Study Design

- Detailed plan to
  - Enroll subjects
  - Collect data
  - Perform analysis

Study Designs Options

- Case Reports
- Ecological Studies
- Cross Sectional Studies
- Experimental Studies
- Cohort Studies
- Case Control Studies

Case-Reports

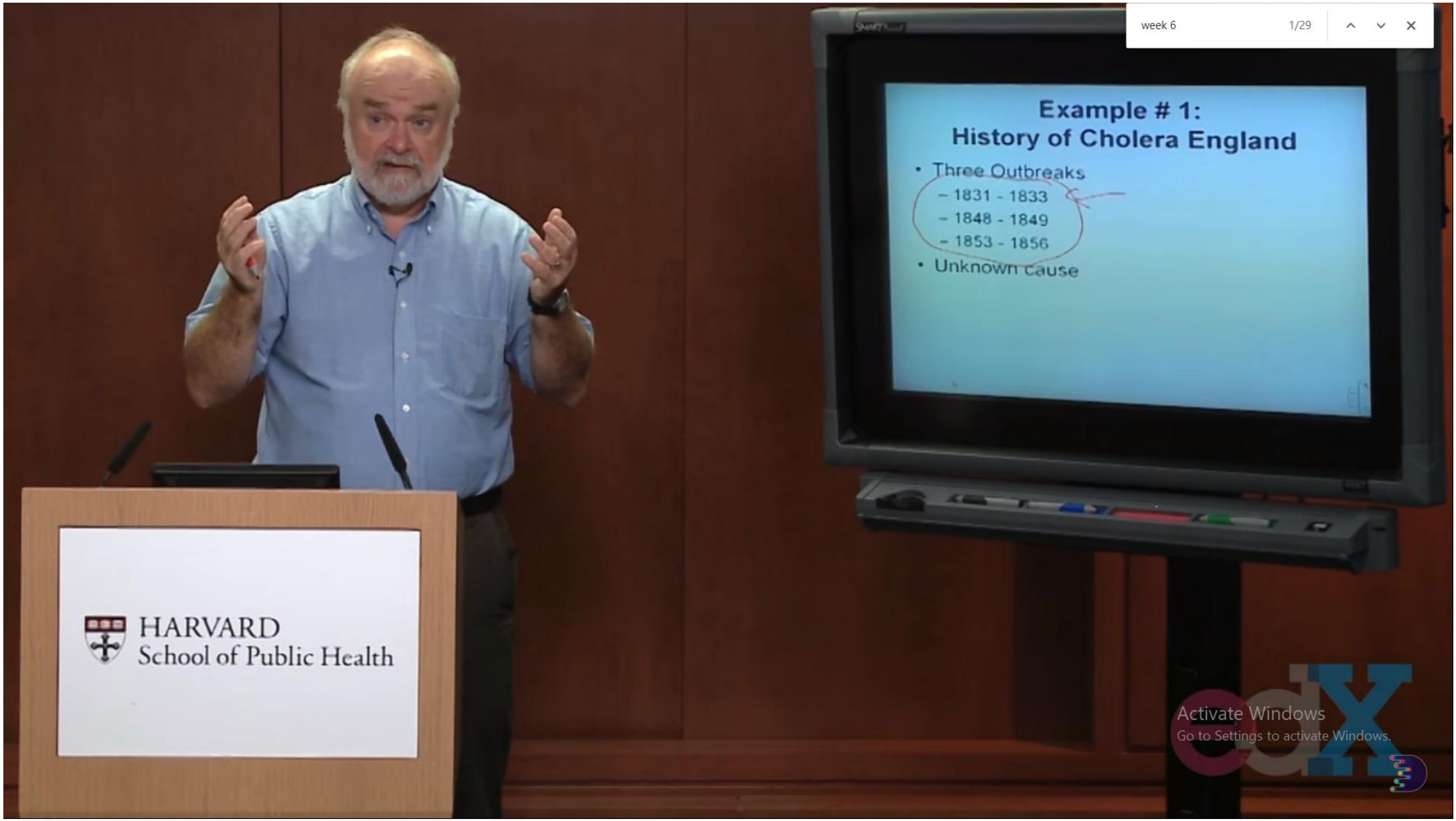
- Detailed report of the symptoms, signs, diagnosis, treatment, and follow-up of an individual patient(s)
- Typically an **unusual/novel occurrence**

http://en.wikipedia.org/wiki/Case_repor

Some Types of Case-Reports

- An **unexpected association** between disease or symptoms.
- An **unexpected event** in the course of observing or treating a patient.
- Findings that shed **new light** on the possible pathogenesis of a disease or an adverse effect.
- **Unique** or **rare** features of a disease.
- **Unique** therapeutic approaches.

http://en.wikipedia.org/wiki/Case_report


week 6
1/29
Example # 1:
History of Cholera England
• Three Outbreaks
– 1831 - 1833
– 1848 - 1849
– 1853 - 1856
• Unknown cause
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.

Advice to Prevent Cholera (NY Board of Health 1832)

"be temperate in eating and drinking, avoid crude vegetables and fruit; abstain from cold water, when heated; and above all from ardent spirits and if habit has rendered it indispensable, take much less than usual … avoid labor in the heat of the day, do not sit or sleep in a draught of air when heated … avoid getting wet"

Magnus: Essentials of Infectious Disease Epidemiology. Jones and Bartlett 20

Advice to Prevent Cholera (NY Board of Health 1832)

"be temperate in eating and drinking, avoid crude vegetables and fruit; abstain from cold water, when heated; and above all from ardent spirits and if habit has rendered it indispensable, take much less than usual … avoid labor in the heat of the day, do not sit or sleep in a draught of air when heated … avoid getting wet"

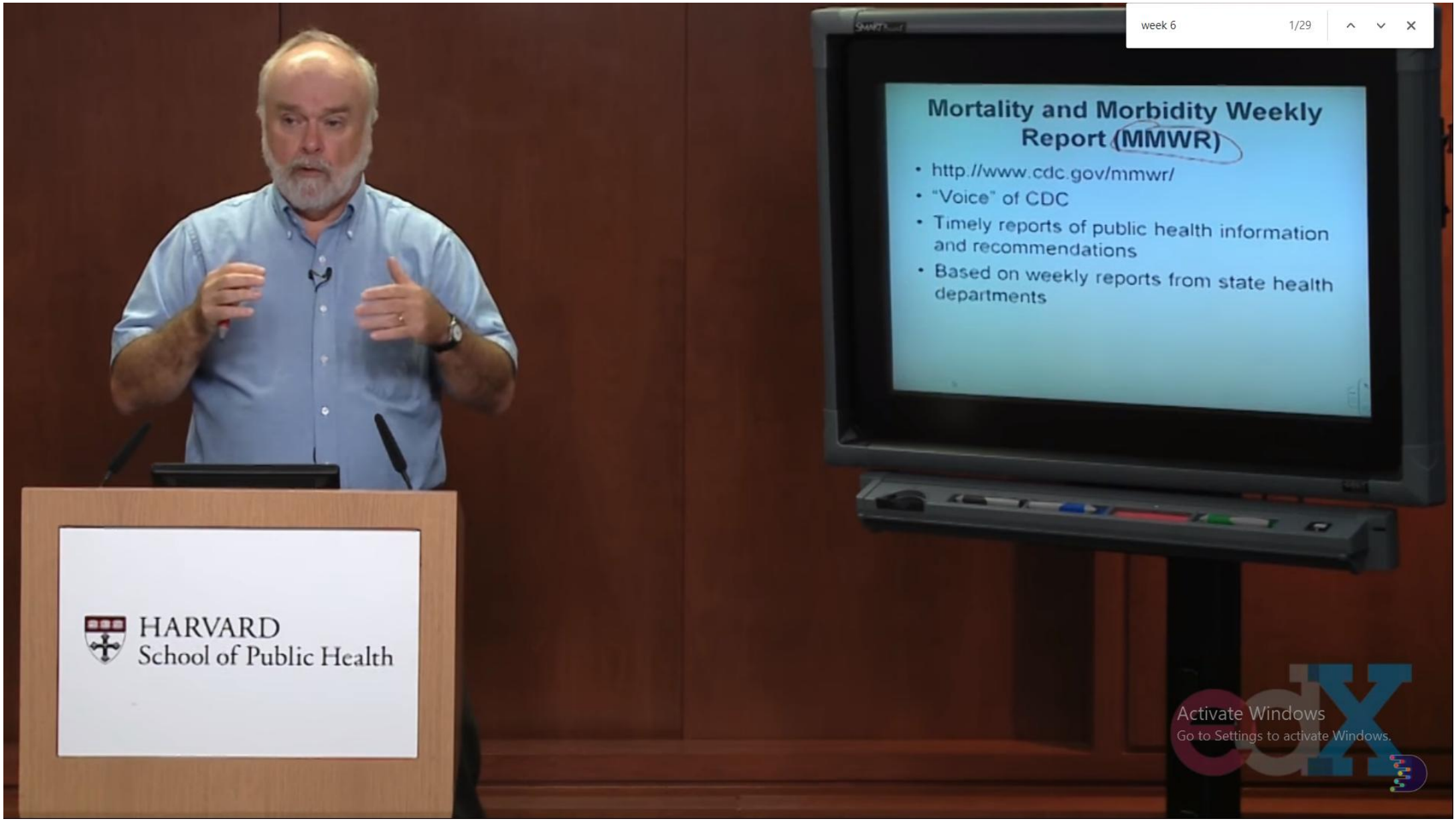
Magnus: Essentials of Infectious Disease Epidemiology. Jones and Bartlett 20

