking. Without doubt this emphasis marks a major improvement over introductory courses of the 1960s, an improvement made possible by the vaunted "computer revolution." Nevertheless, I argue that despite broad acceptance and rapid growth in enrollments, the consensus curriculum is still an unwitting prisoner of history (Cobb, TISE 2007).

Teaching multivariate thinking and confounding

what are we currently teaching?

Advanced Placement Statistics



Data Source: College Board



AP Statistics curriculum

Four broad themes:

- Exploring Data: Describing patterns and departures from patterns
- Sampling and Experimentation: Planning and conducting a study
- Anticipating Patterns: Exploring random phenomena using probability and simulation
- Statistical Inference: Estimating population parameters and testing hypotheses

AP Stats: Exploring data (20-30%)

- Univariate graphics
- Univariate summaries
- Comparing univariate distributions
- Exploring bivariate data
- Exploring categorical data

AP Stats: Sampling and experimentation (10-15%)

- Methods of data collection
- Planning and conducting surveys
- Planning and conducting experiments
- Generalizability of results and types of conclusions

AP Stats: Anticipating patterns (20-30%)

- Probability
- Q Rules for random variables
- Normal tables(!)
- Sampling distributions
- **1** Other distributions (t, χ^2)

AP Stats: Statistical inference (30-40%)

- Estimation (point estimators and confidence intervals)
- 2 Tests of significance

AP Stats: aside on technology

Currently, the graphing calculator is the only computational aid that is available to students for use as a tool for data analysis on the AP Exam (AP Stats course description).

Relatively modern curriculum from circa 1996

MA 113 (Boston University) Basic concepts of estimation and tests of hypotheses, ideas from probability; one-, two-, and multiple-sample problems. Applications in social sciences. Primarily for students in the social sciences who require a one-semester introduction to statistics.

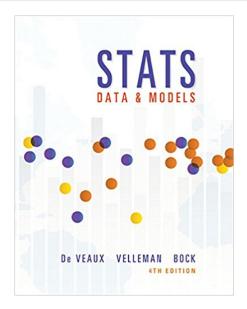
MATH125 (UMass/Boston) Topics include introductory statistics, covering descriptive statistics; introductory probability sufficient to enable development of inferential statistics; and inferential statistics.

STAT101 (Wellesley) An introduction to the fundamental ideas and methods of statistics for analyzing data. Topics include descriptive statistics, basic probability, inference, and hypothesis testing. Emphasis on understanding the use and misuse of statistics in a variety of fields, including medicine and both the physical and social sciences.

STAT100 (Harvard Stat) Introduction to key ideas underlying statistical and quantitative reasoning. Topics covered: methods for organizing, summarizing and displaying data; elements of sample surveys, experimental design and observational studies; methods of parameter estimation and hypothesis testing in one- and two-sample problems; regression with one or more predictors; correlation; and analysis of variance. Explores applications in a wide range of fields, including the social and political sciences, medical research, and business and economics.

BST201 (Harvard Chan) Covers basic statistical techniques that are important for analyzing data arising from epidemiology, environmental health and biomedical and other public health-related research. Major topics include descriptive statistics, elements of probability, introduction to estimation and hypothesis testing, nonparametric methods, techniques for categorical data, regression analysis, analysis of variance, and elements of study design. Applications are stressed. Designed for students desiring more emphasis on theoretical developments.

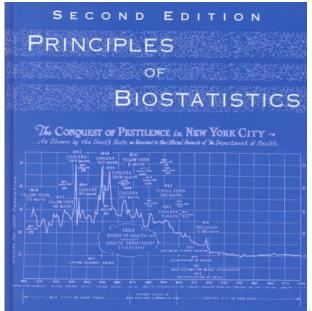
DeVeaux, Velleman, and Bock (SDM4)



DeVeaux, Velleman, and Bock (SDM4)

- Chapter 2: "When averages are taken across different groups, they can appear to contradict the overall averages. This is known as Simpson's paradox"
- Chapter 12: introduce confounding (in the context of clinical trials)
- Chapter 28 (page 817) multiple regression

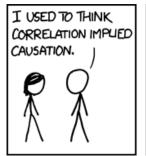
Pagano and Gauvreau



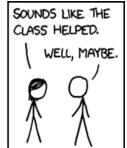
Principles of Biostatistics, second edition

- Chapter 4: Confounding defined (page 71, standardization as an approach to address p. 84–89)
- Chapter 16: Simpson's paradox introduced via multiple 2x2 tables (page 374 of 525)
- Chapter 19: multiple regression to move beyond bivariate questions
- Why wait?

