LECTURE: 3

Measures of Association

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EPIDEMIOLOGIC REASONING

1. **Suspicion that a factor (exposure) may influence occurrence of disease.**

   - **Observations in clinical practice**
   - **Examination of disease patterns**
     - **Do subpopulations have higher or lower rates?**
     - **Are disease rates increased in the presence of certain factors?**
   - **Observations in laboratory research**
   - **Theoretical speculation**

EPIDEMIOLOGIC REASONING

2. Formulation of specific hypotheses

- Based on suspicions concerning influence of a particular factor on disease occurrence

3. Conduct analytic studies

- Hypotheses are tested to determine if statistical associations between factors (exposures) and disease exist
- Study population is assembled from individuals with disease or outcome of interest and an appropriate comparison group

EPIDEMIOLOGIC REASONING

4. **Assess validity of association**

- **Does the observed association really exist?**
  - **Is the association valid?**
  - **Are there alternative explanations for the association?**
    - **Chance**
    - **Bias**
    - **Confounding**

EPIDEMIOLOGIC REASONING

5. Make a judgement of whether a cause-effect relation between factor (exposure) and disease exists

- **What is the magnitude of the association?**
- **Are the findings consistent with previous studies (or conflicting)?**
- **Are the findings biologically credible?**
- **Can underlying biological mechanisms that support the association be identified?**

EPIDEMIOLOGIC MEASURES

- **Measures of disease frequency - measures disease risk or burden in a population**
  - **Prevalence**
  - **Incidence**

EPIDEMIOLOGIC MEASURES

- **Measures of association**
  - **Calculations used to measure disease frequency relative to other factors**
  - **Indications of how more or less likely one is to develop disease as compared to another**

EPIDEMIOLOGIC MEASURES OF ASSOCIATION

- **Absolute**
  - **Risk difference**

    exposed - unexposed

- **Relative**
  - **Risk ratios**
  - **Odds ratios**

    exposed / unexposed

EPIDEMIOLOGIC MEASURES OF ASSOCIATION

- **The relative risk of myocardial infarction in men compared with women is : 5**

$$\text{Risk ratio} = \frac{\text{Risk}_{\text{men}}}{\text{Risk}_{\text{women}}} = \frac{\text{5 cases/1000 PY}}{\text{1 case/1000 PY}} = 5$$

- **The absolute risk difference between men and women is : 4 cases/1000 PY**

5 cases/1000 PY - 1 case/1000 PY = 4 cases/1000 PY

EPIDEMIOLOGIC ASSOCIATION

- **Statistical relationship between two or more events, characteristics, or other variables**

- **Statistical relationship between exposure and disease**

- **Association is not causation!**

RISK FACTOR

- **A factor (exposure) found to be associated with a health condition**
- **an attribute or exposure that increases the probability of occurrence of disease**
  - **behaviour**
  - **genetic**
  - **environmental**
  - **social**

-- time

-- person

-- place

EPIDEMIOLOGIC MEASURES OF ASSOCIATION

- **Relative risk**
- **Odds ratio**
- **Attributable risk/population attributable risk percent**
- **Standardized mortality ratios**

2 X 2 TABLES IN EPIDEMIOLOGY

Used to summarize frequencies of disease and exposure and used for calculation of association

	Disease		
Exposure	Yes	No	Total
Yes	*a*	*b*	*a* + *b*
No	*c*	*d*	*c* + *d*
Total	*a* + *c*	*b* + *c*	*a* + *b* + *c* + *d*

2 X 2 TABLES: CONTENTS OF CELLS

a = number of individuals who are exposed and have the disease

b = number who are exposed and do not have the disease

c = number who are not exposed and have the disease

d = number who are both non-exposed and non-diseased

2 X 2 TABLES IN EPIDEMIOLOGY

Used to summarize frequencies of disease and exposure and used for calculation of association

	Disease		
Exposure	Yes	No	Total
Yes (exposed)	*a*	*b*	*total # exposed*
No (unexposed)	*c*	*d*	*total # unexposed*
Total	*total # with disease*	*total # with no disease*	*Total Population*

RELATIVE RISK

- The ratio of the risk of disease in persons exposed compared to the risk in those unexposed
- Often, a measure of association between incidence of disease and exposure of interest

$$RR = \frac{\text{Incidence rate of disease in exposed}}{\text{Incidence rate of disease in unexposed}}$$