Perceived Causes of Cholera in 1832

- Reference: Craigie D. *An account of the epidemic cholera of Newburn in January and February 1832.* Edinburgh Medical Surgical Journal 1832;37:337-384.
- Describes some of the 92 attacks of Cholera (1/6 of the population) that occurred in a seven-day period in the village of Newburn

Proposed Cause

- Not the spread from the sick to the sound
- "I venture to assert … that the intercourse with the sick went in this case for nothing; and, had Mr. Edmonston secluded himself with his garden wall, the **pickled salmon** would have produced precisely the same effect."


week 6 1/29
Mortality and Morbidity Weekly Report (MMWR)
• http://www.cdc.gov/mmwr/
• "Voice" of CDC
• Timely reports of public health information and recommendations
• Based on weekly reports from state health departments
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.

Mortality and Morbidity Weekly Report (MMWR)

- http://www.cdc.gov/mmwr/
- "Voice" of CDC
- Timely reports of public health information and recommendations
- Based on weekly reports from state health departments

Example #2: CDC MMWR Case Report

"In the period October 1980 – May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California"

Editorial Note: "*Pneumocystis* pneumonia in the United States is almost exclusively limited to severely immunosuppressed patients. The occurrence of Pneumocystis in these 5 previously healthy individuals without a clinically apparent underlying immunodeficiency is unusual"

CDC – MMWR June 5 1981 /30(21); 1-3
www.cdc.gov/hiv/resources/reports/mmwr.1981.htm

Kaposi's Sarcoma and Pneumocystis Pneumonia among Homosexual Men – New York City and California

"During the past 30 months, Kaposi's Sarcoma (KS), an uncommonly reported malignancy in the United States, has been diagnosed in 26 homosexual men (20 in New York; 6 in California)."

Editorial Note: ... "The occurrence of this number of KS cases during a 30 month period among young homosexual men is considered highly unusual."

CDC – MMWR July 4;30:306-8

Follow-up on Karposi's Sarcoma and *Pneumocystis* Pneumonia

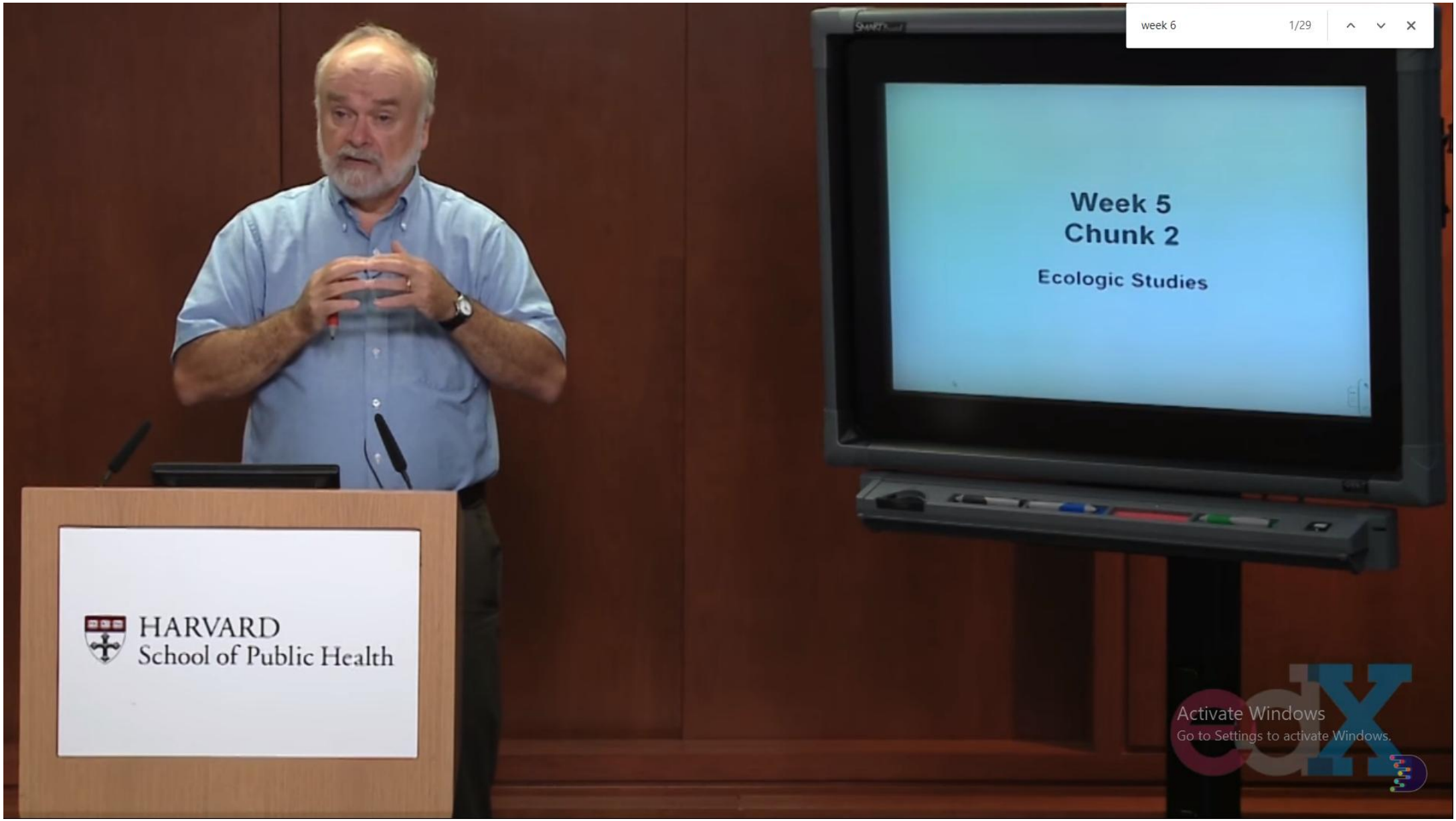
"Twenty-six cases of Karposi's sarcoma (KS) and 15 cases of *Pneumocystis carinii* pneumonia (PCP) among previously healthy homosexual men were recently reported. ... Since July 3, 1981, CDC has received reports of an additional 70 cases of these 2 conditions in persons without known underlying disease."

Editorial Note: "KS is a rare, malignant neoplasm seen predominantly in in elderly men in this country."

CDC – MMWR 1981 August 28;30:409-10

Case-Reports

- **Problem**: Usually no comparison group
- Possible historical/experience comparison group
- **Generates potential hypotheses for future, more detailed investigations**


week 6
1/29
Week 5
Chunk 2
Ecologic Studies
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.

Ecologic Studies

- Correlation Studies
- Examine associations between exposure and disease measures on the **population level**
- Unit of measurement = population group