Do we teach in a way that encourages paralysis?

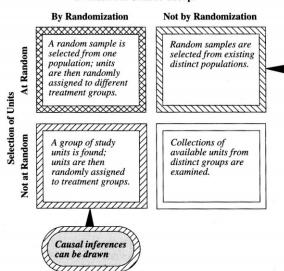






Other factors may be responsible for observed associations

Allocation of Units to Groups



Inferences to

can be drawn

the populations

Example from SDM4 (De Veaux, Velleman, and Bock) p. 575

Exercise 20.41: It's widely believed that regular mammogram screening may detect breast cancer early, resulting in fewer deaths from that disease. One study that investigated this issue over a period of 18 years was published during the 1970's. Among 30,565 who had never had mammograms, 196 died of breast cancer (0.64%) while only 153 of 30,131 who had undergone screening died of breast cancer (0.50%).

Do these results suggest that mammograms may be an effective screening tool to reduce breast cancer deaths?

Solution to Exercise 20.41 SDM4 (De Veaux, Velleman, and Bock) p. 575

 $H_0: p_1-p_2=0$ vs. $H_A: p_1-p_2>0$ (one-sided test? That's a different sermon.)

Solution to Exercise 20.41 SDM4 (De Veaux, Velleman, and Bock) p. 575

 $H_0: p_1 - p_2 = 0$ vs. $H_A: p_1 - p_2 > 0$ (one-sided test? That's a different sermon.) where p_1 is the proportion of women who never had mammograms who died of breast cancer and p_2 is the proportion of women who had undergone screening who died of breast cancer (z=2.17, p=0.0148).

With a p-value this low, we reject H_0 . The data suggest that mammograms may reduce breast cancer deaths.

Solution to Exercise 20.41 SDM4 (De Veaux, Velleman, and Bock) p. 575

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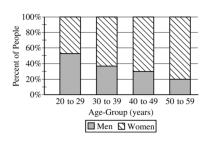
(But what about possible confounders?)

AP Statistics 2017 free response

2017 AP° STATISTICS FREE-RESPONSE QUESTIONS

The table and the bar chart below summarize the age at diagnosis, in years, for a random sample of 207 men and women currently being treated for schizophrenia.

Age-Group (years) 20 to 29 30 to 39 40 to 49 50 to 59 Total 46 21 119 Women 40 12 Men 53 23 88 Total 99 63 30 15 207



Do the data provide convincing statistical evidence of an association between age-group and gender in the diagnosis of schizophrenia?

OpenIntro Statistics

Third Edition



David M Diez Christopher D Barr Mine Cetinkaya-Rundel



Open Intro Statistics

6.34 Prenatal vitamins and Autism. Researchers studying the link between prenatal vitamin use and autism surveyed the mothers of a random sample of children aged 24 - 60 months with autism and conducted another separate random sample for children with typical development. The table below shows the number of mothers in each group who did and did not use prenatal vitamins during the three months before pregnancy (periconceptional period).⁵⁷

		Autism		
		Autism	Typical development	Total
Periconceptional	No vitamin	111	70	181
$prenatal\ vitamin$	Vitamin	143	159	302
	Total	254	229	483

- (a) State appropriate hypotheses to test for independence of use of prenatal vitamins during the three months before pregnancy and autism.
- (b) Complete the hypothesis test and state an appropriate conclusion. (Reminder: Verify any necessary conditions for the test.)
- (c) A New York Times article reporting on this study was titled "Prenatal Vitamins May Ward Off Autism". Do you find the title of this article to be appropriate? Explain your answer. Additionally, propose an alternative title. ⁵⁸

Open Intro Statistics

- **3** Since the p-value $< \alpha$, we reject H_0 . There is strong evidence of a difference in the rates of autism of children of mothers who did and did not use prenatal vitamins during the first three months before pregnancy.
- The p-value is small and we reject H0. The data provide convincing evidence to suggest that caffeinated coffee consumption and depression in women are associated.
- Yes, this is an observational study. Based on this study we can't deduce that drinking more coffee leads to less depression. There may be other factors, lurking variables, that cause decreased depression in women who drink more coffee.

