The Cross-Sectional Study:

Investigating Prevalence and Association

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Lecture Objectives

1. Understand the structure of the cross-sectional study design,
2. Understand the advantages and disadvantages of this design, and
3. Understand the kinds of questions that can be addressed using cross-sectional data.

Outline

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Are Kidney Stones and Hypertension Connected?

Background

- Women age 34–59 with history of kidney stones more likely to also have prior diagnosis of hypertension. (Madore, 1998)
- Men age 40–75 with stone history: same direction of association, but weaker. (Madore, 1998b)
- Multiple studies report relationship between BP and stones; wide variability in size of relationship.

The Gap: What is really going on?

Hypotheses:

- Some subgroups may be more susceptible to increased BP when stones are present than others.
- Heterogeneity of previous results may be due to differences in representation of high-risk subgroups.
- Association of BP and stones varies with (a) sex and (b) body size.

How to test these hypotheses?

- Need to be able to identify and study subgroups of interest.
- Need to avoid selection by stone status or blood pressure (so clinic-based samples are probably out)
- Would like to say something about subgroups as they exist in the adult population.

Investigated by Gillen, Coe, and Worcester using NHANES III: *The Third National Health and Nutrition Examination Survey.*

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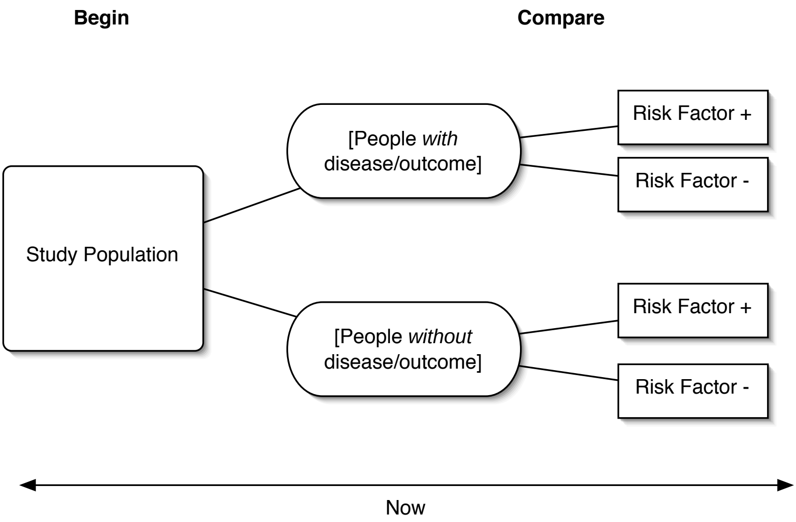
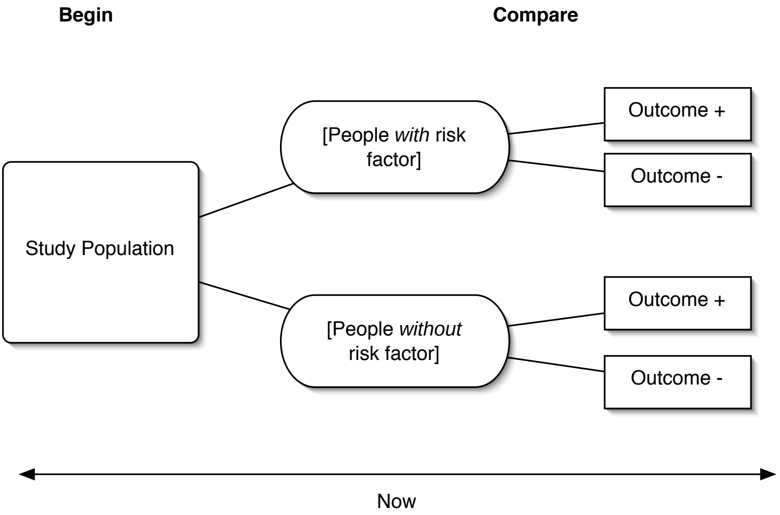
The Logic of Cross-Sectional Studies

- Looks at a "slice" of the population at a single point in time.
- If the selected sample is appropriately selected, composition of the sample reflects that in the population.
  - Simple random sample
  - Cluster sample
  - Stratified random samples
  - Multi-stage sample
- Perform pre-defined measurements and ascertainments.
  Often include questionnaire/survey questions
- What can we do with this sample? We can estimate
  - *Prevalence.* What fraction of the population has a particular characteristic?
    [History of kidney stones? Diagnosed hypertension? SBP > 140?]
  - *Association.* What is the correlation between an "exposure" and an "outcome?"
    [Relationship of kidney stone history to HTN history]

The Structure of a Cross-Sectional Study



The Structure of a Cross-Sectional Study, Continued



Pros and Cons

- Advantages
  - Cheaper/easier than longitudinal study: no follow-up required!
  - Afford good control over the measurement/ascertainment process
  - Can maximize completeness of key data (compared to retrospective study)
  - Have greater control over precision of estimates in subgroups (stratified sampling)
  - Often can be accomplished as *secondary data analysis*, that is, data collected by someone else (possibly for another purpose)

Pros and Cons, Continued

- Disadvantages
  - In secondary data analysis, no control over purpose, choice, or method of data collection
  - Cannot tell us about causal relationships (only correlation)
  - Generalizability limited by sampled population, population definition
  - Sample size requirements may be very large (especially when looking at rare outcomes or exposures)
  - Potential for selection bias.
    Example. "Length-biased sampling" results from the fact that individuals with long courses of a disease are more likely to be the ones identified as prevalent cases than people with courses of short duration.

