Study types & Measures of association

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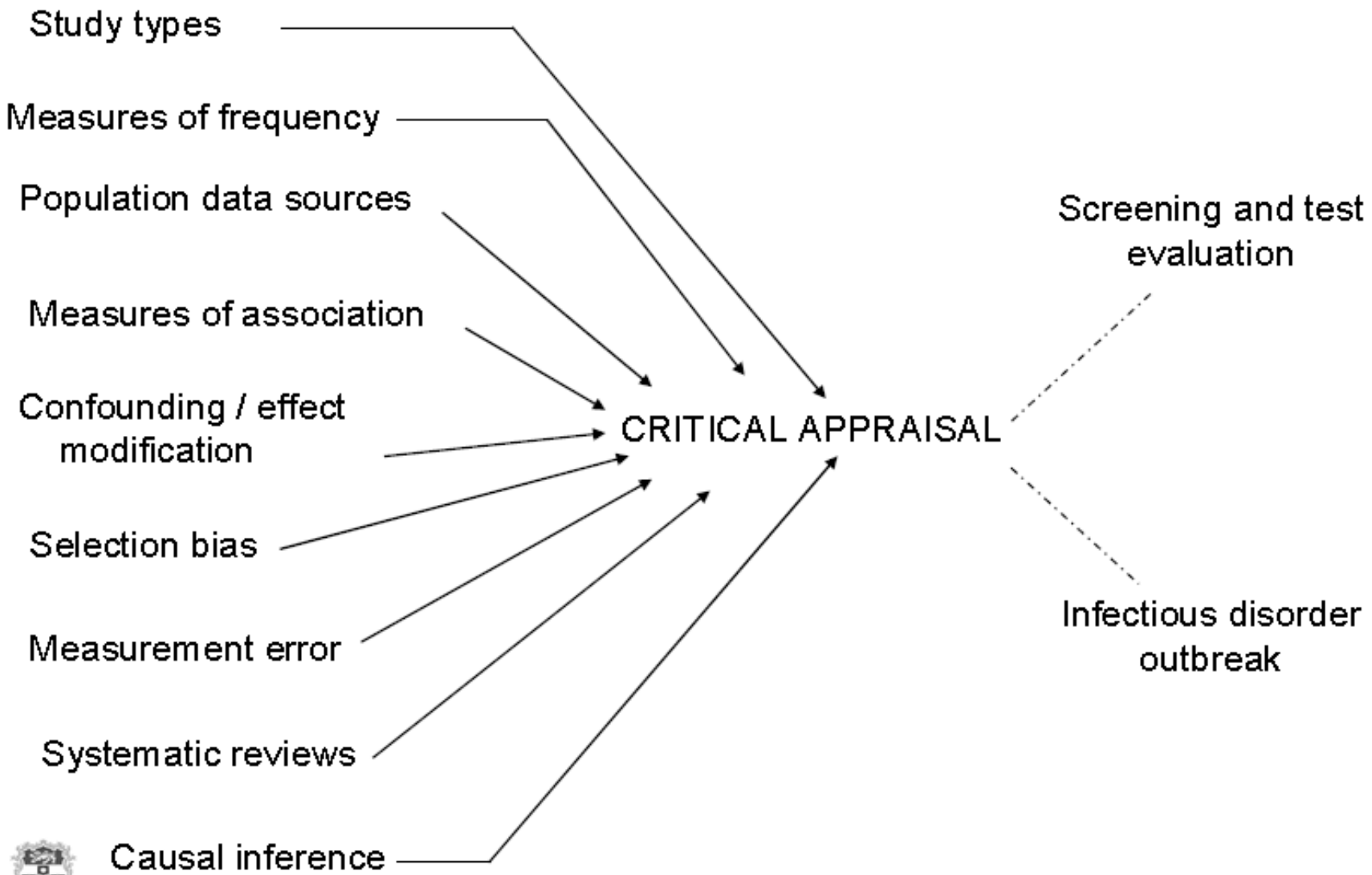
Epidemiological methods map



Measures of association

How big, or how strong is the association between the study factor (exposure) and the outcome factor (disease) ?

- relative risk
- risk difference
- odds ratio
- attributable fraction
- population attributable fraction

STUDY TYPES

Asking questions

1. Australian government needs to provide figures to WHO on the incidence of HIV in Australia	2. Anna's mum is worried about Anna using her mobile phone so much – she's heard they're not safe
3. Mrs Smith's GP is wondering whether acupuncture might help Mrs Smith's shoulder pain	4. Medical Services Advisory Board is considering whether to offer a Medicare rebate for Magnetic Resonance Imaging for investigation of joint problems

What is the research question?

What is the main issue ?

- How common is it? [Frequency]
- What caused it? [Aetiology]
- Does it work? [Intervention]
- How accurate is this test? [Diagnosis or Test evaluation]

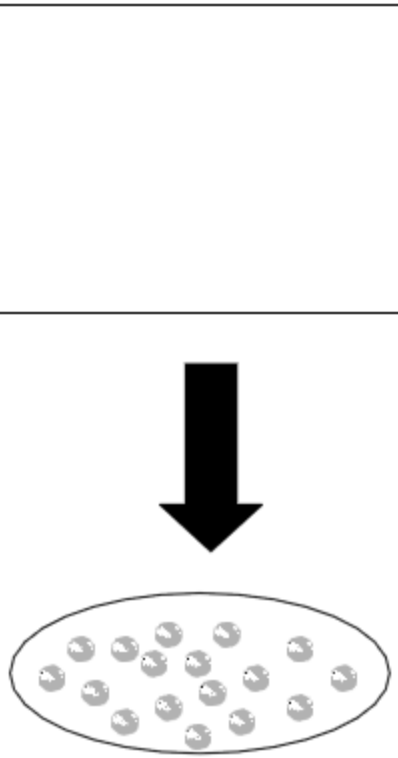
What is the research question?

What is the main issue ?

- How common is it? [Frequency]….HIV
- What caused it? [Aetiology]….Mobile phone
- Does it work? [Intervention]….Acupuncture
- How accurate is this test? [Diagnosis or Test evaluation]….Magnetic resonance imaging

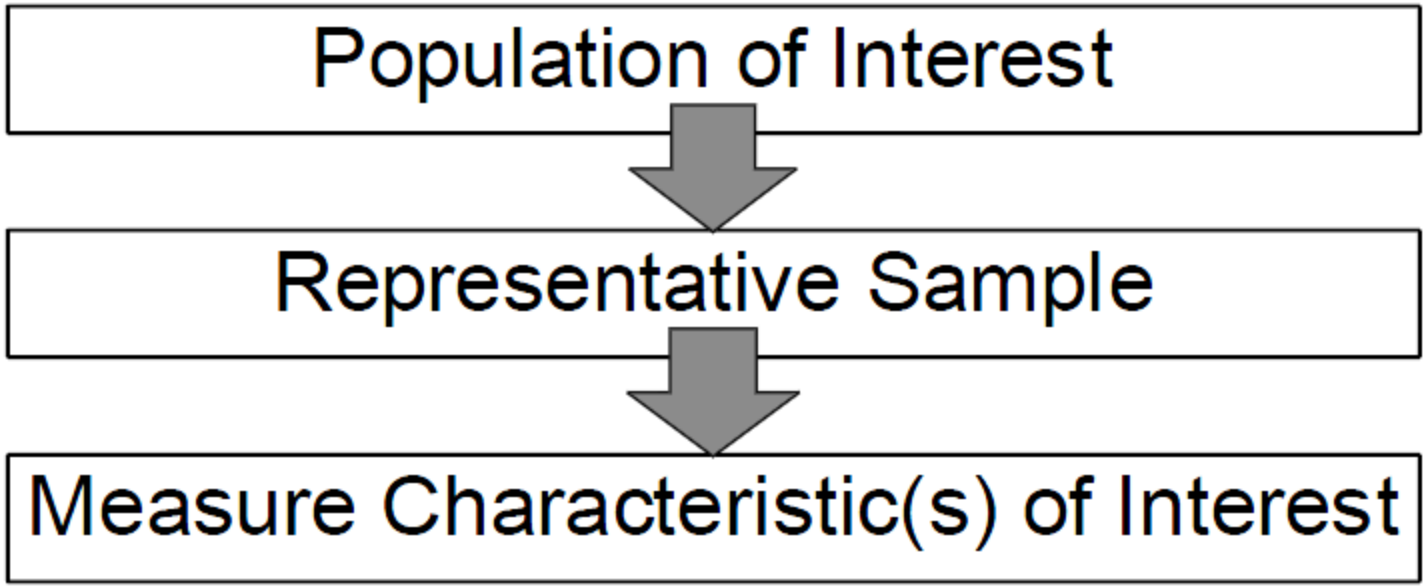
Question/issue	Study designs
Intervention	Randomised controlled trial Cohort study (non-randomised trial) Case-control study Case series Ecological study Before and after study
Aetiology	Randomised controlled trial Cohort study Case-control study Case series Ecological study Before and after study
Diagnosis (one test against reference standard)	Cross-sectional analysis
Diagnosis (comparison of two tests)	Randomized controlled trial Cohort study Case-control study
Frequency of occurrence	Descriptive - cross sectional (eg survey) - cohort

How frequently does it occur?