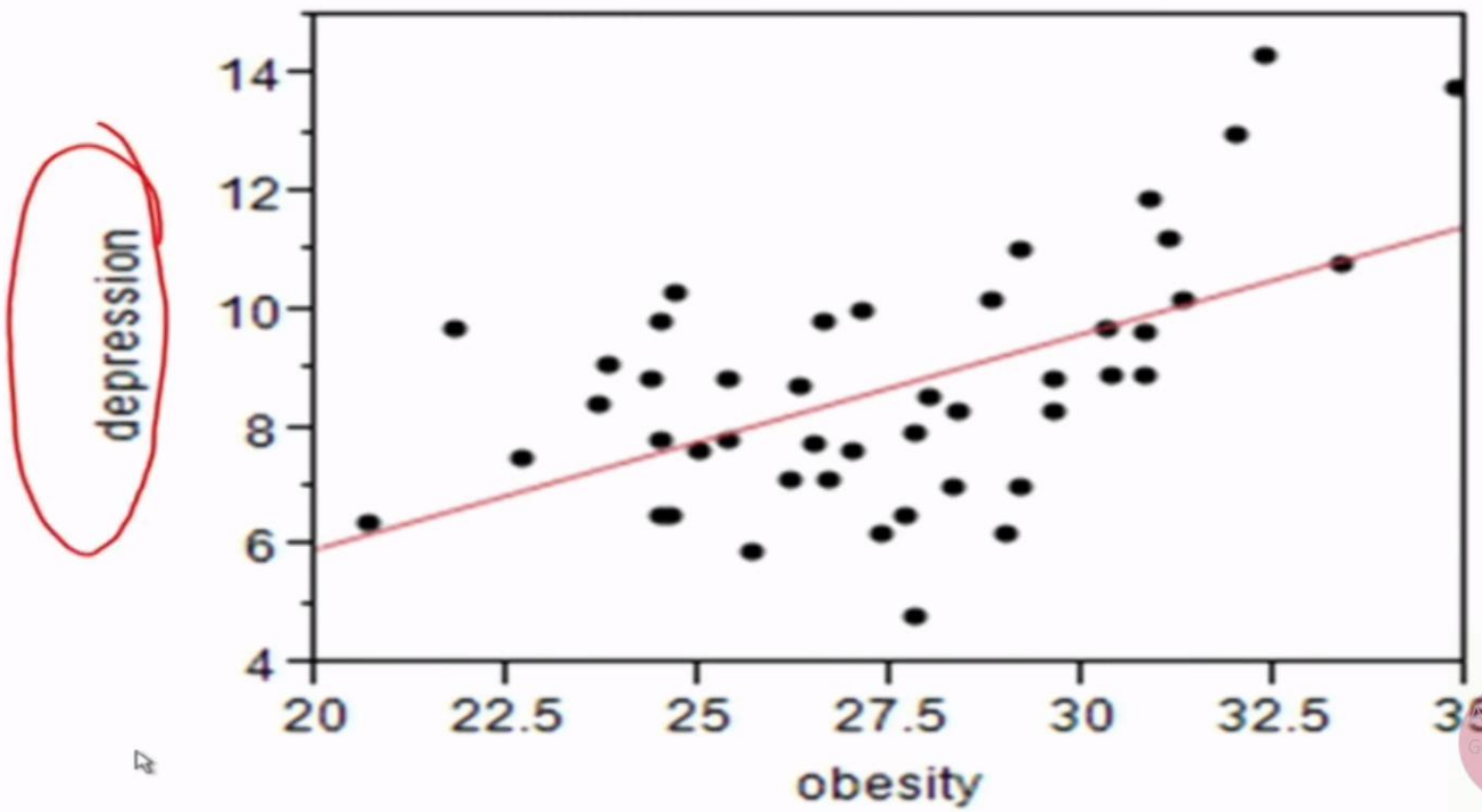
Ecologic Studies

- Correlation Studies
- Examine associations between exposure and disease measures on the **population level**
- Unit of measurement = population group

Example: Obesity and Depression

- CDC data from the **Behavioral Risk Factor Surveillance System (BRFSS)**
- Prevalence of depression from 2006 – 2008
  - http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5938a2.htm
- Prevalence of obesity in 2011
  - www.cdc.gov/obesity/data/adult.html

Prevalence of Depression and Obesity by U.S. States



CDC data

Conclusion

- States with higher prevalence of obesity tend to have higher prevalence of depression
- Does this imply
  - ~~Obesity~~ causes depression **in individuals**?
  - Depression causes obesity **in individuals**?

Conclusion

- States with higher prevalence of obesity tend to have higher prevalence of depression
- Does this imply
  - Obesity causes depression **in individuals**?
  - Depression causes obesity **in individuals**?

Ecologic Studies

- Associations on population levels may not reflect associations on individual levels.
- Example: Don't know whether individuals who are obese tend also to be depressed
- **Ecologic Fallacy**: Incorrectly assuming that an association on a population level reflects an association on an individual

Obesity	Depression		Total
	Yes	No	
Yes	1	3	4
No	3	3	6
Total	4	6	10

P(Obesity)	P(Depression)	OR
0.4	0.4	0.33

Obesity	Depression		Total
	Yes	No	
Yes	2	3	5
No	3	2	5
Total	5	5	10

P(Obesity)	P(Depression)	OR
0.5	0.5	0.44

Obesity	Depression		Total
	Yes	No	
Yes	3	3	6
No	3	1	4
Total	6	4	10

P(Obesity)	P(Depression)	OR
0.6	0.6	0.33

A

Obesity	Depression		Total
	Yes	No	
Yes	1	3	4
No	3	3	6
Total	4	6	10

P(Obesity)	P(Depression)	OR
0.4	0.4	0.33

B

Obesity	Depression		Total
	Yes	No	
Yes	2	3	5
No	3	2	5
Total	5	5	10

P(Obesity)	P(Depression)	OR
0.5	0.5	0.44

C

Obesity	Depression		Total
	Yes	No	
Yes	3	3	6
No	3	1	4
Total	6	4	10

P(Obesity)	P(Depression)	OR
0.6	0.6	0.33

A

Obesity	Depression		Total
	Yes	No	
Yes	1	3	4
No	3	3	6
Total	4	6	10

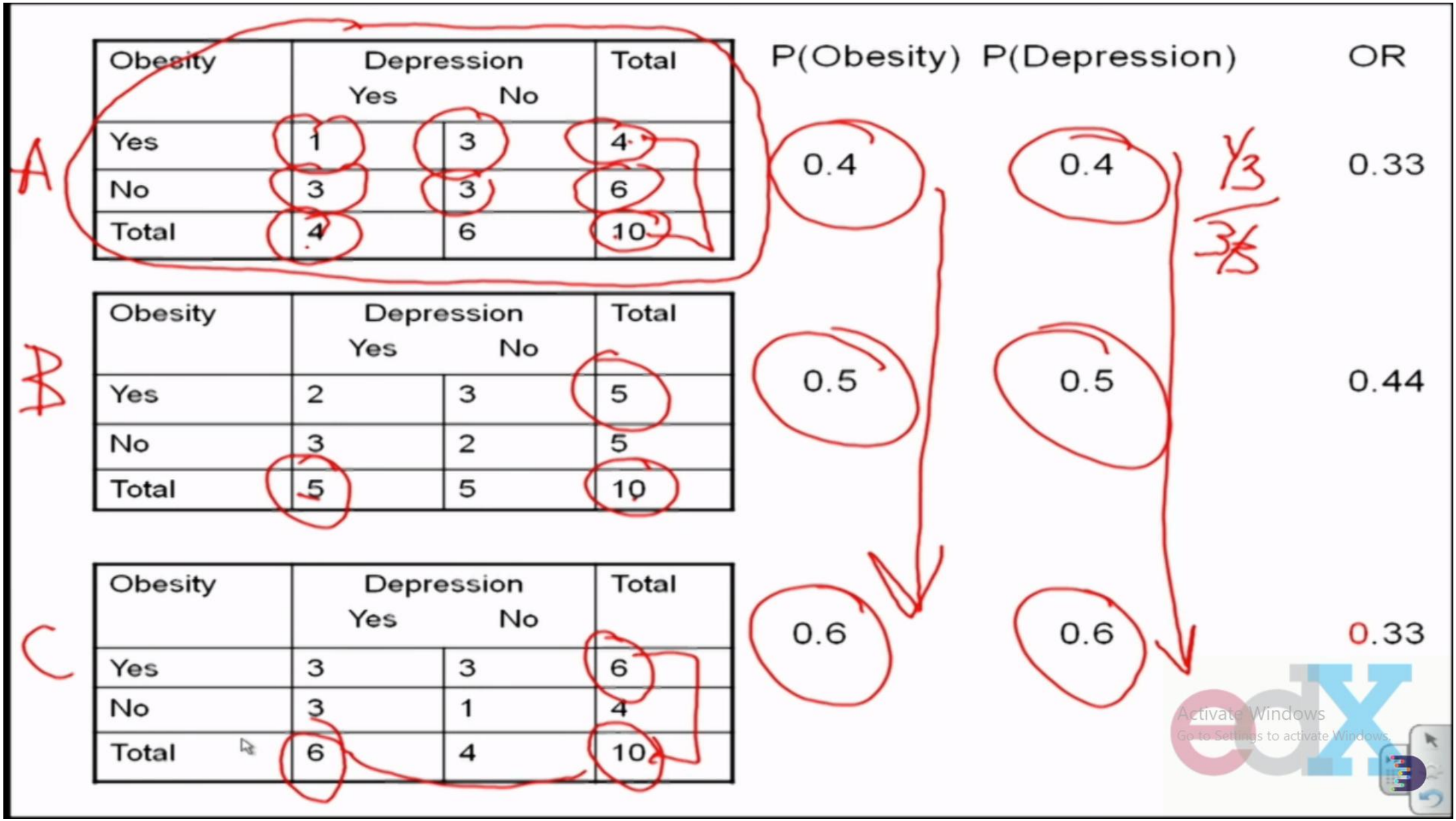
B

Obesity	Depression		Total
	Yes	No	
Yes	2	3	5
No	3	2	5
Total	5	5	10

C

Obesity	Depression		Total
	Yes	No	
Yes	3	3	6
No	3	1	4
Total	6	4	10

	P(Obesity)	P(Depression)	OR
A	0.4	0.4	0.33
B	0.5	0.5	0.44
C	0.6	0.6	0.33


A
Obesity
Depression
Yes
No
Total
Yes 1 3 4
No 3 3 6
Total 4 6 10
P(Obesity) 0.4
P(Depression) 0.4
OR 0.33
B
Obesity
Depression
Yes
No
Total
Yes 2 3 5
No 3 2 5
Total 5 5 10
P(Obesity) 0.5
P(Depression) 0.5
OR 0.44
C
Obesity
Depression
Yes
No
Total
Yes 3 3 6
No 3 1 4
Total 6 4 10
P(Obesity) 0.6
P(Depression) 0.6
OR 0.33