Outline

How to conduct a cross-sectional study

- Identify (and define) population of interest
  [Adults aged 17–90 with knowledge of stone hx].
- Define outcomes
  [Previous diagnosis of HTN; SBP].
- Define exposures (for correlational analysis)
  [Lifetime history of kidney stones]
- Create data collection "instruments"
  [Surveys, interviews, physical measurement procedures: SBP]
  Data collection forms are very useful for
  - Standardization
  - Protocol adherence
- Insure consistent ascertainment
  [Training of staff]

How to conduct a cross-sectional study, Continued

- Sample from population appropriately
  [Multistage sample of households].
- Obtain consent, then "measure"
- Analyze using appropriate statistical methods
  - *May require special techniques to account for sampling design.*
  - Statistical adjustment for *confounders* is usually necessary; we are (usually) after relationships that remain after adjusting for other factors
    [Age, race, sex are differentially associated with both stone formation and blood pressure]

OR...
Ask NORC.

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Practical Issues for the Primary Cross-Sectionalist

- Non response
- Representativeness
- Logistics issues: cluster sampling, household contact
- Defining eligibility (target population)
- Defining measures in advance; respondent burden
- Data collection forms

Outline

Kidney Stones and BP

Gillen, *et al*, used NHANES III data (publicly available) to address their research questions.

- Conducted 1988–1994 by NCHS
- National population-based sample
- Noninsitutionalized persons aged > 2 months
- $n = 33\,994$
- Stone history available on $n = 20\,029$.

Answering key questions

Have you ever had a kidney stone?

919 answer Yes (4.6%)

This is a simple *prevalence* calculation

BP outcomes:

1. *Have you ever been told you have high blood pressure?*
2. SBP, DBP, Pulse pressure

Relationship of sex to stone formation:

Kidney stone Hx $-$: 54% women

Kidney stone Hx $+$: 40% women $p < 0.001$

Odds of stone history 1.73 higher in men than women

Relation of stone formation to hypertension:

"SFs were more likely to report a previous diagnosis of hypertension compared with non-SFs (32.7% vs 24.6%; $P = 0.001$)."

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Confounding: An Issue

- African-Americans less likely to form stones
- African-Americans more likely to have hypertension
- Want to "hold constant" AA effects when exploring stone-HTN effects
- Similarly for other *confounders*

Regression is one approach to confounders

Regression analysis

Table 2. Logistic Regression Results Modeling Self-Reported Diagnosis of Hypertension in the NHANES III Sample

Covariate	Adjusted Odds Ratio* (95% CI)	*P*
History of renal stones (yes *v* no)†		
Women	1.69 (1.33-2.17)	<0.001
Men	1.20 (0.88-1.64)	0.237
Age (/5 y)	1.22 (1.20-1.24)	<0.001
African-American race	1.48 (1.29-1.69)	<0.001
BMI (/kg/m^2)	1.10 (1.09-1.12)	<0.001
Ever smoker (yes *v* no)	1.04 (0.89-1.22)	0.600
History of CVD (yes *v* no)	2.00 (1.66-2.41)	<0.001
Diabetes (yes *v* no)	1.51 (1.25-1.82)	<0.001

*Adjusted for all covariates listed.
†*P* for interaction between history of renal stones and sex = 0.056.

What if degree of association depends on values of another variable?

Interaction effects

- SFs have higher BP than non-SFs
- This is stronger for heavier people
- This is more true for women than for men

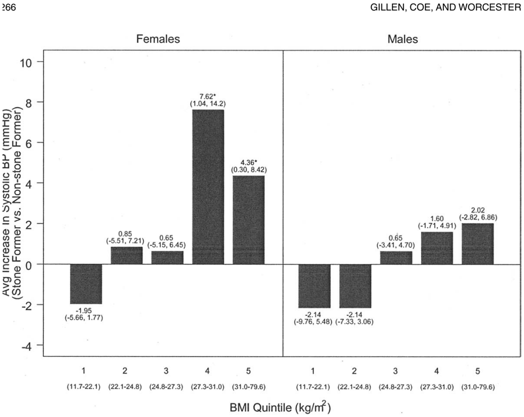

Fig 1. Multiple linear regression estimates (and corresponding 95% CIs) of the average difference in SBP comparing SFs with non-SFs by sex and BMI quintile. All estimates are adjusted for age, race, BMI, smoking status,

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Data Analysis/Statistics/Limitations

- Causality cannot be directly assessed
  - Do stones cause high BP, or does high BP predispose to stones?
  - Can view as "hypothesis generating" studies
  - Causality implies time course assessment
  - No experimental intervention
- Generalizability always an issue
  - Less so for population-based studies
  - Sampling method is key to generalizability
  - Relevance of defined population
    [NHANES: noninstitutionalized population]
  - Particularly important for smaller-scale cross sections: "Cross section of what?"
  - Convenience samples are especially problem-prone since it is hard to know how people "select in" to the population: chart review, clinic waiting rooms, callers to a help line.
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Data Analysis/Statistics/Limitations, Continued

- Confounders
  - Statistical adjustment possible, *if* confounders are measured!
  - Regression methods are most common, although stratification can also be used
  - Unmeasured confounders
    - A major worry, but need to identify
    - Ingenuity may lead to suitable *proxies*
    - Unrecognized confounders = land mine

Outline

Suggested Reading

1. Kantor J, Bilker WB, Glasser DB, Margolis DJ (2002). "Prevalence of erectile dysfunction and active depression: an analytic cross-sectional study of general medical patients," *Am J Epidemiol* 2002 Dec 1;156(11): 1035–42.

   An example of a community-based prevalence and correlation study.

2. Delgado-Rodriquez M, Llorca J (2004). "Bias," *Journal of Epidemiology and Community Health* 2004;58: 635–641.

   A useful paper cataloging important sources of bias.
   Available on the course website:
   `http://health.bsd.uchicago.edu/thisted/epor/`