Descriptive study: cross-sectional study / survey

Descriptive Studies



Descriptive Studies

Used for answering questions about frequency

Usually cross-sectional studies

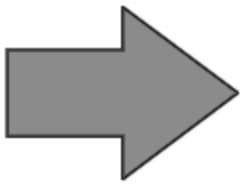
May be cohort studies

Examples

- Prevalence survey of TB
- Prevalence of domestic violence
- Incidence of playground injury in a school population over one year

Causal relationships

???

Study factor (exposure)  Outcome factor

Analytic studies

Analytic studies are used to work out the answers to questions about cause and effect:

- "What caused this?"
- "Does this intervention work?"
- "Is this test better than another test?".

Analytic studies allow you to analyse the relationship between two factors:

- exposure and outcome
- treatment and outcome
- test and disease

Analytic studies

Used for answering questions of aetiology or the effect of intervention (causality):

- Randomised controlled trial
- Cohort study
- Case control study
- Cross sectional analytic study
- Before and after study
- Ecological study

Analytic studies - RCT

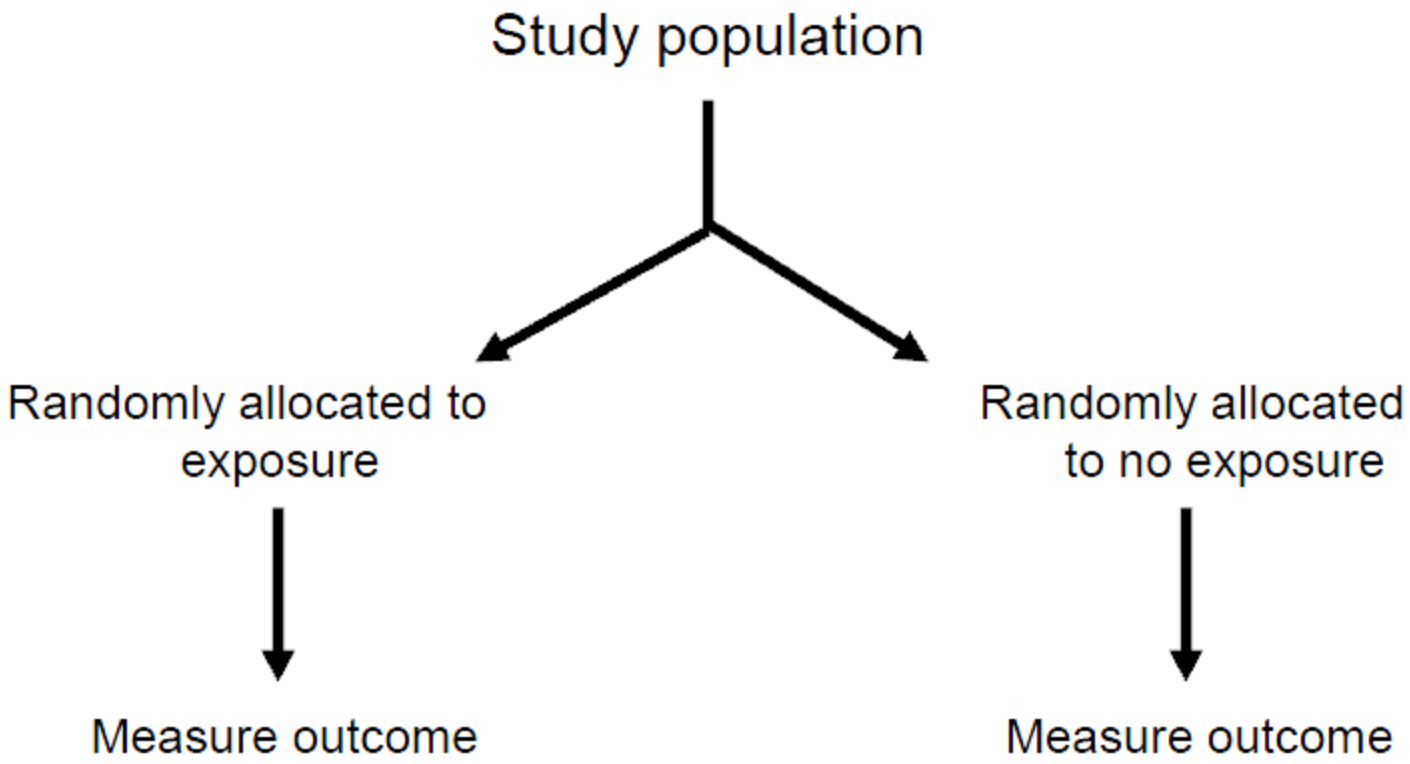
Chance alone determines exposure to study factor

Outcome is measured later

MAJOR STRENGTH:

There is no difference between the exposed and unexposed group EXCEPT for the study factor

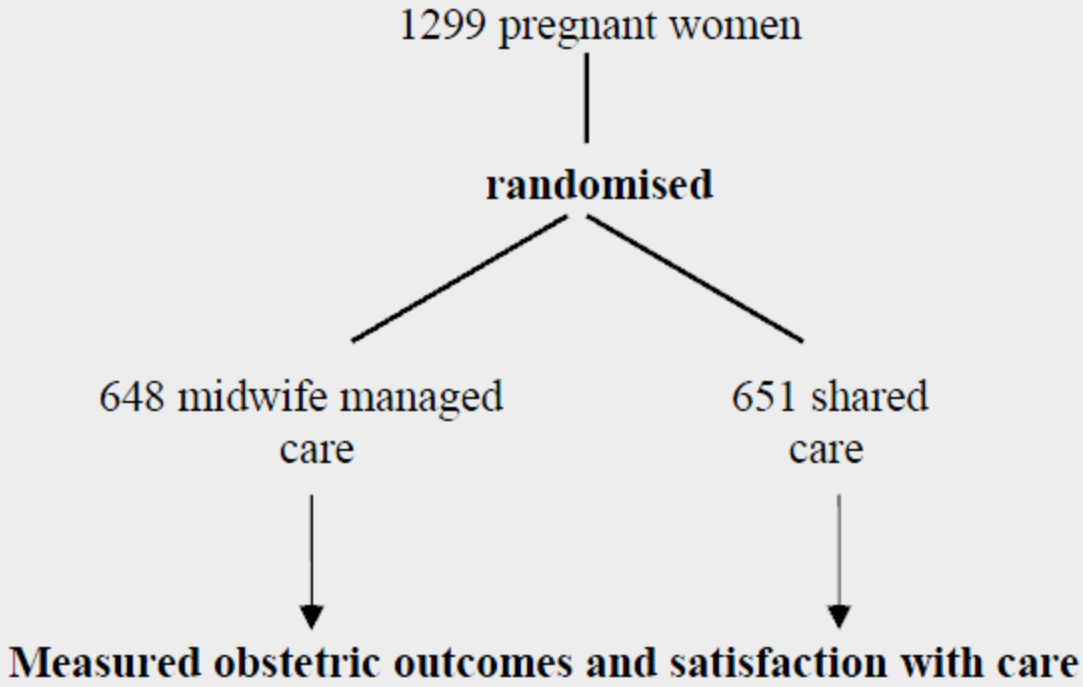
Randomised controlled trial



Analytic studies - RCT

Randomised control trial of efficacy of midwife-managed care

Lancet 1996;348:213-218



Characteristic	Shared care (n=635)	Midwife care (n=643)
Mean age	25.5 yrs	25.8 yrs
Current smokers	38.6%	37.9%
Married	54.8%	53.6%
1st baby	53.5%	54.7%
Subsequent baby	46.5%	45.3%
Star sign = Gemini	**8.1%**	**8.3%**