A

Obesity	Depression		Total
	Yes	No	
Yes	1	3	4
No	3	3	6
Total	4	6	10

B

Obesity	Depression		Total
	Yes	No	
Yes	2	3	5
No	3	2	5
Total	5	5	10

C

Obesity	Depression		Total
	Yes	No	
Yes	3	3	6
No	3	1	4
Total	6	4	10

	P(Obesity)	P(Depression)	OR
A	0.4	0.4	0.33
B	0.5	0.5	0.44
C	0.6	0.6	0.33

A

Obesity	Depression		Total
	Yes	No	
Yes	1	3	4
No	3	3	6
Total	4	6	10

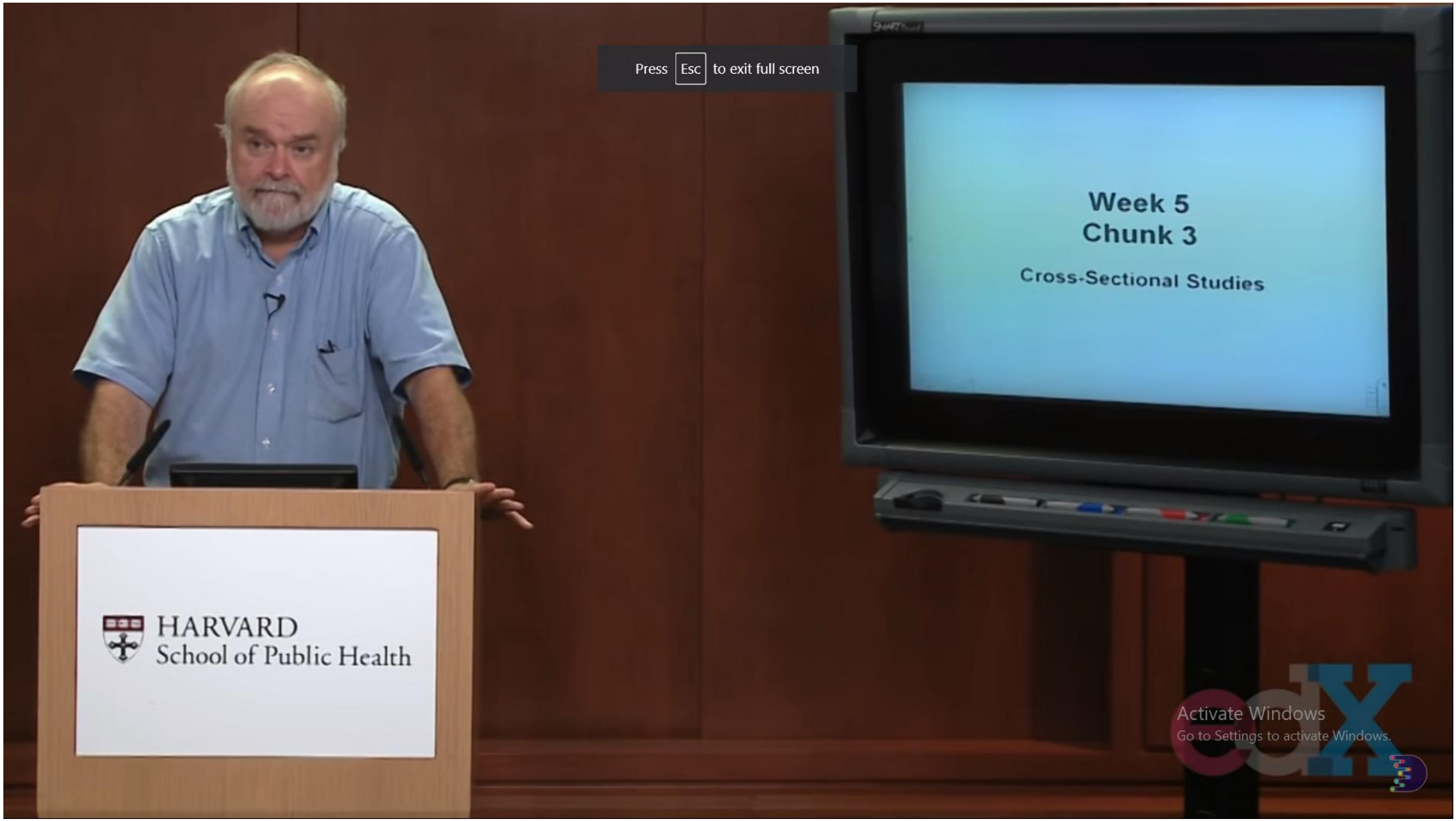
B

Obesity	Depression		Total
	Yes	No	
Yes	2	3	5
No	3	2	5
Total	5	5	10

C

Obesity	Depression		Total
	Yes	No	
Yes	3	3	6
No	3	1	4
Total	6	4	10

	P(Obesity)	P(Depression)	OR
A	0.4	0.4	0.33
B	0.5	0.5	0.44
C	0.6	0.6	0.33


Press Esc to exit full screen
Week 5
Chunk 3
Cross-Sectional Studies
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.

Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.8226

Prevalence Odds Ratio = (86/2095)/(108/2145) = 0.8153

Question: Can we conclude from these data that smokers are at lower risk of developing CHD?

Potential Reasons for Association between Smoking and Prevalence of CHD

- Incidence
- Unlikely that smoking prevents CHD

Incidence of first CHD among Smokers and Non-Smokers

	Incident CHD	Person-yrs	Incidence Rate
Smokers	531	39636.77	531/(39636.77py) = 1.34/(100py)
Non-Smokers	515	41288.39	515/(41288.39py) = 1.25/(100py)

Rate Ratio = [531/(39636.77py)] / [515/(41288.39py)] = 1.07

Incidence of first CHD among Smokers and Non-Smokers

	Incident CHD	Person-yrs	Incidence Rate
Smokers	531	39636.77	531/(39636.77py) = 1.34/(100py)
Non-Smokers	515	41288.39	515/(41288.39py) = 1.25/(100py)

Rate Ratio = [531/(39636.77py)] / [515/(41288.39py)] = 1.07

Potential Reasons for Association between Smoking and Prevalence of CHD

- **Duration of CHD**
- Unlikely that duration of CHD that develops among smokers is shorter than that of non-smokers