(Non-scientific) survey of isolated statisticians and Stat Edsection members

question: "what assumptions do you have students check when using the two sample t-test?"

(Non-scientific) survey of isolated statisticians and Stat Ed section members

- question: "what assumptions do you have students check when using the two sample t-test?"
- representative answer: (instructor using Gould and Ryan [first edition])
 - Randomness in the data collection process (either random samples or experiment)
 - Independent samples
 - Sither normal looking samples or sample sizes larger than 25

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- Independent samples
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What about possible confounders? (Only one other respondent out of more than 20 mentioned "random assignment": almost all emphasis was on technical conditions).



EPI202b (circa 1995)

•
$$Z^2 = \frac{[X - E(X|H_0)]^2}{Var(X|H_0)} = \frac{(0.1310 - 0)^2}{0.00106} = 16.25$$

$$Pr[\chi^2 > 16.25] = 0.00006$$

We conclude that there is statistically significant evidence of an association betwee CAT level and CHD risk in these data.

(assuming no confounding, no selection bias, no information bias)

revised GAISE College report

Guidelines for Assessment and Instruction in Statistics Education (GAISE)

College Report 2016

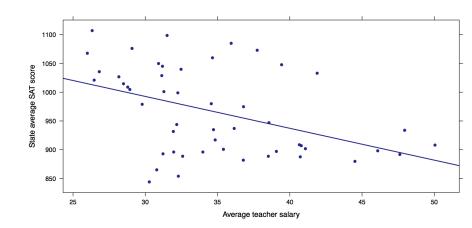
revised GAISE College Report (2016)

- Teach statistical thinking.
 - Teach statistics as an investigative process of problem-solving and decision-making.
 - Give students experience with multivariable thinking.
- Focus on conceptual understanding.
- Integrate real data with a context and purpose.
- Foster active learning.
- Use technology to explore concepts and analyze data.
- Use assessments to improve and evaluate student learning.

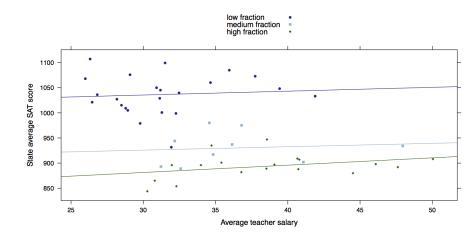
Teaching multivariate thinking and confounding

- what are we currently teaching?
- motivating multivariate examples

SAT scores and teacher salaries (state data from 2010)

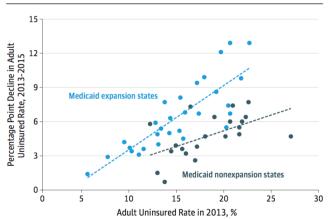


SAT scores and teacher salaries (state data from 2010)



stratification and/or multiple regression: Obama's 2016 single author JAMA paper

Figure 2. Decline in Adult Uninsured Rate From 2013 to 2015 vs 2013 Uninsured Rate by State



See also "Statistical methods in the NEJM" (2007)

Whickham cohort: smoking and mortality

Association of smoking and mortality



Smoking status

Whickham cohort: smoking and mortality

Results for 18-64 year olds at baseline



Whickham cohort: smoking and mortality

Results for those 65+ years old at baseling



Smoking status

Kidney stones (Wikipedia Simpson's Paradox)

	Treatment A	Treatment B	
Small stones	Group 1 93% (81/87)	Group 2 87% (234/270)	
Large stones	Group 3 73% (192/263)	Group 4 69% (55/80)	
Both	78% (273/350)	83% (289/350)	

How to handle more than two variables?