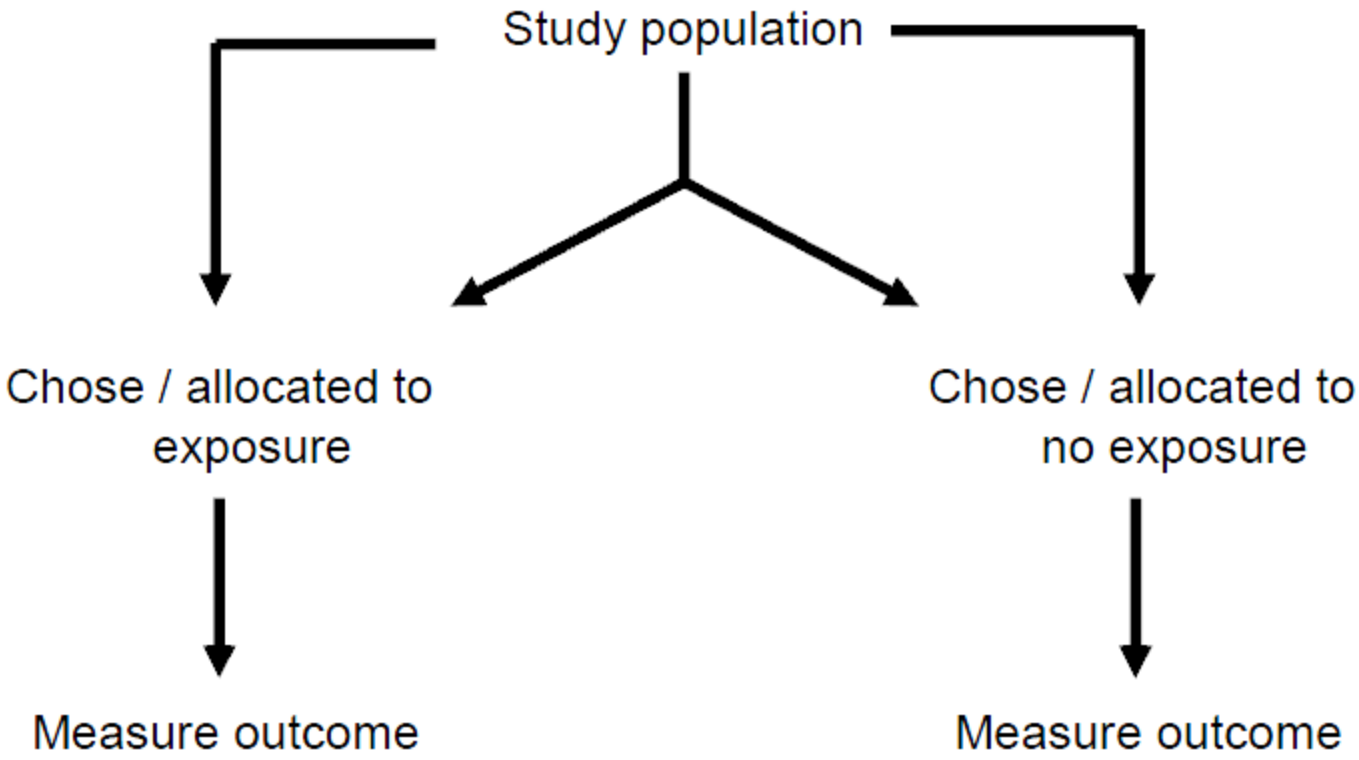
Analytic studies - cohort

Exposure to study factor determined by subjects

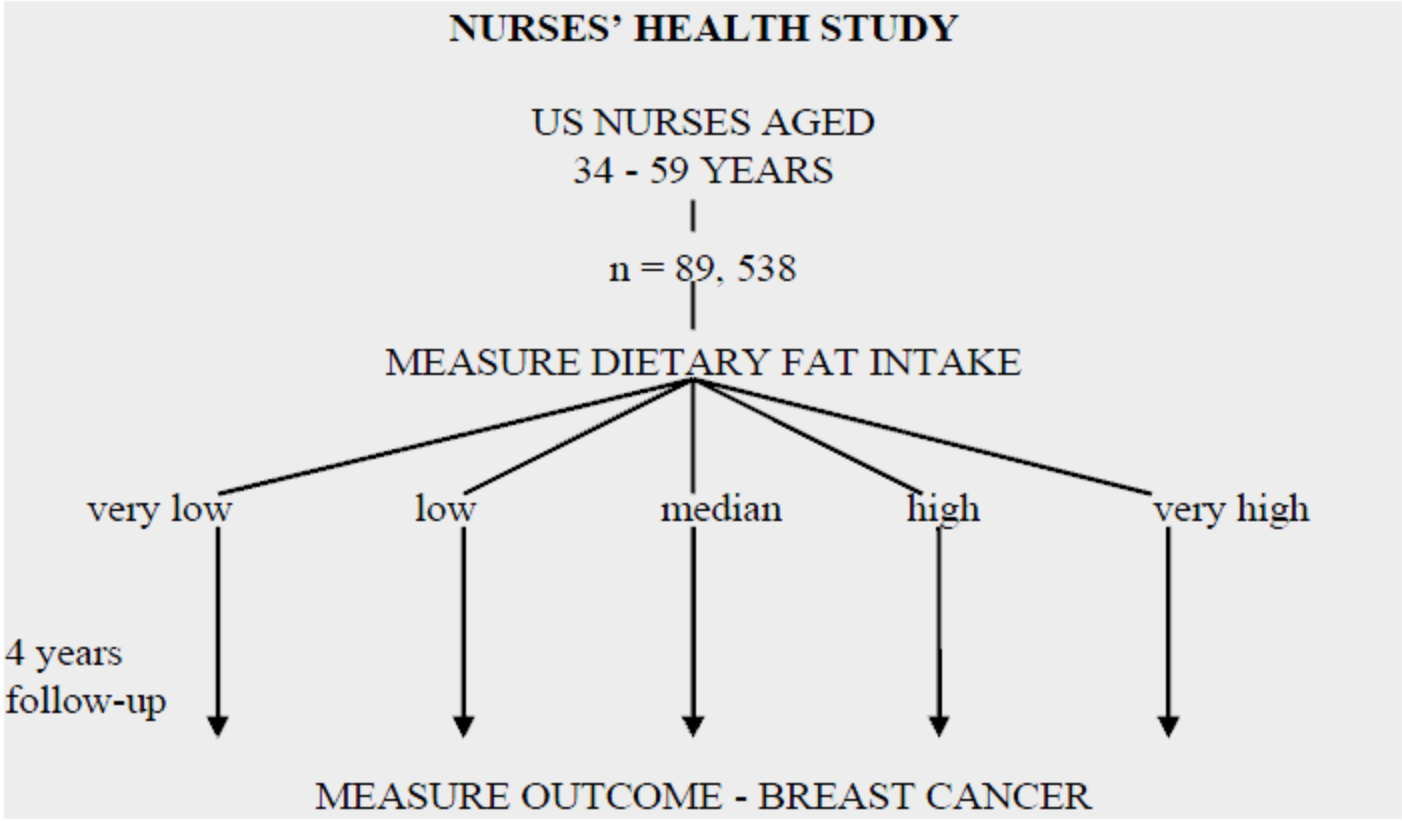
Investigators measure the extent of exposure

Outcome is measured LATER

Cohort study



Analytic studies - cohort



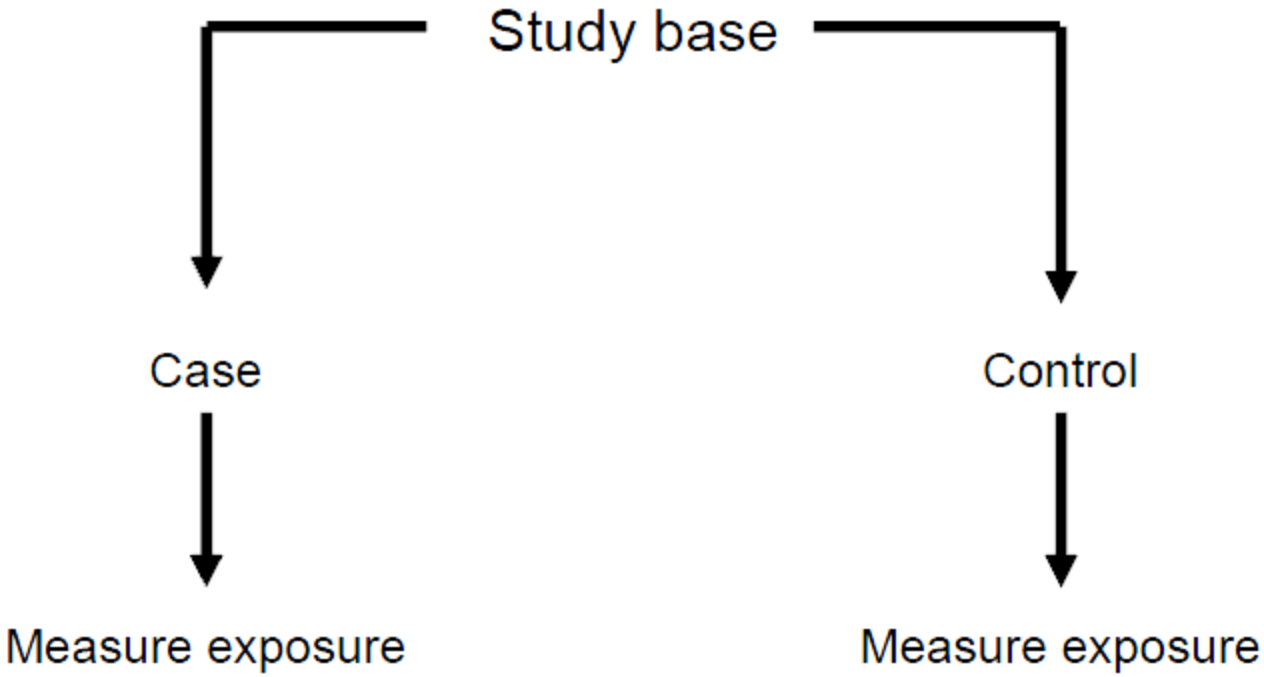
Analytic studies - case control

Subjects selected on presence [cases] or absence [controls] of the outcome factor

Then exposure factor[s] is measured in cases and controls [ie after outcome is known].

Relative frequency of the exposure in cases and controls is compared.