Potential Reasons for Association between Smoking and Prevalence of CHD

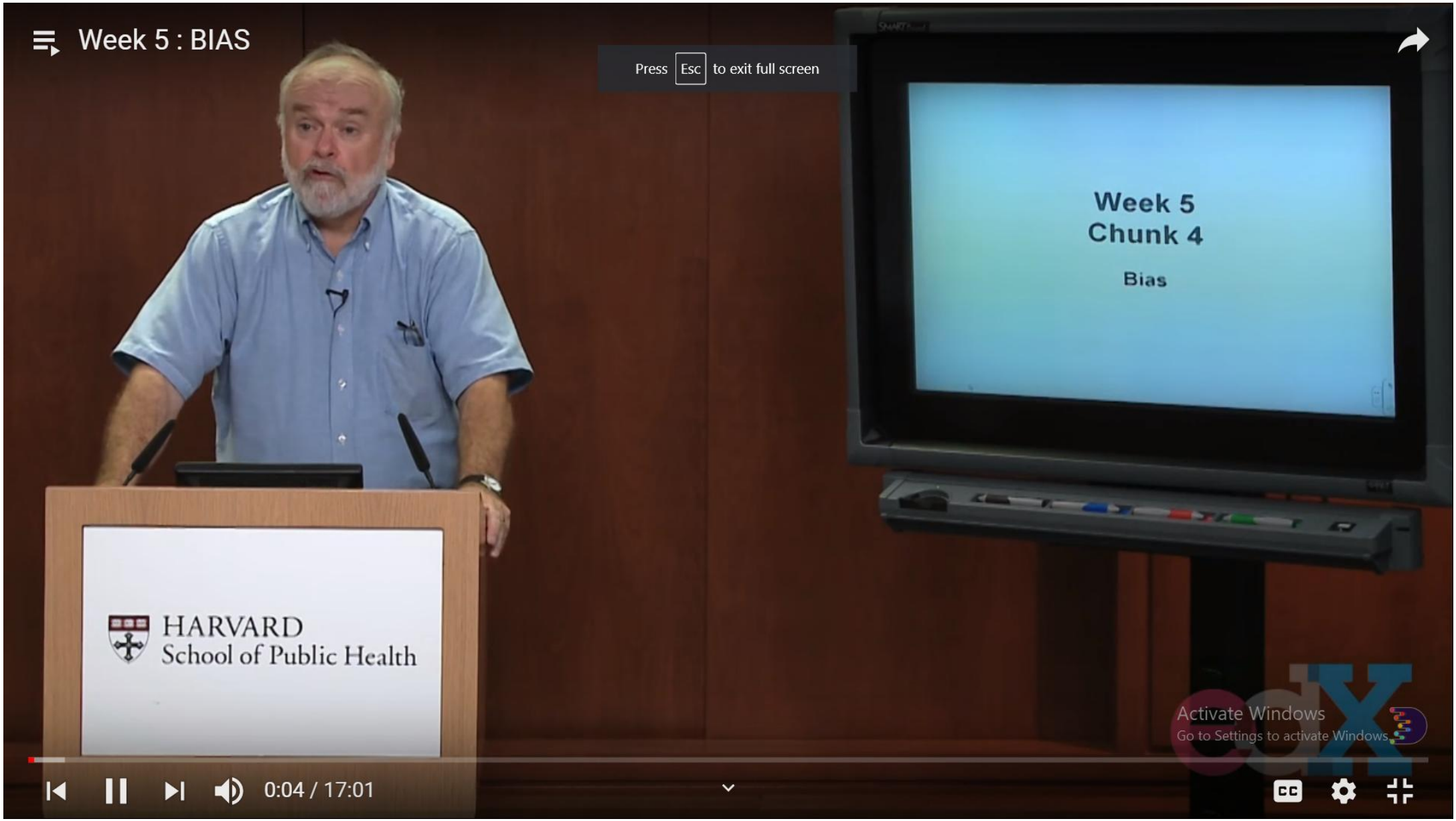
- **Reverse Causation**
- Likely that CHD development causes individuals to stop or not start smoke

Potential Reasons for Association between Smoking and Prevalence of CHD

- **Reverse Causation**
- Likely that CHD development causes individuals to stop or not start smoke

Potential Reasons for Any Association in Epidemiology

- Truth
- Bias
- Confounding
- Chance


Week 5 : BIAS
Press Esc to exit full screen
Week 5
Chunk 4
Bias
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.
0:04 / 17:01

Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.82

Potential Reasons for Association between Smoking and Prevalence of CHD

- **Bias**
- Error in design/implementation of a study
  - Error in enrolling subjects
  - Error in collecting data
- Results in an incorrect value for a measure of association

Potential Reasons for Association between Smoking and Prevalence of CHD

- General Types
  - Selection Bias
  - Measurement Bias

Selection Bias

- 5209 participants enrolled at start of study
- 4434 participants in 1956 exam in data set
- Possible reasons for 5209 – 4434 = 775 missing participants
  - Death
  - Loss-to-follow-up
  - Removed from data set by NIH (NHLBI)

Selection Bias

- Problem: Missing data may be related to smoking status and CHD status
- Implications: Biased estimates of the prevalence of CHD among smokers and/or non-smokers

Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.82

Measurement Bias

- Suppose smokers see physicians less often and undergo less testing than non-smokers
- Possible implications: Under-reporting of CHD among smokers

Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

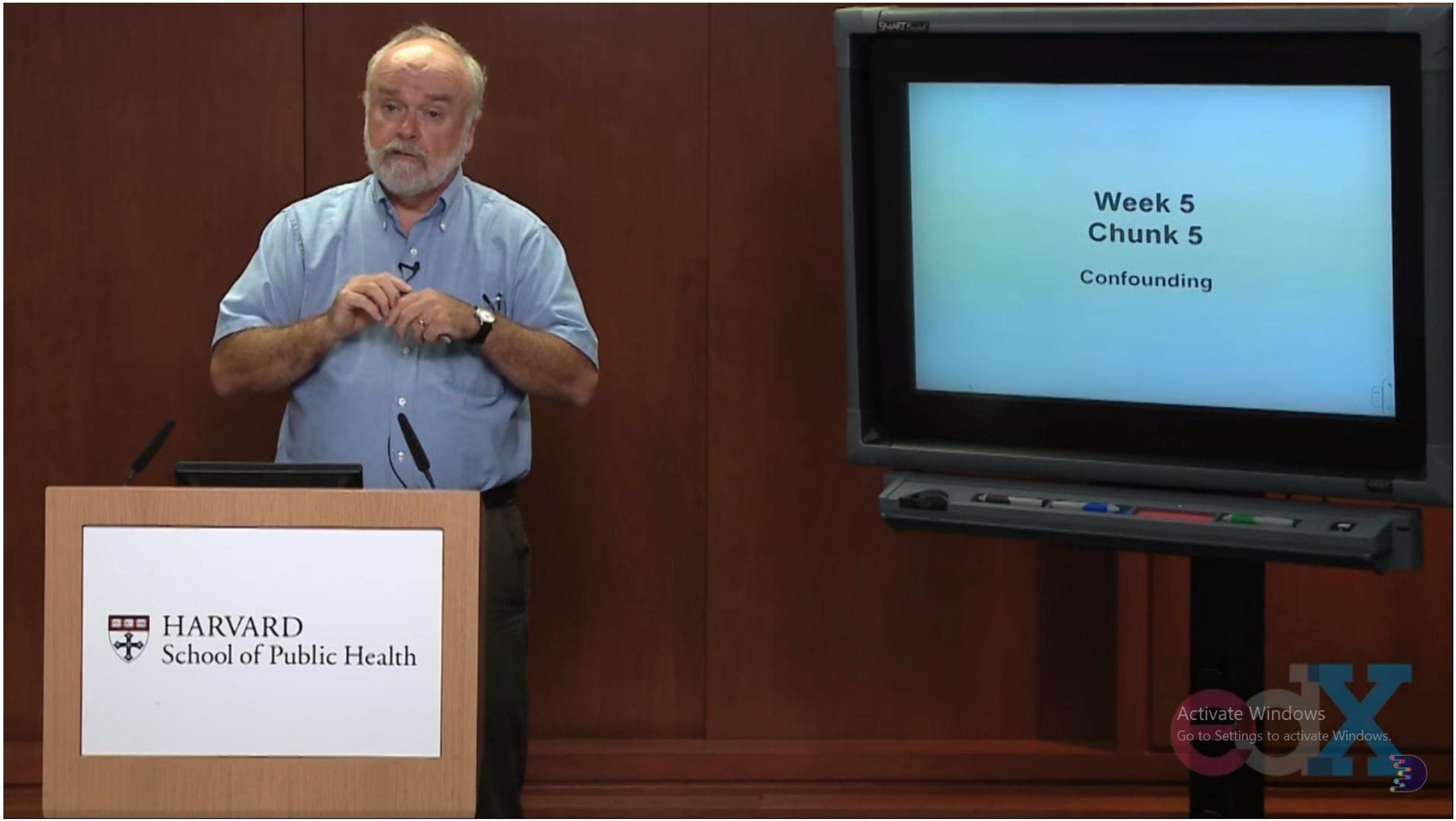
Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.82

Types of Misclassification

- **Random Misclassification**
  - Misclassification of CHD unrelated to smoking status
  - Usual implication: Bias of Prevalence Ratio towards its null value (underestimation)
- **Non-Random Misclassification**
  - Misclassification is related to smoking status
  - Implication: Bias in any direction (underestimation or overestimation)

Addressing Bias

- **Evaluate**
  - Source
  - Likely magnitude/strength
  - Direction (over-estimate versus under-estimate)
- Possible Correction/Adjustment
  - Usually very little in the analysis