- stratification
- multiple regression (early and often)
- straightforward to use mosaic package "Less Volume, More Creativity" approach to modeling (https: //journal.r-project.org/archive/2017/RJ-2017-024 and related Little Books)
- "Data Viz on Day One" (http://escholarship.org/uc/item/84v3774z)
- causal graphs and confounding

Teaching multivariate thinking and confounding

- what are we currently teaching?
- motivating multivariate examples
- confounding 101 and 201

Multivariate thinking and confounding

AP Statistics Vocabulary

55 DC (I)



confounding

when the levels of one factor are associated with the levels of another factor so their effects cannot be separated

Utts: Seeing through Statistics (4th edition)

Jessica M. Utts

Seeing Through Statistics

Fourth Edition



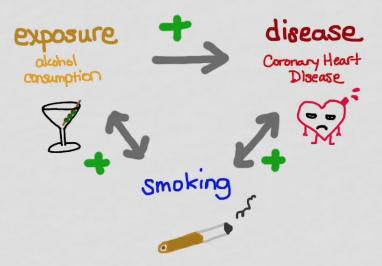
Utts: Seeing through Statistics (4th edition)

A confounding variable is one that has two properties.

- A confounding variable is related to the explanatory variable in the sense that individuals who differ for the explanatory variable are also likely to differ for the confounding variables.
- A confounding variable affects the response variable. Because of these two properties, the effect of a confounding variable on the response variable cannot be separated from the effect of the explanatory variable on the response variable.

causal graphs (Elizabeth Lynch)

Confounding Variable



Learning outcomes (Hernan and Swanson, EPI 524)

Confounding is a ubiquitous bias that arises when non-comparable groups are compared. It is one of the greatest threats to valid causal inferences from observational data. Therefore, controlling for confounding is a fundamental component of epidemiologic research.

Wikipedia definition

In statistics, a confounder (also confounding variable or confounding factor) is a variable that influences both the dependent variable and independent variable causing a spurious association. Confounding is a causal concept, and as such, cannot be described in terms of correlations or associations.

Wikipedia talk page



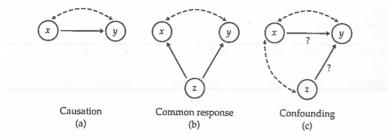


Moore et al (IPS, 7th edition)

Explaining association: causation

Figure 2.29 shows in outline form how a variety of underlying links between variables can explain association. The dashed double-arrow line represents an observed association between the variables x and y. Some associations are explained by a direct cause-and-effect link between these variables. The first diagram in Figure 2.28 shows "x causes y" by a solid arrow running from x to y.

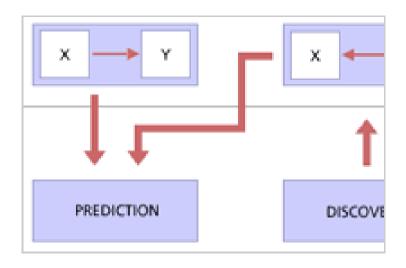
Items 1 and 2 in Example 2.42 are examples of direct causation. Even when direct causation is present, very often it is not a complete explanation of an association between two variables. The best evidence for causation comes from experiments that actually change x while holding all other factors fixed. If y changes, we have good reason to think that x caused the change in y.



What to teach?

We need to go beyond these informal definitions...

CMU Open Learning Initiative (OLI): Causal and Statistical Reasoning



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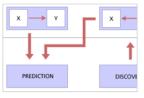
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SOC

CMU OLI: Causal and Statistical Reasoning



Causal & Statistical Reasoning [Enter Course]

Overview:

This course provides an introduction to causal and statistical reasoning. After taking this course, students will be better prepared to make rational decisions about their own lives and about matters of social policy. They will be able to assess critically—even if informally—claims that they encounter during discussions or when considering a

news article or report. A variety of materials are presented, including Case Studies where students are given the opportunity to examine a causal claim, and the Causality Lab, a virtual environment to simulate the science of causal discovery. Students have frequent opportunities to check their understanding and practice their skills.