Case-control study



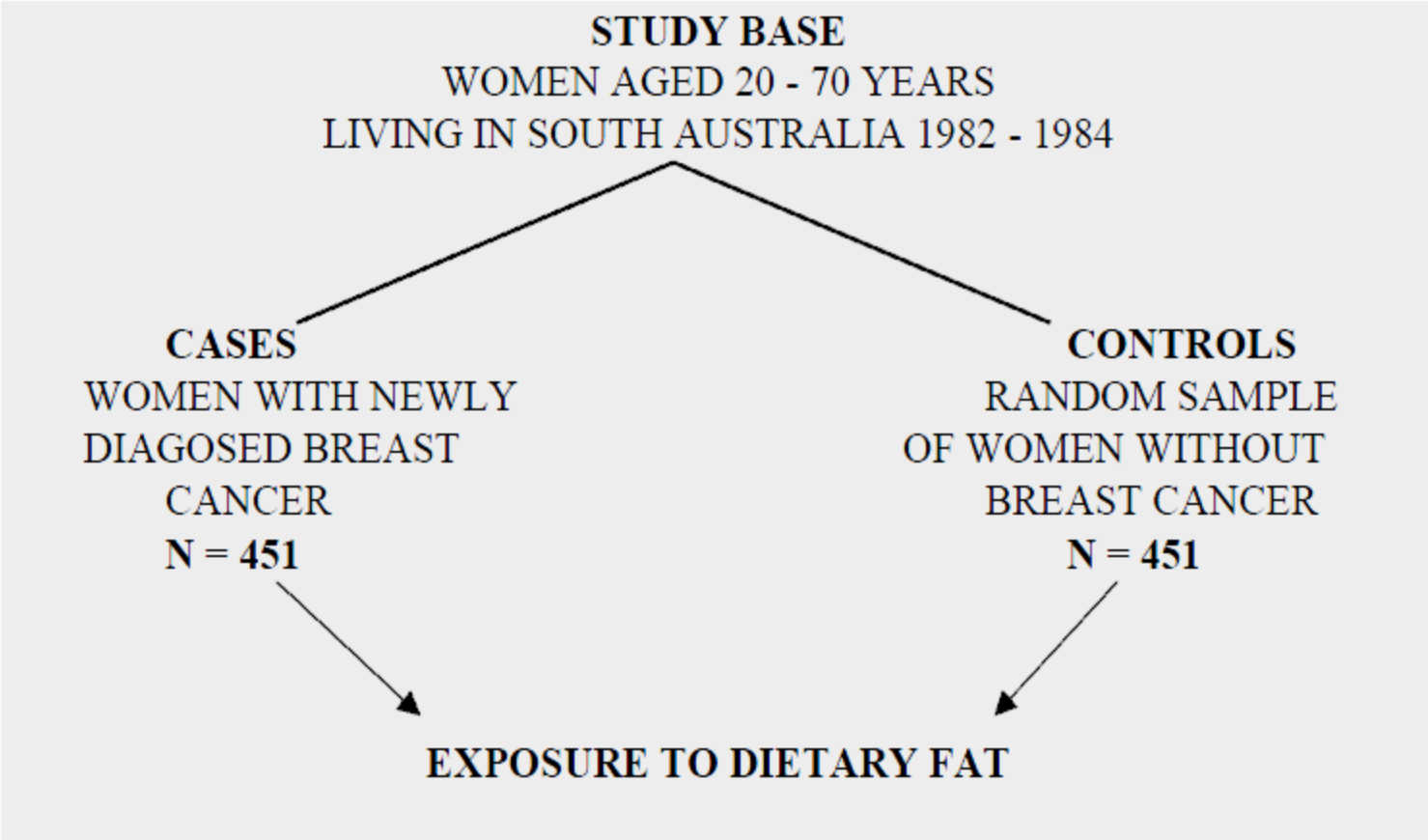
What is a study base?

- Defined place
- Defined time
- Defined group
- E.g. All children under 15 living in Brisbane between 1 Jan 1990 and 31 Dec 2003

Is the study base well defined?

Is the study base poorly defined?

Analytic studies - Case Control



Analytic Studies: cross sectional analytic

Subjects selected because they were present at the time of the study.

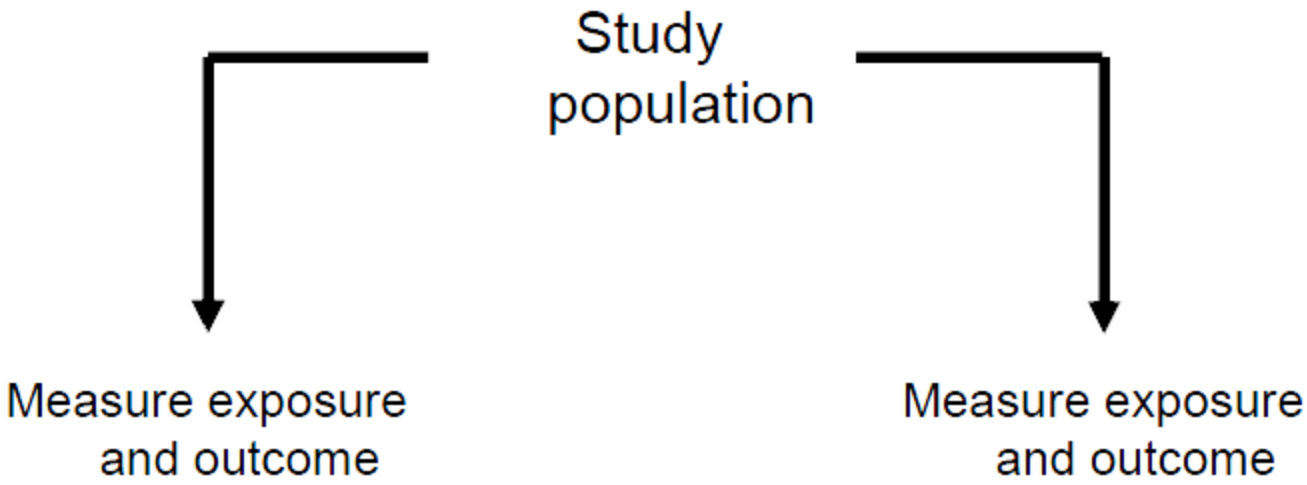
Selection is NOT on the basis of either exposure or outcome.

Example:

- Does being overweight cause arthritis?

This could be examined in a study in which both weight and arthritis symptoms are measured at the same time

Cross-sectional study

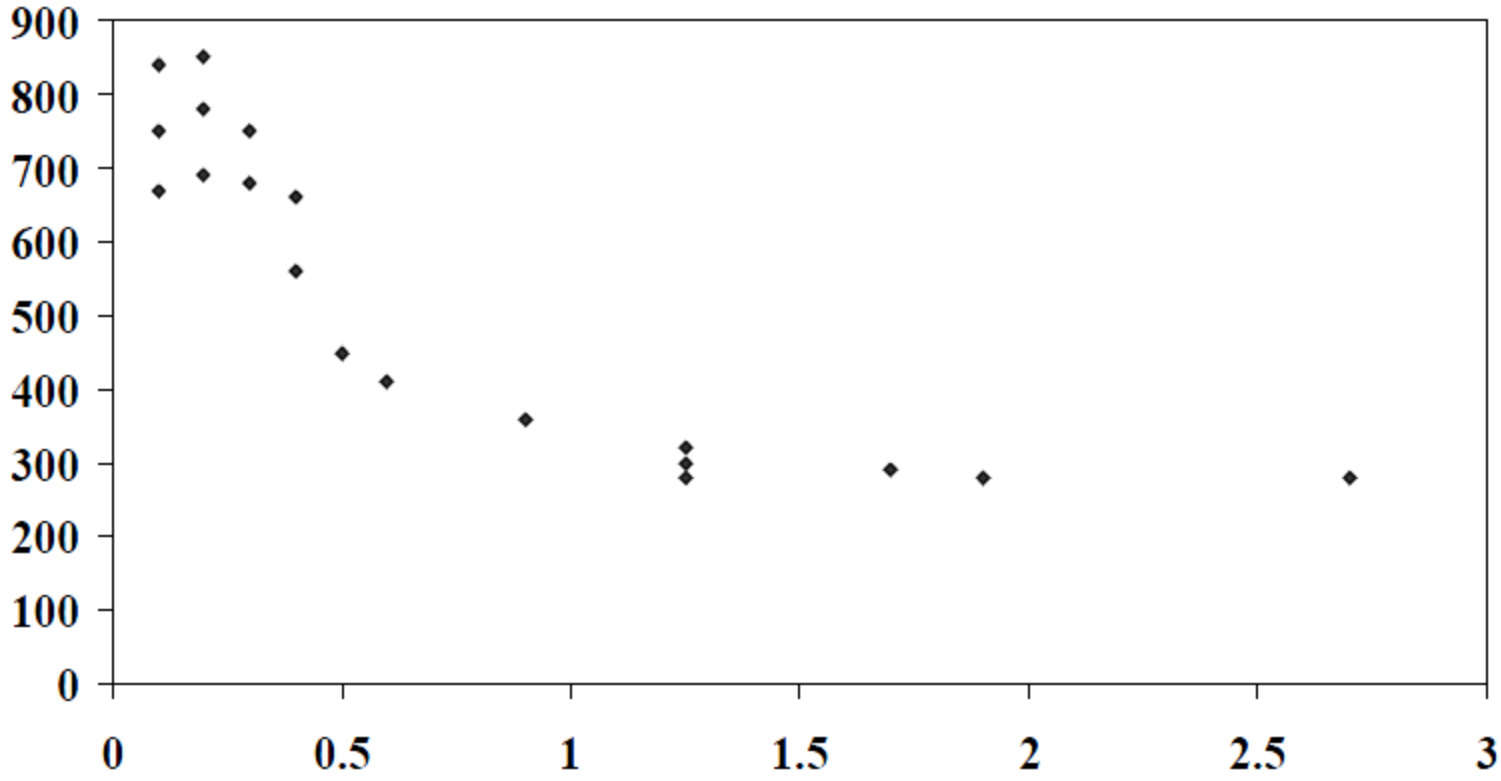


Ecological studies

The group is the unit of analysis

Individual exposure and outcome are not considered

Dental caries per 100 children by Fluoride content of water supply (parts per million) Pub Health Rep 57;1155-1179, 1942



Case-control versus cohort studies

In a COHORT STUDY of smoking (exposure) and lung cancer (outcome):

- begin with a group of smokers (exposed to study factor) and a group of non-smokers (not exposed to study factor; "controls")
- follow them forward in time to see who develops lung cancer (outcome factor)

Case-control versus cohort studies

In a CASE-CONTROL STUDY of smoking and lung cancer

- begin with a group in whom outcome is known: eg lung cancer patients (cases) and a group of people without lung cancer (controls)

- assess their past history of smoking (exposure factor)

Case-control versus cohort studies

Cohort study:

- "Control" = person without the exposure

Case-control study:

- "Control" = person without the outcome

- "Control" = "Referent"

Analytic studies – test evaluation

For answering questions of diagnosis (test evaluation) :

Evaluating one test against a reference standard:

- Cross sectional analytic study

Comparing two tests:

- Randomised controlled trial
- Cohort study
- Case control study

Questions about diagnosis: How accurate is the test?