Week 5
Chunk 5
Confounding
HARVARD
School of Public Health

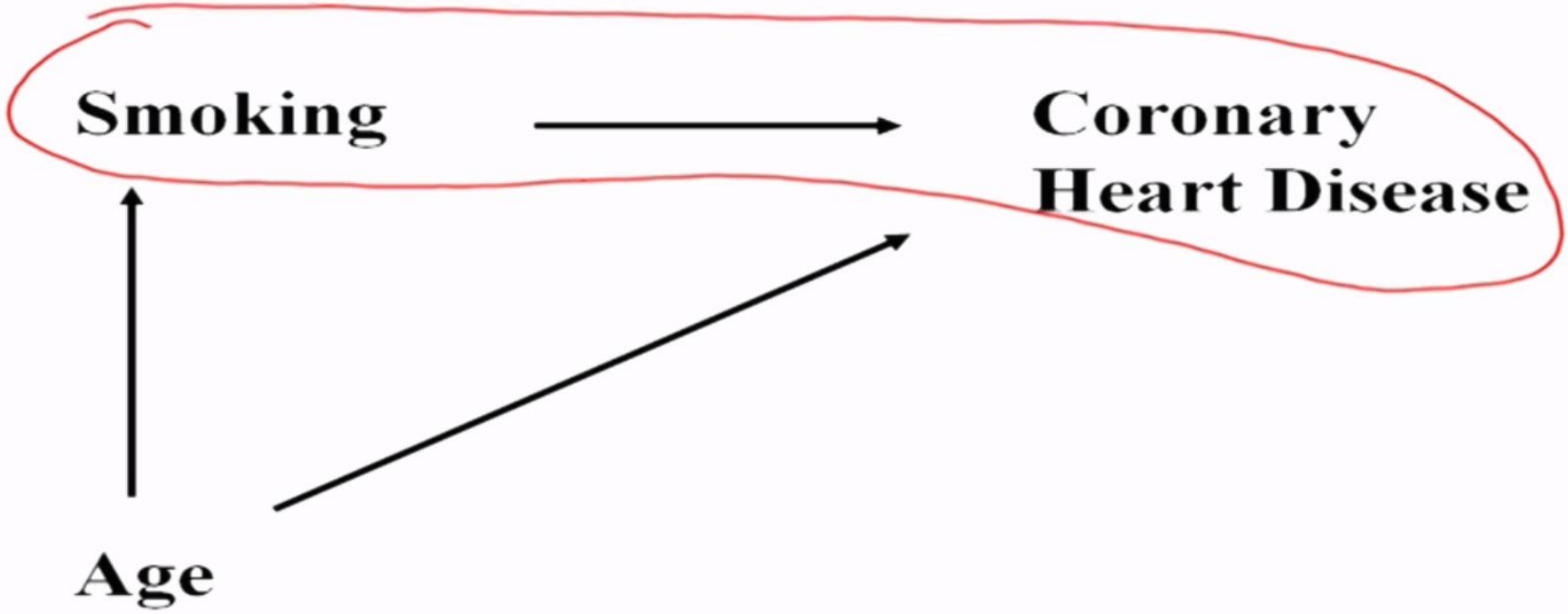
Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.82

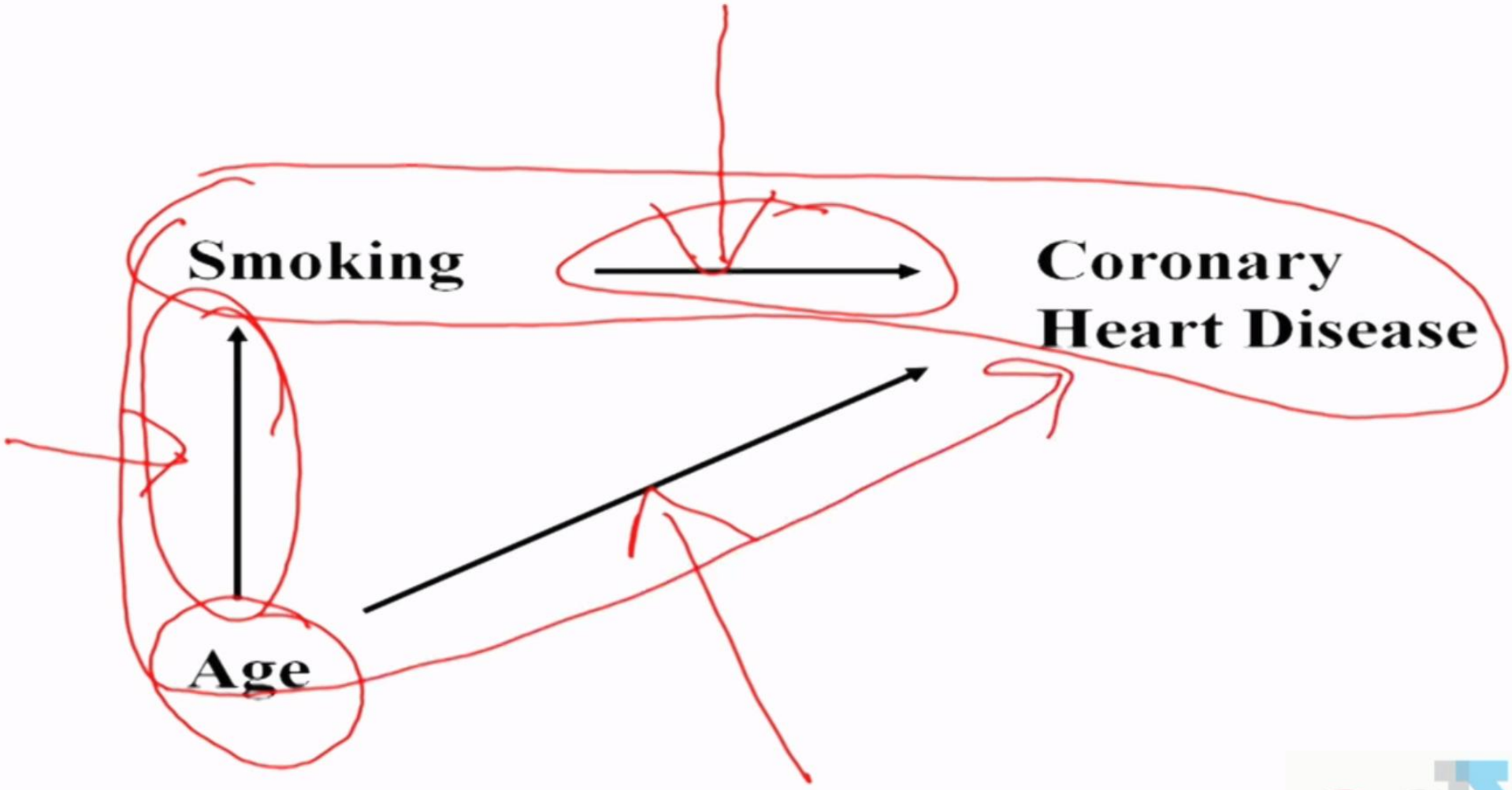
Confounding

- Suppose 2181 smokers are younger than the 2253 non-smokers
- Does the Prevalence Ratio (0.82) reflect
  - Effect of Smoking?
  - Effect of Age?
  - Both?



Confounding: Concept

- **Lack of exchangeability**
  - Non-smokers are different from smokers in regards to a determinant (age) of CHD
- Existence of **backdoor pathway** in a causal diagram
  - Prevalence Ratio reflects the mixture of the effects of smoking and age