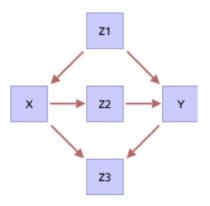
CMU OLI: Causal and Statistical Reasoning criteria

- X and Y are D-separated by Z just in case there are no undirected paths between X and Y that are active relative to Z
- A path is active iff all the variable on the path are active
- Non-colliders are active if they are not in the conditioning set
 Z, and inactive if they are in Z
- Colliders are active if they are in Z or have an effect in Z, and inactive otherwise

CMU OLI: Causal and Statistical Reasoning calculating

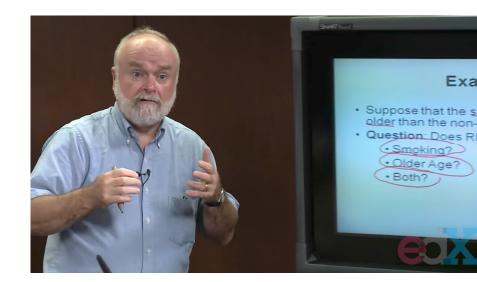
- First identify all undirected paths
- Count number of active (causally connected) paths
 - No mediators or common causes in Z
 - All common effects in Z
- If an active path exists, it is D-connected by that path
- If not, D separated

CMU OLI: Causal and Statistical Reasoning

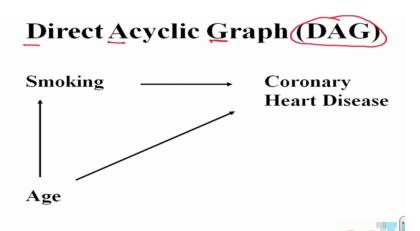


Used these materials (with some success) in a second course in statistics (2009)

Causal graphs (Fran Cook videos)

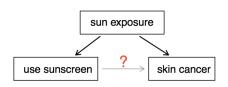


Causal graphs (Fran Cook videos)



Example

Suppose an observational study tracked sunscreen use and skin cancer, and it was found that the more sunscreen someone used, the more likely the person was to have skin cancer. Does this mean sunscreen causes skin cancer?



Sun exposure is what is called a **confounding variable**, ¹³ which is a variable that is correlated with both the explanatory and response variables. While one method to justify making causal conclusions from observational studies is to exhaust the search for confounding variables, there is no guarantee that all confounding variables can be examined or measured.

Fast forward



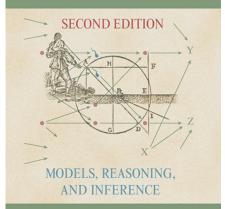
Jewell (2003)

Texts in Statistical Science

Statistics for Epidemiology

Nicholas P. Jewell

CAUSALITY



JUDEA PEARL

van der Laan and Rose (2011)

Springer Series in Statistics

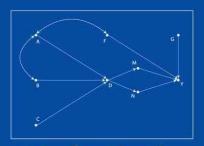
Mark J. van der Laan Sherri Rose

Targeted Learning

Causal Inference for Observational and Experimental Data

Winship and Morgan, second edition (2015)

ANALYTICAL METHODS FOR SOCIAL RESEARCH



Counterfactuals and Causal Inference

Methods and Principles for Social Research SECOND EDITION

STEPHEN L. MORGAN CHRISTOPHER WINSHIP

Vanderweele (2015)

EXPLANATION IN CAUSAL INFERENCE

Methods for Mediation and Interaction

TYLER J. VANDERWEELE

Wikipedia definition

Definition [edit | edit source]

Confounding is defined in terms of the data generating model (as in the Figure above). Let X be some independent variable, Y some dependent variable. To estimate the effect of X on Y, the statistician must suppress the effects of extraneous variables that influence both X and Y. We say that, X and Y are confounded by some other variable Z whenever Z is a cause of both X and Y.