	Reference standard	
	Disease present	Disease absent
Test positive	True positive	False positive
Test negative	False negative	True negative

Questions about diagnosis: How accurate is the test?

	Blood alcohol concentration (= "Truth")		
Police assessment	>0.1 mg/dl	<0.1 mg/dl	Total
Intoxicated	444	85	529
Sober	45	762	807
Total	489	847	1,336

Systematic reviews and meta-analysis

Examines results from different studies

Meta-analysis is a statistical method of combining results from multiple studies

MEASURES OF ASSOCIATION

Incidence

CUMULATIVE INCIDENCE

$$I = \frac{\text{\# of individuals experiencing a NEW event during a time period}}{\text{\# of susceptible individuals at the beginning of the time period}}$$

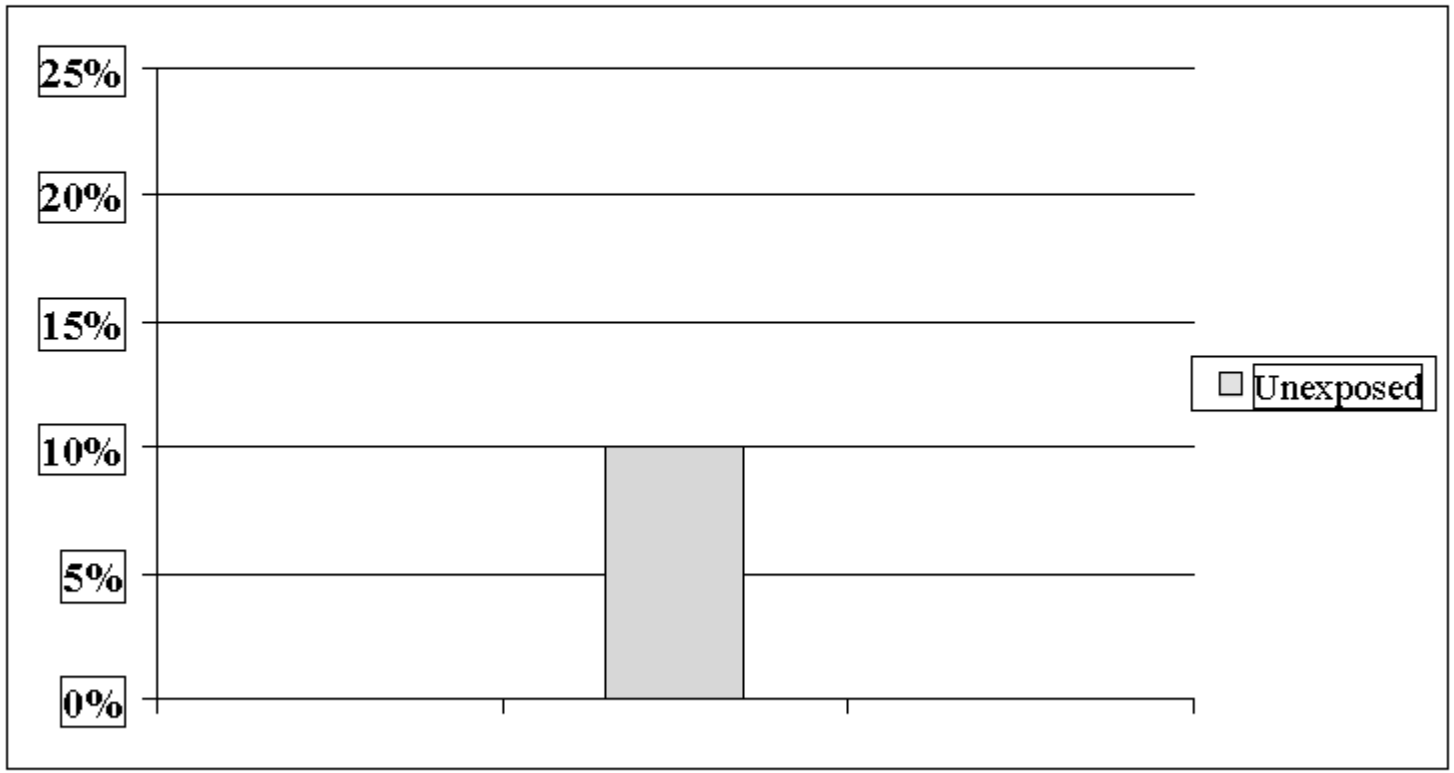
Incidence is a measure of events (event rate)

Incidence is a measure of risk

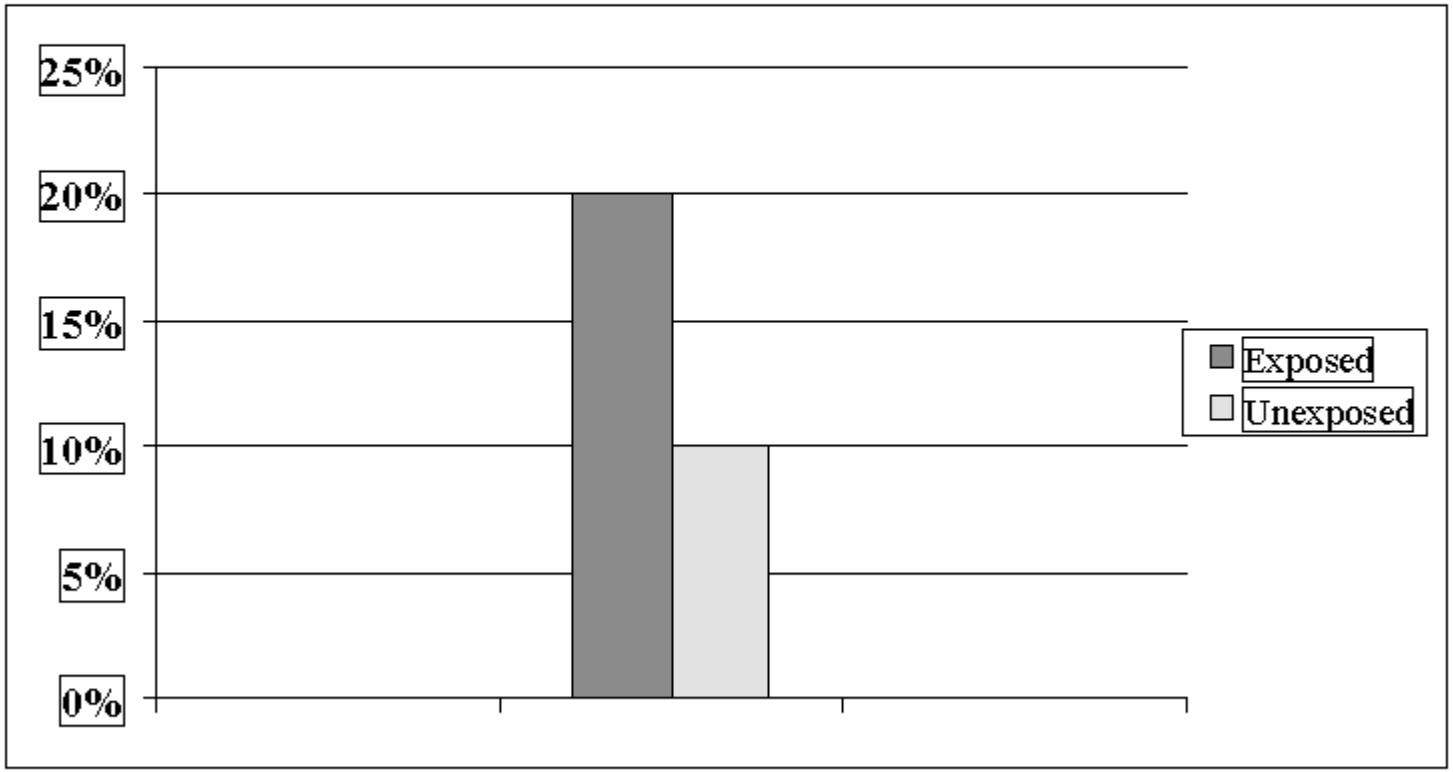
Relative Risk (risk ratio)

