

Introduction to Clinical Epidemiology

Kristen A. Stafford, MPH, PhD
Associate Professor
Department of Epidemiology and Public Health

Special thanks to Dr. Mona Baumgarten for the use of her slides

What is Epidemiology?

*Epidemiology is the **study** of the **distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems***

Dictionary of epidemiology. 4th ed. 2001

What is Clinical Epidemiology?

Clinical Epidemiology is the application of principles of epidemiology to clinical medicine. While classical epidemiology is the study of the distribution and determinants of diseases in populations, clinical epidemiology is the application of the principles and methods of epidemiology to conduct, appraise or apply clinical research studies focusing on prevention, diagnosis, prognosis, and treatment of disease. Clinical Epidemiology is the basic science of Evidence-based Medicine.

Outline

- Measures of disease occurrence
- Measures of association

“We owe all the great advances in knowledge to those who endeavor to find out how much there is of anything.”

- James Maxwell, physicist (1831-1879)

“One’s knowledge of science begins when he can measure what he is speaking about and express it in numbers”

- Lord Kelvin, mathematician and physicist (1824 – 1907)

Measures of Disease Occurrence

- Prevalence
- Cumulative incidence
- Incidence rate

The occurrence of disease can be measured using rates or proportions

Rates tell us how “fast” a disease is occurring in a population

Proportions tell us what fraction of the population is affected

**So you mean to tell
me...**

**Epidemiologist don't know how
many cases there really are?**

quickmeme.com

Prevalence

Number of diseased individuals in population at a specified time

Total population at same specified time

Prevalence

- Is a proportion and therefore has no units
- Ranges from 0 to 1
- Numerator includes both new and ongoing cases of disease
- Represents a cross-sectional “snapshot” of the population

Prevalence

- Does not estimate risk of disease
- Is not useful for studies of risk factors
- Estimates burden of disease
- Is useful in planning of health services

Example

- 10,600 men age 50-59 were examined in 2002 as part of a large heart health study
- 842 men were found to have coronary heart disease
- Prevalence of CHD = $0.079 \approx 8\%$

Cumulative Incidence

Number of new cases of disease during specified time period

Number of individuals at risk of disease at start of time period

At Risk

Individuals are at risk of disease if they:

- Do not have the disease at the start of the follow-up period
- Are capable of developing the disease
 - Have the organ of interest