	Disease		
Exposure	Yes	No	Total
Yes	*a*	*b*	*a* + *b*
No	*c*	*d*	*c* + *d*
Total	*a* + *c*	*b* + *c*	*a* + *b* + *c* + *d*

$$\text{Relative Risk} = \frac{a / (a + b)}{c / (c + d)}$$

RELATIVE RISK

	Develop CHD	Do Not Develop CHD	Totals	Incidence per 1000/yr
Smokers	84	2916	3000	28.0
Non-smokers	87	4913	5000	17.4

Incidence in smokers = 84/3000 = 28.0
Incidence in non-smokers = 87/5000 = 17.4
Relative risk = 28.0/17.4 = 1.61

INTERPRETATION OF RELATIVE RISK

- 1 = No association between exposure and disease
  - incidence rates are identical between groups
- > 1 = Positive association
  - exposed group has higher incidence than non-exposed group
- < 1 = Negative association or protective effect
  - non-exposed group has higher incidence
  - example: .5 = half as likely to experience disease

- A relative risk of 1.0 or greater indicates an increased risk
- A relative risk less than 1.0 indicates a decreased risk

AT TIMES, EPIDEMIOLOGISTS WILL CHOOSE TO EXPRESS DISEASE FREQUENCY IN TERMS OF ODDS

WHAT ARE ODDS?

MEASURES OF DISEASE ASSOCIATION

The chance of something happening can be expressed as a risk and/or as an odds:

Risk = the chances of something happening

the chances of *all* things happening

Odds = the chances of something happening

the chances of it *not* happening

EXAMPLE: IF I CHOOSE A STUDENT RANDOMLY FROM THIS CLASS, HOW LIKELY IS IT THAT I WILL CHOOSE YOU?

RISK (PROBABILITY) = 1/9 = .111

ODDS = 1/8 = .125

MEASURES OF DISEASE ASSOCIATION

<u>Example:</u> Among 100 people at baseline, 20 develop influenza over a year.

The risk is 1 in 5 (i.e. 20 among 100) = .2 The odds is 1 to 4 (i.e. 20 compared to 80) = .25

ODDS

- **What are odds?**
- **Let p = the probability of an event**
- **1-p = the probability that the event does not occur**
- **Odds of the event = p/1-p**
  - **If the probability of an event is 0.7, the the odds of winning are 0.7/0.3 = 2.33**

ODDS RATIO

- **The ratio of the odds of a condition in the exposed compared with the odds of the condition in the unexposed**

- **Usually applied to prevalence studies rather than incidence studies**

$$\text{OR} = \frac{\text{odds of disease in exposed}}{\text{odds of disease in unexposed}}$$

Exposure	Disease: Yes	Disease: No	Total
Yes	*a*	*b*	*a* + *b*
No	*c*	*d*	*c* + *d*
Total	*a* + *c*	*b* + *c*	*a* + *b* + *c* + *d*

$$\text{Odds Ratio} = \frac{[a / (a + b)] / [1 - (a/(a+b))]}{[c / (c + d)] / [1 - (c/(c+d))]}$$

Odds Ratio

Exposure	Disease: Yes	Disease: No	Total
Yes	a	b	$a + b$
No	c	d	$c + d$
Total	$a + c$	$b + c$	$a + b + c + d$

$$\text{Odds Ratio} = \frac{[\,a / b\,]}{[\,c / d\,]} = \frac{[\,ad\,]}{[\,bc\,]}$$

Based on the Odds Ratio formula, what is the Odds Ratio for each disease status in this famous smoking study?

Smoking and Carcinoma of the Lung			
Disease Status	**# of smokers**	**# of nonsmokers**	
Males Lung cancer	**647**	**2**	
Males Controls	**622**	**27**	
Females Lung cancer	**41**	**19**	
Females Controls	**28**	**32**	

Doll R. Bradford, Hill A. Smoking and carcinoma of the lung: preliminary report. British Medical Journal 1950, 2: 739-748.