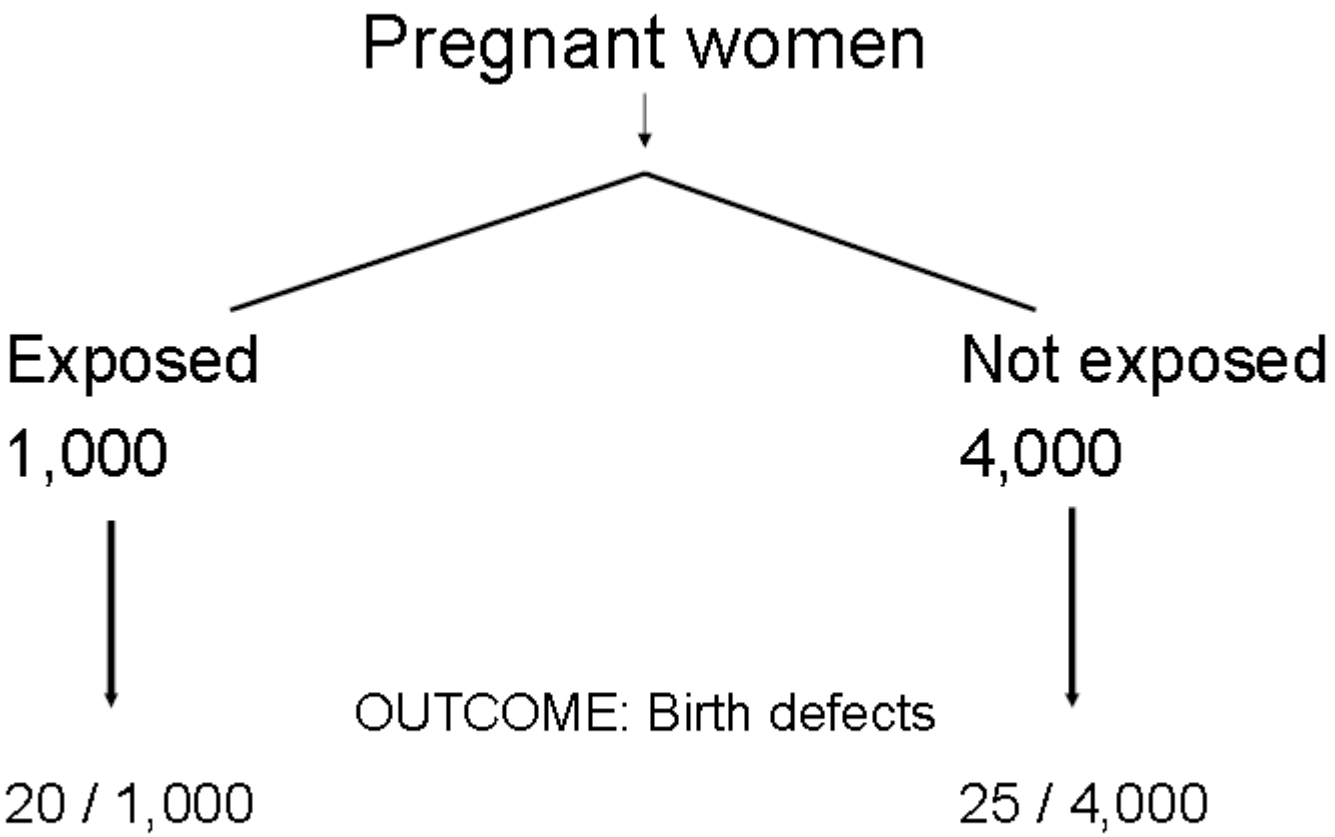
$$\frac{\text{Incidence in the exposed group}}{\text{Incidence in the control group}}$$

How large is the effect: relative risk



How large is the effect: relative risk




Pregnant women
Exposed
1,000
Not exposed
4,000
OUTCOME: Birth defects
20 / 1,000
25 / 4,000

Cohort study of effect of pesticide on risk of birth defects

	Birth defect present	Birth defect absent	Total
Exposed	20		1,000
Unexposed	25		4,000
Total	45		5,000

Cohort study of effect of pesticide on risk of birth defects

	Birth defect present	Birth defect absent	Total
Exposed	20		1,000
Unexposed	25		4,000
Total	45		5,000

Incidence in exposed group: 20 / 1,000 = 0.02 = 2%

Incidence in unexposed group: 25 / 4,000 = 0.00625 = 0.625%

Relative risk = 2% / 0.625%

= 3.2

Trial of folate to reduce birth defects

	Birth defect present	Birth defect absent	Total
Exposed	343		10,335
Unexposed	398		10,320
Total	741		20,655

Incidence in exposed group: 343 / 10,335 = 0.033 = 3.32%

Incidence in unexposed group: 398 / 10,320 = 0.039 = 3.86%

Relative risk = 3.3% / 3.9%

= 0.86

Trial of folate to reduce birth defects

	Birth defect present	Birth defect absent	Total
Exposed	343		10,335
Unexposed	398		10,320
Total	741		20,655

Relative risk = 0.86

Relative risk reduction = 0.14

RRR = (1-RR)

Risk Difference (Absolute Risk Increase)

- Risk in exposed group minus risk in the unexposed group
- How many extra outcomes are due to the exposure?

$$\text{Risk Difference} = I_{exposed} - I_{unexposed}$$

Cohort study of effect of pesticide on risk of birth defects

	Birth defect present	Birth defect absent	Total
Exposed	20	980	1,000
Unexposed	25	3,975	4,000
Total	45	4,955	5,000

Risk Difference = 2%-0.625%
= 1.375%

Trial of folate to reduce birth defects

	Birth defect present	Birth defect absent	Total
Exposed	343	9,992	10,335
Unexposed	398	9,922	10,320
Total	741	19,914	20,655

Risk Difference = $I_{UE} - I_E$

= 3.9% - 3.3%

= 0.6%

Number needed to treat

- How many people must be treated (exposed) to prevent one person from developing the outcome?

NNT = 1 / Risk Difference (ARR)

Trial of folate to reduce birth defects

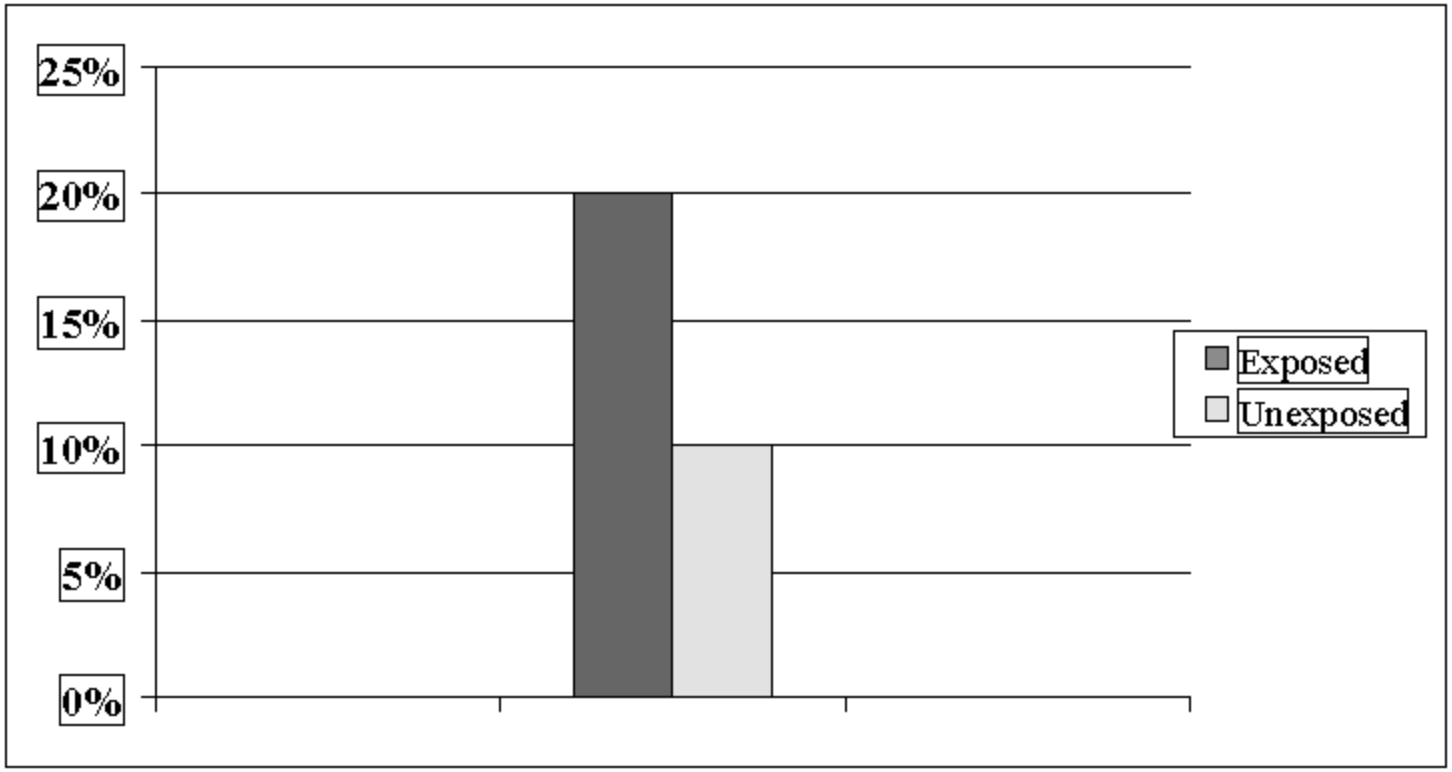
	Birth defect present	Birth defect absent	Total
Exposed	343		10,335
Unexposed	398		10,320
Total			