Cumulative Incidence

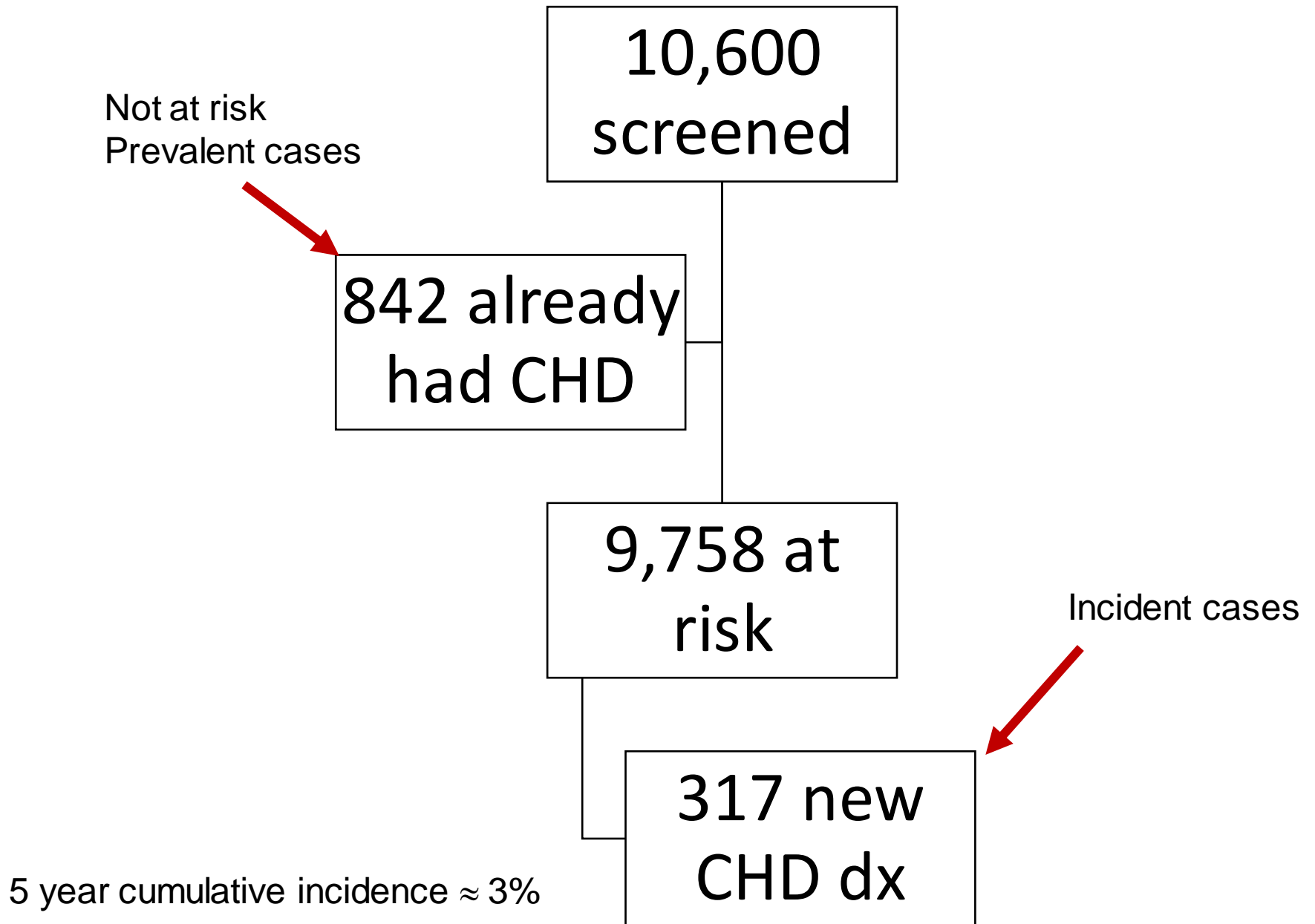
- Represents the probability that an individual will develop the disease over a specified time period
- Is a measure of disease risk
- Is a proportion and therefore has no units
- Ranges from 0 to 1

Cumulative Incidence

- Based on assumption that all at-risk individuals are followed until they develop the disease or the observation period ends
- Does not reflect effect of differing lengths of follow-up
- *Syn.:* Incidence proportion

Example

- 10,600 men age 50-59 were examined in 2002 as part of a large heart health study
- 842 men were found to have coronary heart disease
- During the period 2002 to 2007, 317 men developed CHD
- Five-year cumulative incidence of CHD = ?



Incidence Rate

Number of new cases of disease during specified time period

Person-time of observation among people at risk during same time period

Incidence Rate

- Average rate at which a disease develops in a population over a specified time period
- Is a true rate and has the units of time
- Ranges from 0 to infinity
- Accounts for differing lengths of follow-up
- *Syn.:* Incidence density, hazard rate

Person-Time

Sum, over all individuals, of time at risk until the event of interest, loss to follow-up, or the end of the study

Example

<u>Subject</u>	<u>Years of Follow-up</u>	<u>Got Disease</u>
A	2	N
B	2	Y
C	1	N
D	1	N
E	1	Y
F	3	N
G	1	Y
H	1	Y
I	1	N
J	2	Y

Example

$$\begin{aligned}\text{Incidence rate} &= \frac{5 \text{ cases of disease}}{15 \text{ person-years}} \\ &= 0.33 \text{ cases per person-year} \\ &= 33 \text{ cases per 100 person-years}\end{aligned}$$

Challenge: person-years is epidemiologic jargon

33 new cases per 100 persons per year

Example

Interpretation:

New cases of the disease appear at the rate of

- 0.33 cases per person per year *or*
- 33 cases per 100 persons per year *or*
- 33 cases per 100 person-years

Incidence and Prevalence

- Change in incidence reflects change in etiologic factors (risk factors or protective factors)
- Change in prevalence reflects change in incidence or duration or both

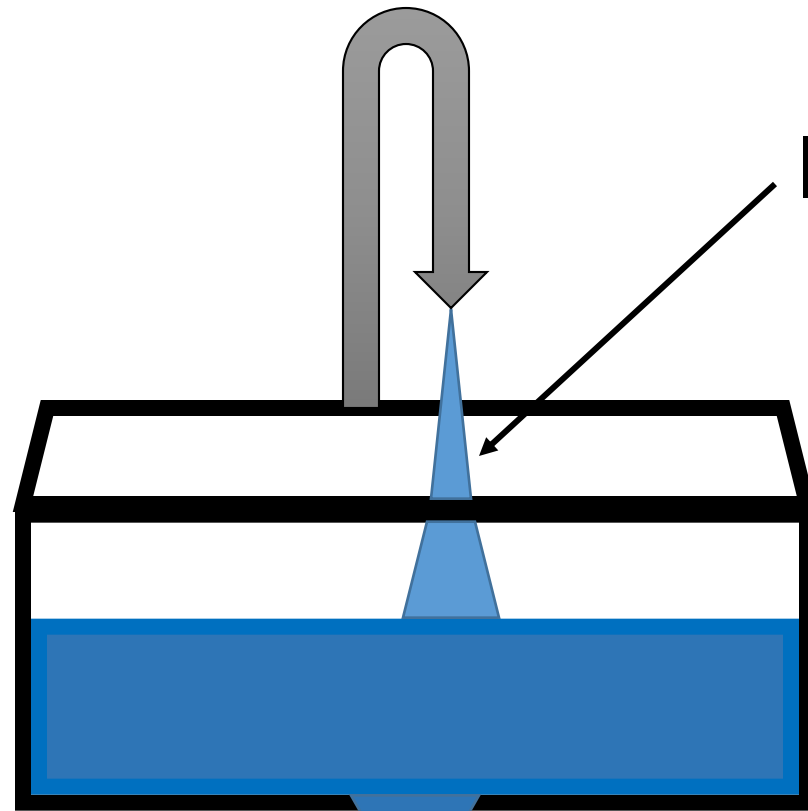
Incidence and Prevalence

Prevalence \approx
incidence rate \times average duration of disease

- Assumes incidence, prevalence, duration are stable over time
- Assumes prevalence $< 10\%$

Prevalence

Not supposed to be
a fish tank



Incidence

Death

Recovery

Measures of Association

- Relative Risk (RR)
- Odds Ratio (OR)

Ways to express the results of an RCT

- Relative Risk Reduction (RRR)
- Absolute Risk Reduction (ARR)
- Number Needed to Treat (NNT)
- Number Needed to Harm (NNH)



Oh no -
not again!
When somebody
down there fools
people with biased
relative risks, an
angel loses its
wings

HEAVEN'S DEPARTMENT OF EPIDEMIOLOGY

Pastier

Statistically-funny.blogspot.com

Relative Risk

- Ratio of disease incidence among exposed individuals to disease incidence among unexposed individuals
- Useful in research on disease etiology
- Quantifies magnitude of the association between an exposure and a disease
- *Syn.:* Risk ratio

Relative Risk

		CHD		
		Yes	No	
Smoking	Yes	a	b	a+b
	No	c	d	c+d
		a+c	b+d	

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

Relative Risk

- Varies from 0 to infinity
- When $RR=1$, there is no association between exposure and disease
- When $RR > 1$, the exposure is a risk factor for the disease, i.e., increases the risk of disease
- When $RR < 1$, the exposure is a protective factor for the disease, i.e., decreases the risk of disease

Example

		CHD		
		Yes	No	
Smoking	Yes	100	900	1,000
	No	20	980	1,000
		120	1,880	

Relative risk = ?