Let $P(y \mid do(x))$ be the probability of event Y = y under the hypothetical intervention X = x. X and Y are not confounded if and only if the following holds:

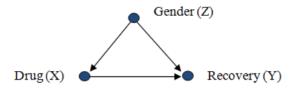
$$P(y \mid do(x)) = P(y \mid x) \tag{1}$$

for all values X = x and Y = y, where $P(y \mid x)$ is the conditional probability upon seeing X = x. Intuitively, this equality states that X and Y are not confounded whenever the observationally witnessed association between them is the same as the association that would be measured in a controlled experiment, with x randomized.

Wikipedia example

Control [edit | edit source]

Consider a researcher attempting to assess the effectiveness of drug X, from population data in which drug usage was a patient's choice. Data show that gender(Z) differences influence a patient's choice of drug as well as their chances of recovery (Y). In this scenario, gender Z confounds the relation between X and Y since Z is a cause of both X and Y:



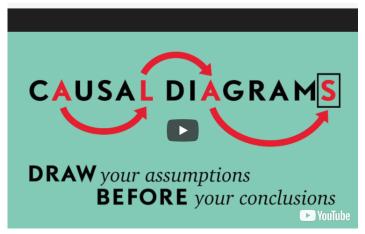
We have that

$$P(y \mid do(x)) \neq P(y \mid x)$$
 (2)

because the observational quantity contains information about the correlation between X and Z, and the interventional quantity does not (since X is not correlated with Z in a randomized experiment). Clearly the statistician desires the unbiased estimate

EdX Causal Diagrams: Draw Your Assumptions Before Your Conclusions course

2. What is a DAG?



EdX Causal Diagrams: Draw Your Assumptions Before Your Conclusions course

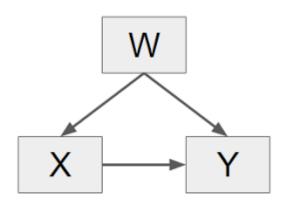
Association vs. Causation



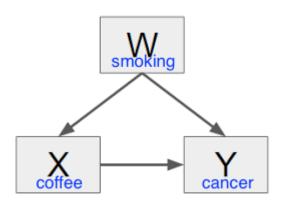
EdX Causal Diagrams: Draw Your Assumptions Before Your Conclusions course

- Causal DAGs
- 2 Confounding
- Selection Bias
- Measurement Bias and putting it all together

Coffee (X), Cancer (Y), and Smoking (W)



Coffee (X), Cancer (Y), and Smoking (W)



Chapters 6 and 7 of Hernan and Robins

6.6 The structure of effect modification

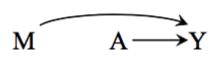


Figure 6.11

Identifying por use our causal association bet to illustrate th

Suppose he identify the average that there is a Computing the association is

$$\Pr\left[Y = 1 \middle| A = \right]$$

7.1 The structure of confounding



Confounding : a cause. The diagrams. For a treatment A diagram show the path $A \rightarrow$ $A \leftarrow L \rightarrow Y$ graph theory, cause L is an

EPI524 Description (Hernan and Swanson)

EPI524 describes models for confounding control (or adjustment), their application to epidemiologic data, and the assumptions required to endow the parameter estimates with a causal interpretation. The course introduces students to two broad sets of methods for confounding control: methods that require measuring and appropriately adjusting for confounders, and methods that do not require measuring the confounders. Specifically, the course introduces outcome regression, propensity score methods, the parametric g-formula, inverse probability weighting of marginal structural models, and instrumental variable methods as means for confounding control. The models described in EPI524 are for time-fixed dichotomous exposures and dichotomous, continuous, and failure time (e.g., survival) outcomes.

Learning outcomes (Hernan and Swanson)

At the completion of the course, you will be able to:

- Explain why models are necessary for confounding control
- Control for confounding using various modeling approaches
- Identify the relative advantages and disadvantages of each modeling approach
- Recognize and formulate well defined questions concerning causal effects

Causality in Statistics Award

Home » Member News, People News

2017 Causality in Statistics Award Announced

1 AUGUST 2017 219 VIEWS NO COMMENT

The American Statistical Association will award the fifth Causality in Statistics Shpitser, John C. Malone Assistant Professor of Computer Science at The John 2017 Joint Statistical Meetings in Baltimore.