Risk Difference = 0.6% = 0.006 = 6/1000

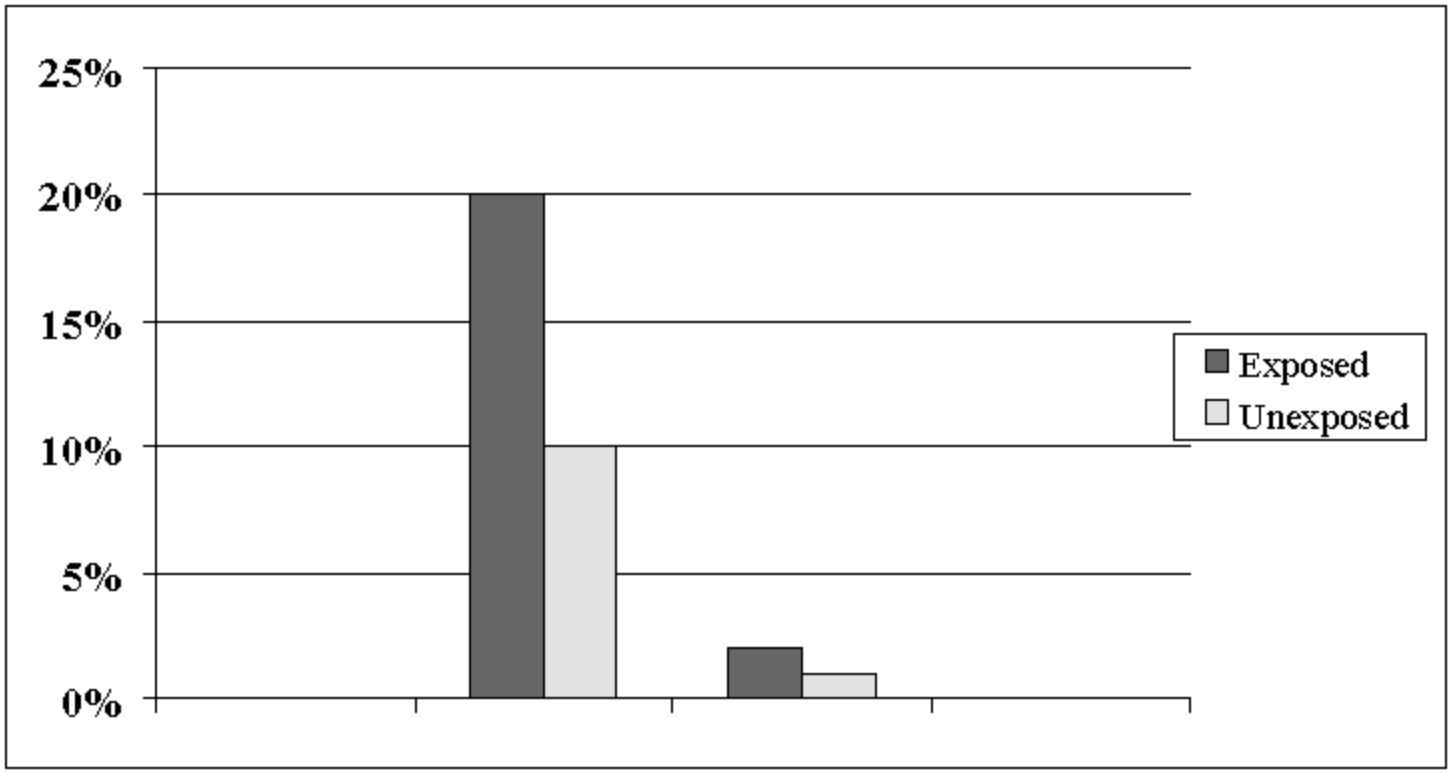
Number needed to treat = 1 / 0.006 (or 1000 / 6)

= 167

How large is the effect?



How large is the effect: relative risk



Measures of effect

- Measures of effect based on INCIDENCE or EVENT RATES can only be calculated for studies that:
  - involve some form of follow-up
  - have known numbers of at-risk subjects
  - have high rates of follow-up ….ie

- RANDOMIZED TRIALS
- COHORT STUDIES

Odds ratio for case-control studies

	Lung cancer		
Smoking	Yes	No	Total
Yes	a	b	a + b
No	c	d	c + d
Total	a + c	b + d	a + b + c + d

$$\text{Odds Ratio (OR)} = \frac{a * d}{b * c}$$

Odds ratio for case-control studies

	Lung cancer		
Smoking	Yes	No	Total
Yes	a	b	a + b
No	c	d	c + d
Total	a + c	b + d	a + b + c + d

$$\text{Odds Ratio (OR)} = \frac{a / c}{b / d} = \frac{a * d}{b * c}$$

Case control study of lung cancer

	Lung cancer		
Smoking	Yes	No	Total
Yes	647	622	1,269
No	2	27	29
Total	649	649	1,298

$$\text{Odds Ratio (OR)} = \frac{647 * 27}{622 * 2} = 14.0$$

Case control study of birth defects

	Birth defect		
Exposure	Yes	No	Total
Yes	20	98	118
No	25	398	423
Total	45	496	541

$$\text{Odds Ratio (OR)} = \frac{20 * 398}{98 * 25} = 3.25$$

Attributable risk

Incidence (unexposed) = Background rate (ie Incidence due to OTHER exposures)

Incidence (exposed) = Incidence (DUE TO exposure) PLUS Incidence (unexposed)

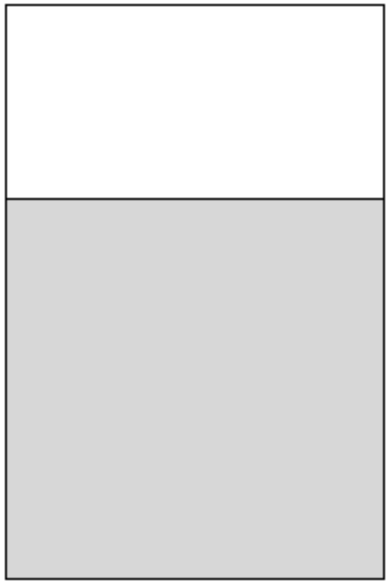
Therefore, incidence due to the exposure (attributable risk):

Incidence (exposed) - Incidence (unexposed)

So Risk Difference, Absolute Risk Increase and Attributable Risk are all words for the same measure of effect

Incidence in unexposed population

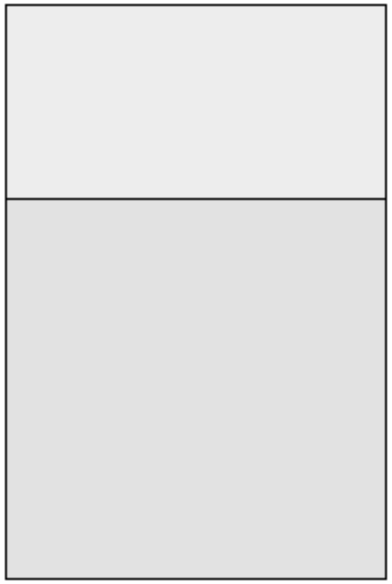
Incidence due to other exposures or background rate



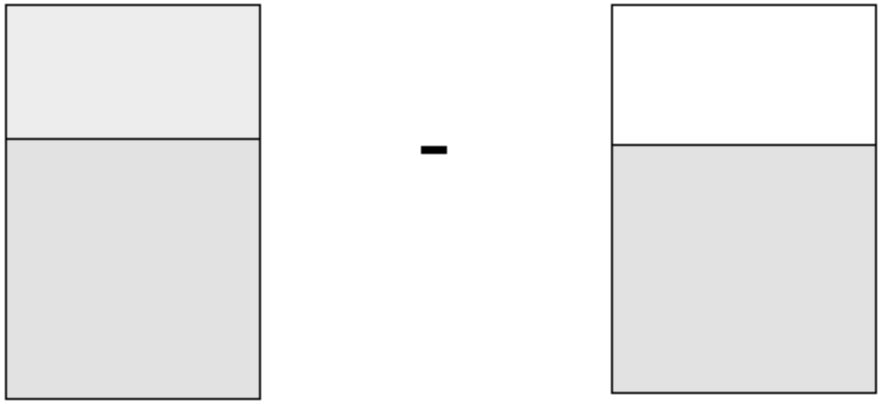
Incidence in exposed population

Incidence due to exposure

Background Incidence



Attributable risk



Attributable risk

$$AR = I_{exposed} - I_{unexposed}$$

Attributable fraction (Attributable risk %)

$$AF = \frac{I_{exposed} - I_{unexposed}}{I_{exposed}} \times 100$$

The percentage of outcomes in the exposed group that are due to exposure

Cohort study of effect of pesticide on risk of birth defects

	Birth defect present	Birth defect absent	Total
Exposed	20	980	1,000
Unexposed	25	3,975	4,000
Total	45	4,955	5,000

Incidence in exposed group: 20 / 1,000 = 2%
Incidence in unexposed group: 25 / 4,000 = 0.625%

Attributable risk = 2%–0.625% = 1.375%

AF = $I_E - I_{UE} / I_E * 100$

= 2%–0.625% / 2% *100

= 69%

The interpretation of Attributable Fraction

- If the AF = 69%,
- this means that 69% of the birth defects observed in the babies of women exposed to the pesticide are attributable to exposure to the pesticide.