DIFFERENCE MEASURES

- **Attributable risk**

  No. of cases among the exposed that could be eliminated if the exposure were removed

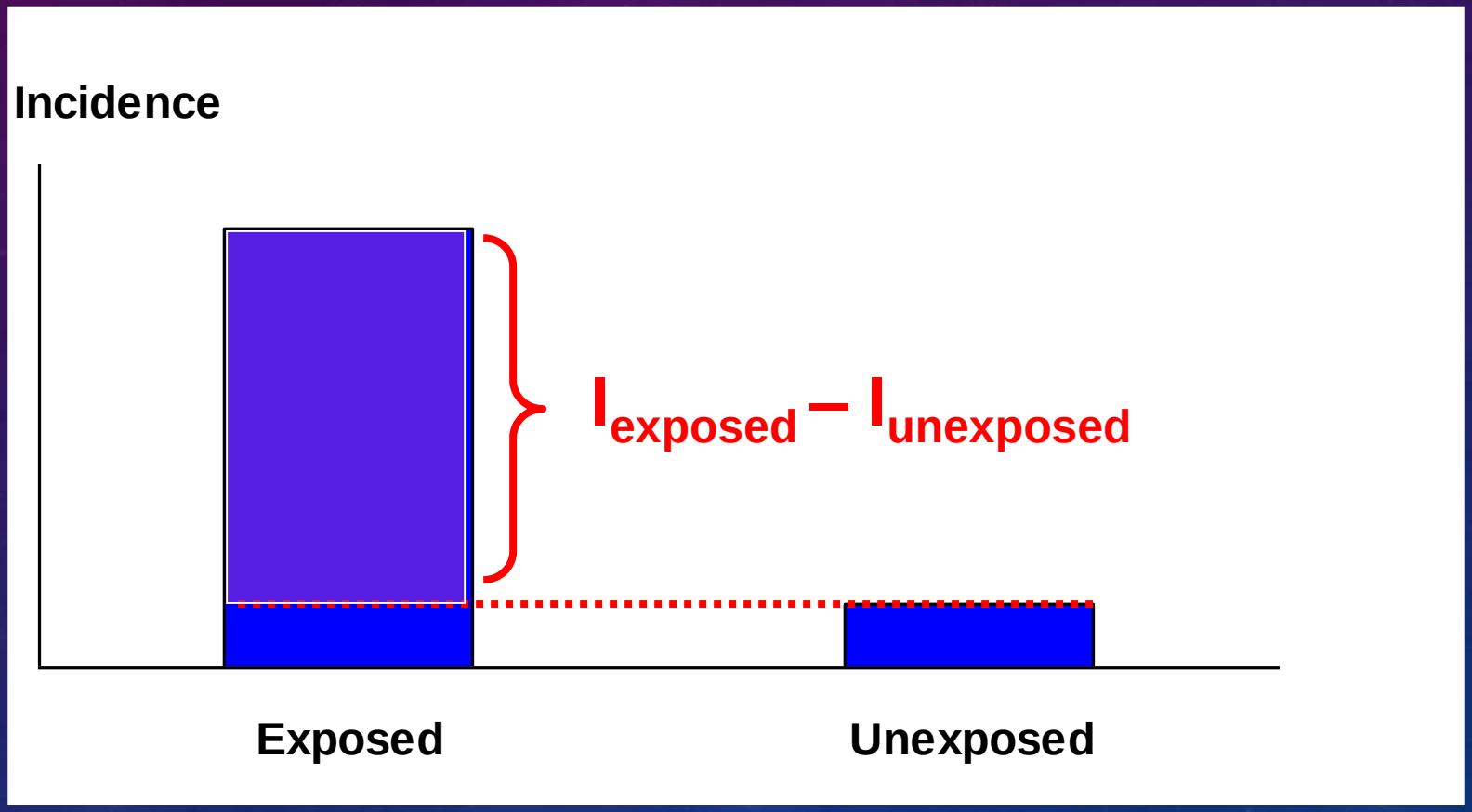
  = Incidence in exposed - Incidence in unexposed

- **Population attributable risk percent**

  Proportion of disease in the study population that could be eliminated if exposure were removed

$$= \frac{\text{Incidence in total population - Incidence in unexposed}}{\text{incidence in total population}}$$

ATTRIBUTABLE RISK



I = Incidence

ATTRIBUTABLE RISK

- **Rate of disease in the population that can be directly attributed to the exposure**