Next steps

- Rich and sophisticated literature on causal inference now exists
- New curricular models and materials have been created (more needed)
- Need to rethink how we integrate this material into our courses (and promulgate the approach)

Teaching multivariate thinking and confounding

- what are we currently teaching?
- 2 motivating multivariate examples
- confounding 101 and 201
- closing thoughts: threats and opportunities

AP Computer Science Principles: an end-run around intro stat?

Big Idea 3: Data and Information

Data and information facilitate the creation of knowledge. Computing enables and empowers new methods of information processing, driving monumental change across many disciplines — from art to business to science. Managing and interpreting an overwhelming amount of raw data is part of the foundation of our information society and economy. People use computers and computation to translate, process, and visualize raw data and to create information. Computation and computer science facilitate and enable new understanding of

computation and computer science facilitate and enable new understanding of data and information that contributes knowledge to the world. Students in this course work with data using a variety of computational tools and techniques to better understand the many ways in which data is transformed into information and knowledge.

AP Computer Science Principles: taught for first time this year

Enduring Understandings

(Students will understand that ...)

EU 3.1 People
use computer
programs to process
information to
gain insight and
knowledge.

Learning Objectives

(Students will be able to ...)

LO 3.1.1 Find patterns and test hypotheses about digitally processed information to gain insight and knowledge. [P4]

AP Computer Science Principles: project based learning

LO 3.1.3 Explain the insight and knowledge gained from digitally processed data by using appropriate visualizations, notations, and precise language. [P5]

EK 3.1.3A Visualization tools and software can communicate information about data.

EK 3.1.3B Tables, diagrams, and textual displays can be used in communicating insight and knowledge gained from data.

EK 3.1.3C Summaries of data analyzed computationally can be effective in communicating insight and knowledge gained from digitally represented information.

EK 3.1.3DTransforming information can be effective in communicating knowledge gained from data.

EK 3.1.3E Interactivity with data is an aspect of communicating.

AP Computer Science Principles: 200 page course description

EU 3.2 Computing facilitates exploration and the discovery of connections in information.

LO 3.2.1 Extract information from data to discover and explain connections or trends. [P1]

AP Computer Science Principles: example question

- 8 of 9 Biologists often attach tracking collars to wild animals. For each animal, the following geolocation data is collected at frequent intervals.
 - The time
 - The date
 - · The location of the animal

Which of the following questions about a particular animal could NOT be answered using only the data collected from the tracking collars?

AP Computer Science Principles: example question

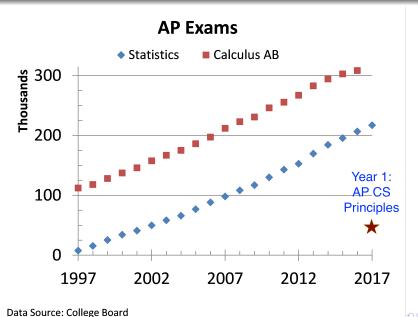
Approximately how many miles did the animal travel in one week?

Does the animal travel in groups with other tracked animals?

Do the movement patterns of the animal vary according to the weather?

In what geographic locations does the animal typically travel?

Advanced Placement Statistics



Moore et al (IPS, 7th edition)

2.6 The Question of Causation*

In many studies of the relationship between two variables, the goal is to establish that changes in the explanatory variable *cause* changes in the response variable. Even when a strong association is present, the conclusion that this association is due to a causal link between the variables is often hard to find. What ties between two variables (and others lurking in the background) can

^{*}This section is optional.

Avoiding paralysis

- Ensure that students don't get stuck (conclude they can't make any headway if data don't arise from a randomized trial)
- Teach (modern) design early and often
- Reinforce key aspects (observational data vs. randomized trials) when we teach inference
- Teach techniques to move beyond two-sample t-test (stratification and multiple regression)
- Make room by simplifying (what if all datasets were n > 100? what if p-values were de-emphasized?)

Multivariate thinking and the introductory (bio)statistics course: preparing students to make sense of a world of observational data

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