Relative Risk

- Can be calculated from cohort studies
 - Including RCTs

Odds

- Ratio of the probability that an event will occur to the probability that the event will not occur
- Risk = ratio of part to the whole
- Odds = ratio of part to the remainder
- Odds always higher than risk

Example

Rolling a die:

- Risk of rolling a 3 = $1/6 = 16.7\%$
- Odds of rolling a 3 = $1/5 = 20\%$

Example

- 20 smokers develop bronchitis while 30 do not
- Odds of bronchitis = ? $20/30 = 0.67$
- Probability of bronchitis = ? $20/50 = 0.4$

Odds Ratio

- Ratio of the odds of exposure among diseased to the odds of exposure among nondiseased

Odds Ratio

		CHD	
		Yes	No
Smoking	Yes	a	b
	No	c	d

$$\text{Odds ratio} = \frac{a/c}{b/d} = \frac{ad}{bc}$$

Odds Ratio

- Varies from 0 to infinity
- When $OR=1$, there is no association between exposure and disease
- When $OR > 1$, the exposure is a risk factor for the disease, i.e., increases the odds of disease
- When $OR < 1$, the exposure is a protective factor for the disease, i.e., decreases the odds of disease

Odds Ratio

- Only measure of association available from case-control studies
- Good estimate of the relative risk when the incidence is low ($< 5\%$ in the general population)

Example

		CHD	
		Yes	No
Smoking	Yes	25	10
	No	75	90
		100	100

Odds ratio = ?

Odds Ratio

- Only measure of association you can get from a case-control study
- Commonly presented in the literature from cohort studies with a dichotomous outcome
 - Because that's what logistic regression produces
 - There are ways around this with modern statistical packages

Expressing the results of a RCT

- Relative Risk Reduction
- Absolute Risk Reduction
- Number Needed to Treat
- Number Needed to Harm

Relative Risk Reduction

- By how much does the treatment reduce the risk of a bad outcome **RELATIVE** to the control group?

Outcome	Control Event Rate (CER)	Experimental Event Rate (EER)	Relative Risk (RR)	Relative Risk Reduction (RRR)
90-day mortality	$138/239 = 0.58$	$122/238 = 0.54$	$EER/CER = 0.54/0.58 = 0.93$	$1 - RR = 1.0 - 0.93 = 0.07$

Absolute Risk Reduction

- Also called the risk difference. How many bad outcomes does the treatment prevent?

Outcome	Control Event Rate (CER)	Experimental Event Rate (EER)	Relative Risk (RR)	Relative Risk Reduction (RRR)	Absolute Risk Reduction (ARR)
90-day mortality	138/239 = 0.58	122/238 = 0.54	EER/CER 0.54/0.58 = 0.93	1 - RR 1.0 - 0.93 = 0.07	CER - EER 0.58 - 0.54 = 0.04

Number Needed to Treat

- How many people do you need to treat for one person to benefit

Outcome	Control Event Rate (CER)	Experimental Event Rate (EER)	Relative Risk (RR)	Relative Risk Reduction (RRR)	Absolute Risk Reduction (ARR)	Number needed to Treat
90-day mortality	$138/239 = 0.58$	$122/238 = 0.54$	$EER/CER = 0.54/0.58 = 0.93$	$1 - RR = 1.0 - 0.93 = 0.07$	$CER - EER = 0.58 - 0.54 = 0.04$	$1/ARR = 1/0.04 = 25$

Number Needed to Harm

- How many people need to be treated for one person to have an adverse event?
- You calculate one for each specific adverse event
- $1/\text{absolute risk increase}$
- $1/(I_t - I_c)$ where t is treatment and c is control

Problems with NNH

- Subject to considerable error
- Should be presented with 95% confidence intervals for proper interpretation
- Does not take quality of life into account
- Limited value to patients
- Can help a practitioners estimate potential impact of a drug or intervention

Other cool measures we don't have time to discuss

- Hazard Ratios
- Attributable risks and fractions