- **equals incidence rate in exposed minus incidence rate in the unexposed**

$$= \quad A / (A + B) \quad - \quad C / (C + D)$$

AR: FAST DRIVING AND AUTOMOBILE DEATHS

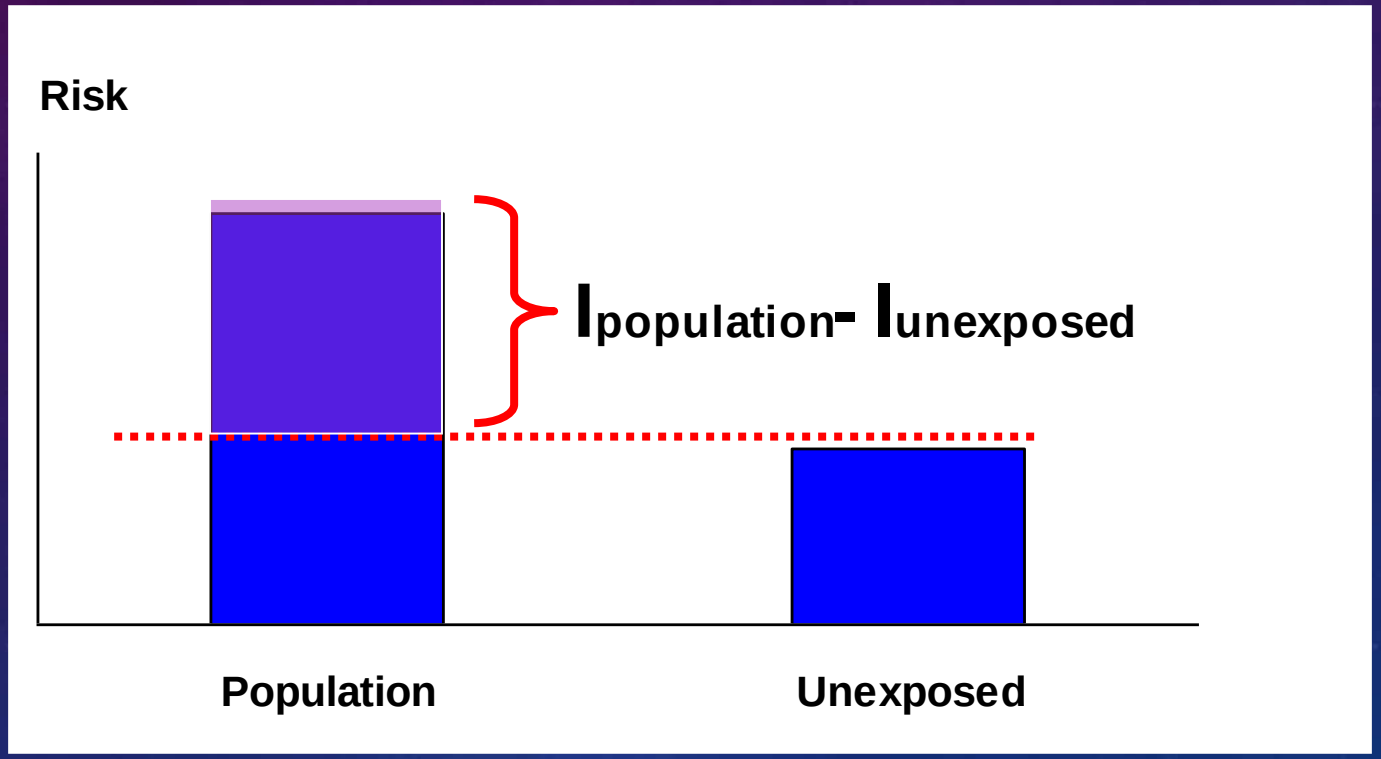
	Dead	Not dead		Risk	RD
Fast	100	1900	2000	0.05	
					0.04
Slow	80	7920	8000	0.01	
	180	9820	10000		

POPULATION ATTRIBUTABLE RISK (PAR)

- **Excess risk of disease in total population attributable to exposure**
- **Reduction in risk which would be achieved if population entirely unexposed**
- **Helps determining which exposures relevant to public health in community**

$$PAR = I_{population} - I_{unexposed}$$

POPULATION ATTRIBUTABLE RISK



POPULATION ATTRIBUTABLE RISK PERCENT (PAR%)

- **PAR expressed as a percentage of total risk in population**

$$PAR\% = \frac{I_{population} - I_{unexposed}}{I_{population}} \times 100$$

PAR: FAST DRIVING

	Dead	Not dead		Risk
Fast	100	1900	2000	0.050
Slow	80	7920	8000	0.010
	180	9820	10000	0.018

$$PAR = 0.018 - 0.010 = 0.008$$

$$PAR\% = \frac{0.018 - 0.010}{0.018} \times 100 = 44\%$$

CONCLUDE

- **44% of driving-related deaths in population were presumably due to fast driving**