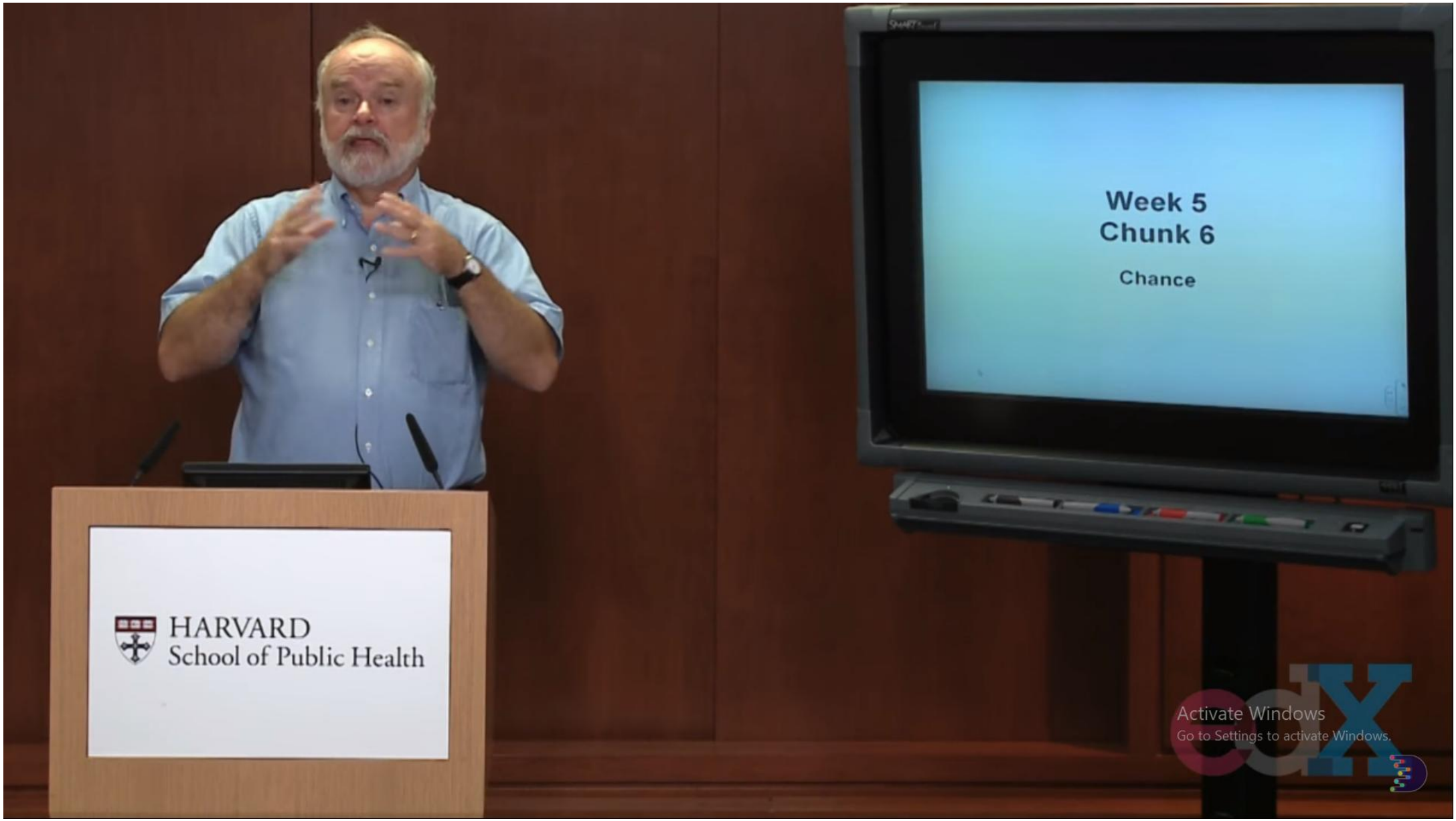

Smoking
Coronary
Heart Disease
Age

Confounding: Implied Definition

- Confounder is related to the exposure
  - Smokers are younger than non-smokers
- Confounder is a determinant of disease, independent of the exposure
  - Age is related to risk of developing CHD
- Confounder is not part of the causal pathway linking exposure to disease

Confounding: Implied Definition

- Confounder is related to the exposure
  - Smokers are younger than non-smokers
- Confounder is a determinant of disease, independent of the exposure
  - Age is related to risk of developing CHD
- Confounder is not part of the causal pathway linking exposure to disease



Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.82

Quantifying the Role of Chance:

- Test of Significance
  - Measure consistency of data with null hypothesis
  - H_0: P(CHD|smokers) = P(CHD|non-smokers)
  - H_0: True Prevalence Ratio = 1.0
- P-Value
  - Large p-values support H_0
  - Small p-values do not support H_0

Quantifying the Role of Chance:

- Confidence Interval
  - Range of estimates for true Prevalence Ratio supported by the data

Example: Prevalence of CHD among Smokers and Non-Smokers at 1956 exam

	CHD		Total	Prevalence of CHD
	Yes	No		
Smokers	86	2095	2181	86/2181 = 0.0394
Non-Smokers	108	2145	2253	108/2253 = 0.0479

Prevalence Ratio = PR = (86/2181) / (108/2253) = 0.8226
95% Confidence Interval (0.6235, 1.0852)
P-value = 0.17

U.S. National Health Surveys

- **National Center for Health Statistic (NCHS)**
  - Centers for Disease Control and Prevention (CDC)
  - http://www.cdc.gov/nchs/
- Schedule
  - Some ongoing annual data collection systems
  - Others conducted periodically
- Types
  - Data collected through personal interviews or examinations
  - Data collected from vital and medical records

NCHS Surveys

- Four major data collection programs
- **National Health and Nutrition Examination Survey (NHANES)**
  - Detailed survey of health and nutrition status of Americans
- **National Health Interview Survey (NHIS)**
  - Interviews of household members

NCHS Surveys

- **National Health Care Surveys**
  - Survey of health care providers and organizations
- **National Vital Statistics System (NVSS)**
  - Records information on births and deaths

NCHS Surveys

- Targeted Surveys
  - National Survey of Family Growth
  - State and Local Area Integrated Telephone Surveys
  - National Immunization Survey

National Health and Nutrition Examination Survey

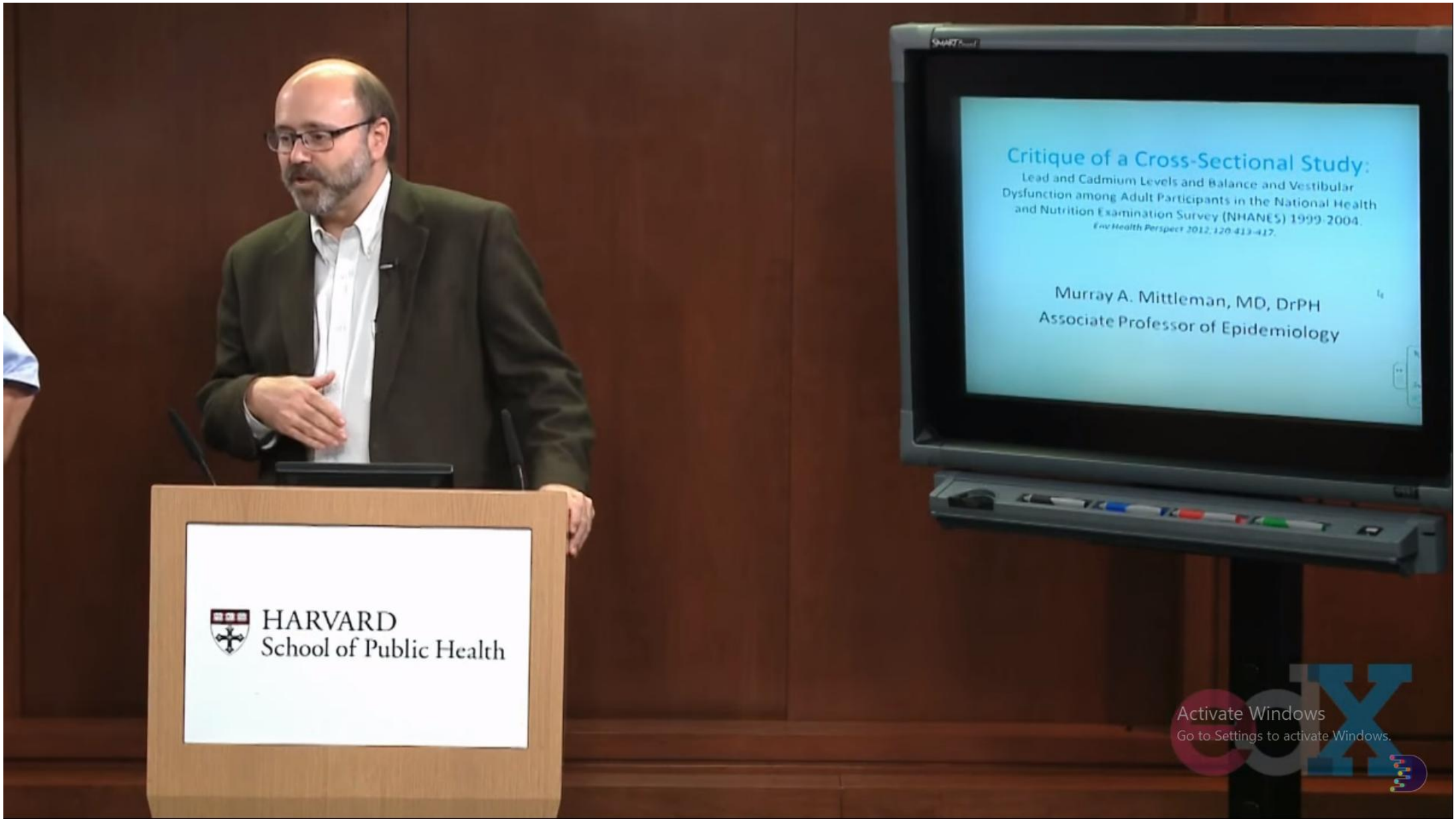
- http://www.cdc.gov/nchs/nhanes/about_nhanes.htm
  - Video history
  - Video tour of Mobile Examination Centers
- Assesses health and nutritional status of adults and children in the US
- National representative sample of 15 counties with 5000 people each year

National Health and Nutrition Examination Survey

- http://www.cdc.gov/nchs/nhanes/about_nhanes.htm
  - Video history
  - Video tour of Mobile Examination Centers
- Assesses health and nutritional status of adults and children in the US
- National representative sample of 15 counties with 5000 people each year

Behavioral Risk Factor Surveillance System (BRFSS)

- Established in 1984 by the Centers for Disease Control and Prevention (CDC)
- http://www.cdc.gov/brfss/
- State-based system of telephone health surveys
  - More than 350,000 adults are interviewed each year
  - Largest telephone health survey in the world


Critique of a Cross-Sectional Study:
Lead and Cadmium Levels and Balance and Vestibular Dysfunction among Adult Participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2004.
Env Health Perspect 2012;120:413-417.
Murray A. Mittleman, MD, DrPH
Associate Professor of Epidemiology
HARVARD
School of Public Health
Activate Windows
Go to Settings to activate Windows.

Critique of a Cross-Sectional Study:

Lead and Cadmium Levels and Balance and Vestibular Dysfunction among Adult Participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2004.

Env Health Perspect 2012;120:413-417.

Murray A. Mittleman, MD, DrPH

Associate Professor of Epidemiology

Cross-sectional Studies

- Cross-sectional studies include data on study subjects at a single point in *time*.

- In epidemiologic studies, *time* can be defined on a variety of scales:
  - Calendar time
  - Age
  - Time of a life event
  - Enrollment in a study
  - ...

Cross-sectional Studies

- In cross-sectional studies information on exposures and outcomes are measured at the same point in time.
- Prevalence is the measure of disease frequency that can be measured in cross-sectional studies; Likewise, prevalence of exposure or the distribution of exposure(s) are measured at a single time point.
- The prevalence (or distribution) of exposures and outcomes can be compared in cross-sectional studies.

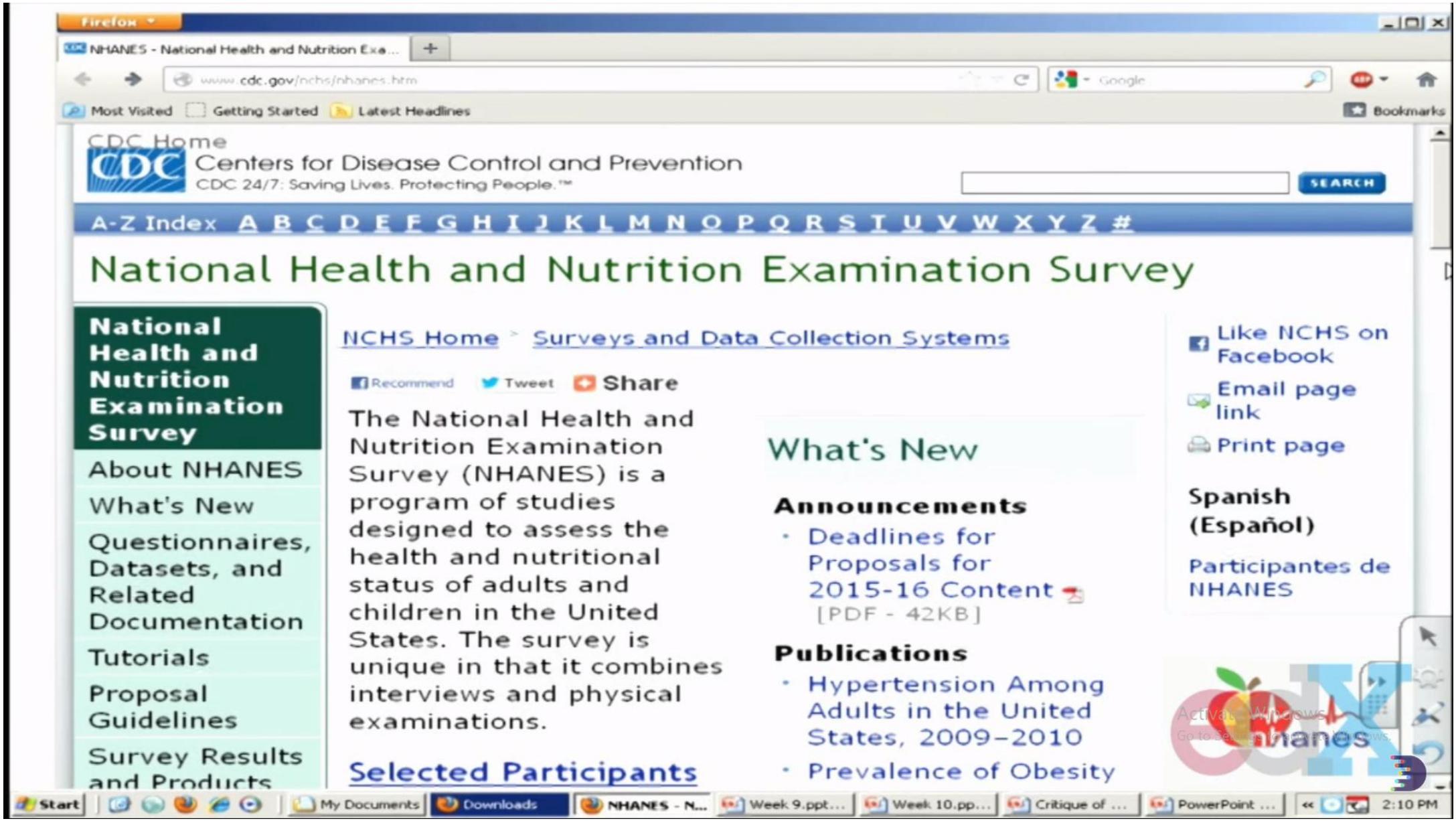
Cross-sectional Studies:
Limitations

- Because exposures and outcomes are measured simultaneously, it is not always possible to know the order of events; this limits the utility of cross-sectional studies in identifying cause-effect relationships.

- Another limitation of cross-sectional studies is that they will over-represent individuals with a longer duration of disease.

- An exposure that is unrelated to the incidence of disease, but increases the duration of disease (say by improving survival), will be associated with a higher prevalence of disease in a cross-sectional study.

http://www.cdc.gov/nchs/nhanes.htm


Firefox
NHANES - National Health and Nutrition Exa...
www.cdc.gov/nchs/nhanes.htm
Most Visited
Getting Started
Latest Headlines
Bookmarks
CDC Home
Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™
SEARCH
A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #
National Health and Nutrition Examination Survey
National Health and Nutrition Examination Survey
About NHANES
What's New
Questionnaires, Datasets, and Related Documentation
Tutorials
Proposal Guidelines
Survey Results and Products
NCHS Home > Surveys and Data Collection Systems
Recommend
Tweet
Share
The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations.
Selected Participants
What's New
Announcements
Deadlines for Proposals for 2015-16 Content [PDF - 42KB]
Publications
Hypertension Among Adults in the United States, 2009–2010
Prevalence of Obesity
Like NCHS on Facebook
Email page link
Print page
Spanish (Español)
Participantes de NHANES
Start
My Documents
Downloads
NHANES - N...
Week 9.ppt...
Week 10.pp...
Critique of ...
PowerPoint ...
2:10 PM

Lead and Cadmium Levels and Balance and Vestibular Dysfunction among Adult Participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2004.

Env Health Perspect 2012;120:413-417.

- Prior studies have indicated that exposure to heavy metals including lead and cadmium is associated with adverse neurobehavioral outcomes and hearing loss, but little is known about the relationship to balance and vestibular function.

- In this study, the authors used data from NHANES to evaluate the cross-sectional relationship between lead and cadmium levels and balance.

- The Romberg test was used to assess balance: http://www.youtube.com/watch?v=wnJ-8u8bEfU

Questions to be Considered

1. How was the study population selected?
2. What was the time frame in assessing the relationship between exposures and outcomes?
3. What was/were the exposure(s) of interest and how were they measured?
4. What was/were the outcome(s) of interest and how was they measured?
5. What was the main result of the study?

Questions to be Considered

6. Did the authors consider the possibility that the observed result may have been influenced by confounding? If so, what were the potential confounders considered?

7. What analytical methods did the authors use to take account of the potential confounding?

8. Did the authors assess the possibility that the observed associations were due to chance?

9. Did the authors evaluate whether the association between the heavy metals and the outcome varied across subgroups of participants (was there evidence of effect modification)?

Questions to be Considered

10. On a scale of 1 to 10, what is your degree of agreement with the assertion "Exposure to lead and/or cadmium causes an increased risk of developing problems with balance and vestibular disturbance"? Base your answer on your understanding of sound epidemiologic principles.

Critique of a Cross-Sectional Study:

Lead and Cadmium Levels and Balance and Vestibular Dysfunction among Adult Participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2004.

Env Health Perspect 2012;120:413-417.

Murray A. Mittleman, MD, DrPH

Associate Professor of Epidemiology