Attributable Fraction

$$AF = \frac{RR - 1}{RR} \times 100$$

Attributable Fraction from Relative Risk

- RR = 3.2
- $AF = \frac{3.2 - 1}{3.2} \times 100$

= 69%

Case control study of birth defects

	Birth defect		
Exposure	Yes	No	Total
Yes	20	98	118
No	25	398	423
Total	45	496	541

Odds Ratio (OR) = (20 * 398) / (98 * 25) = 3.25

AF = [(RR – 1) / RR] * 100 = [(OR – 1) / OR] *100

= [(3.25 – 1) / 3.25] * 100

= 69%

Population Attributable Fraction

- Estimates the effect of the exposure in the whole population
- Includes both a measure of the size of the effect of the exposure and a measure of the frequency (prevalence of exposure)

Population Attributable Fraction

$$PAF = \frac{F(RR - 1)}{1 + F(RR - 1)} \times 100$$

where F is the prevalence of exposure in the population

Population attributable fraction

- Example:

Community A is using a pesticide called "Dead Weed". In a cohort study, Dead Weed was found to increase the risk of birth deformity (RR = 3.2). It is estimated that 10% of women of child bearing age are exposed to Dead Weed.

Population attributable fraction

- $PAF = \frac{0.1\,(3.2-1)}{1+\,0.1\,(3.2-1)} \times 100$

$= \frac{0.22}{1.22} \times 100$

$= 18.0\%$

ie 18.0% of birth defects in the town are attributable to exposure to Dead Weed

Measures of effect

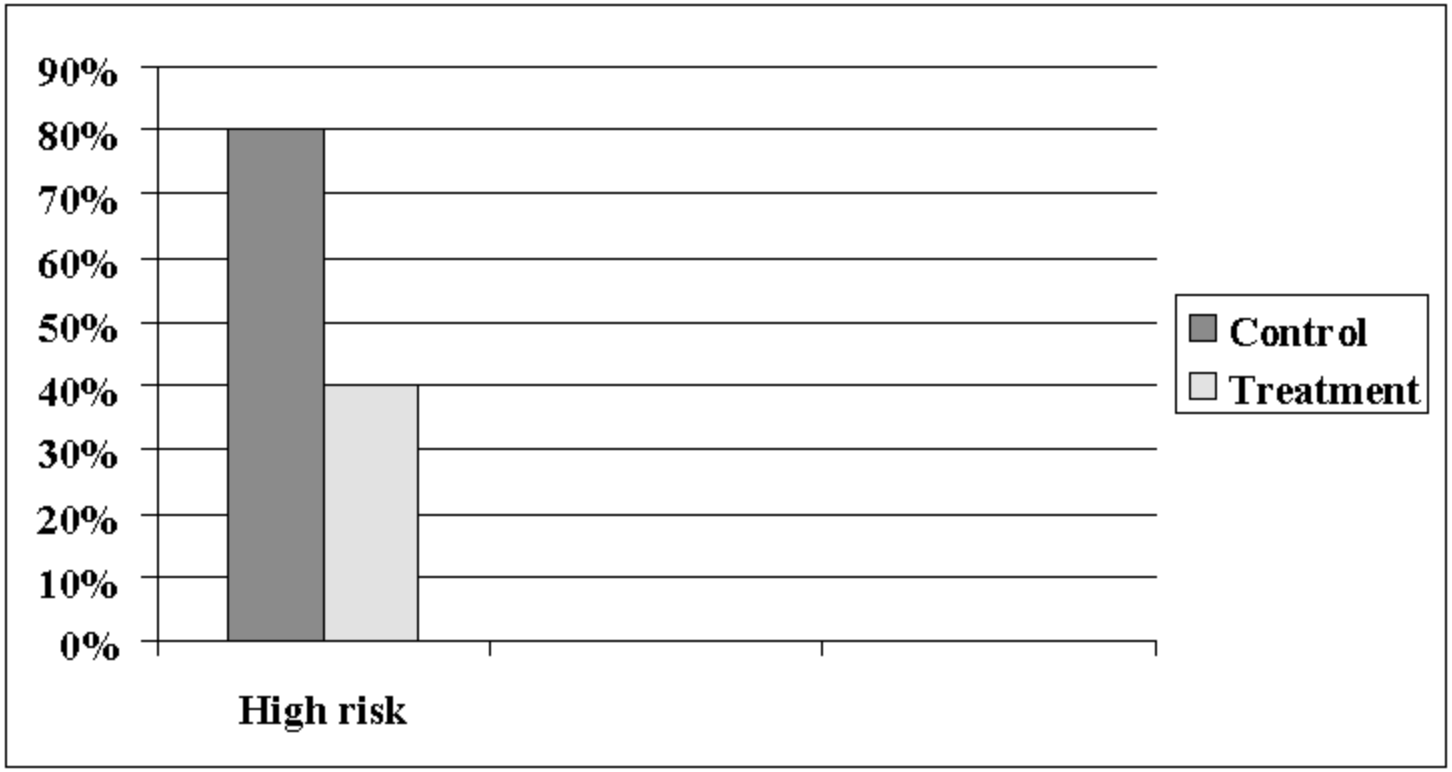
- Randomized trials
- Cohort studies

- Relative risk
- Risk difference (Absolute Risk Increase or Reduction, Attributable Risk)
- Number needed to treat

Measures of effect

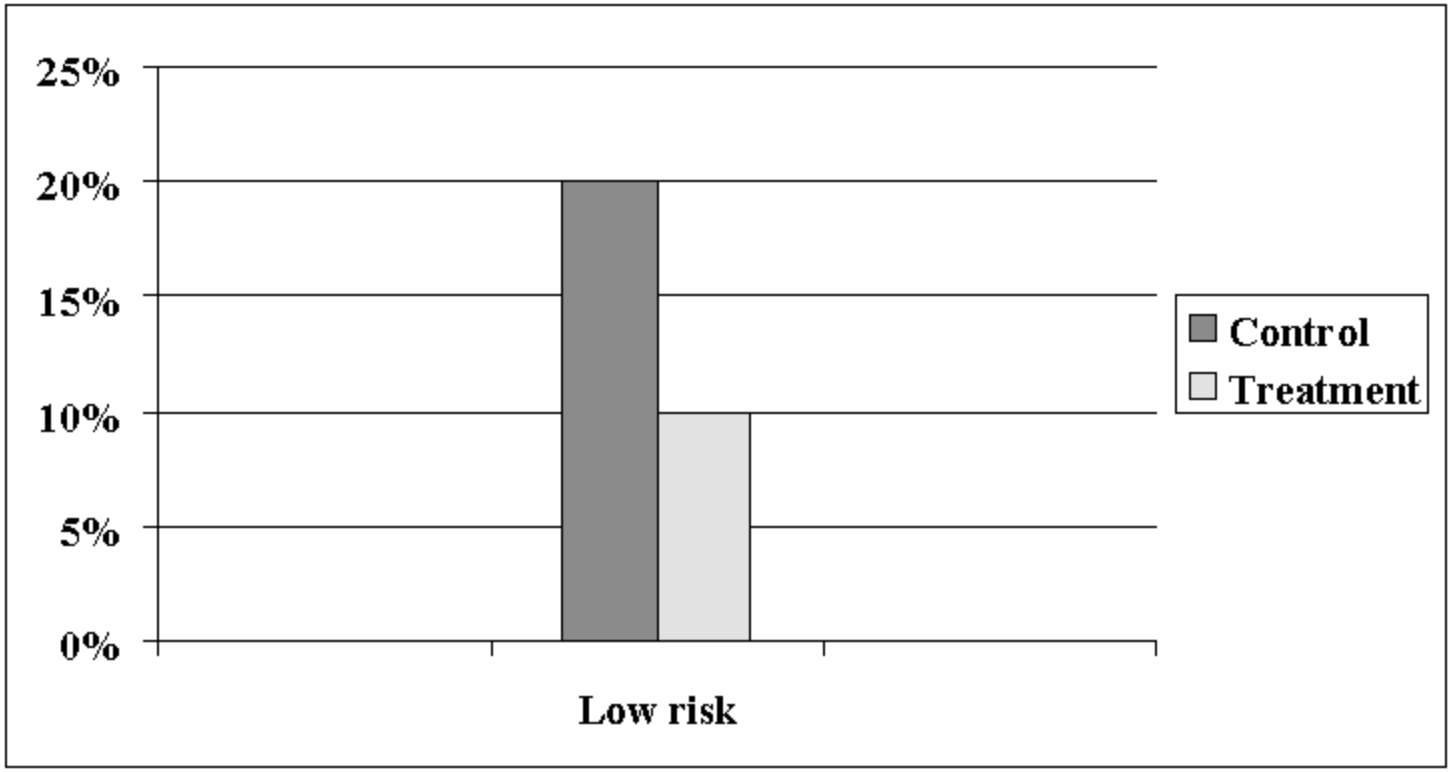
- Case control studies
- Odds ratio
- RCTs, cohort studies and case control studies
- AF and PAF can be calculated from RCTs and COHORT studies, and estimated from the odds ratio in CASE-CONTROL studies.

How large is the treatment effect: relative and absolute risk



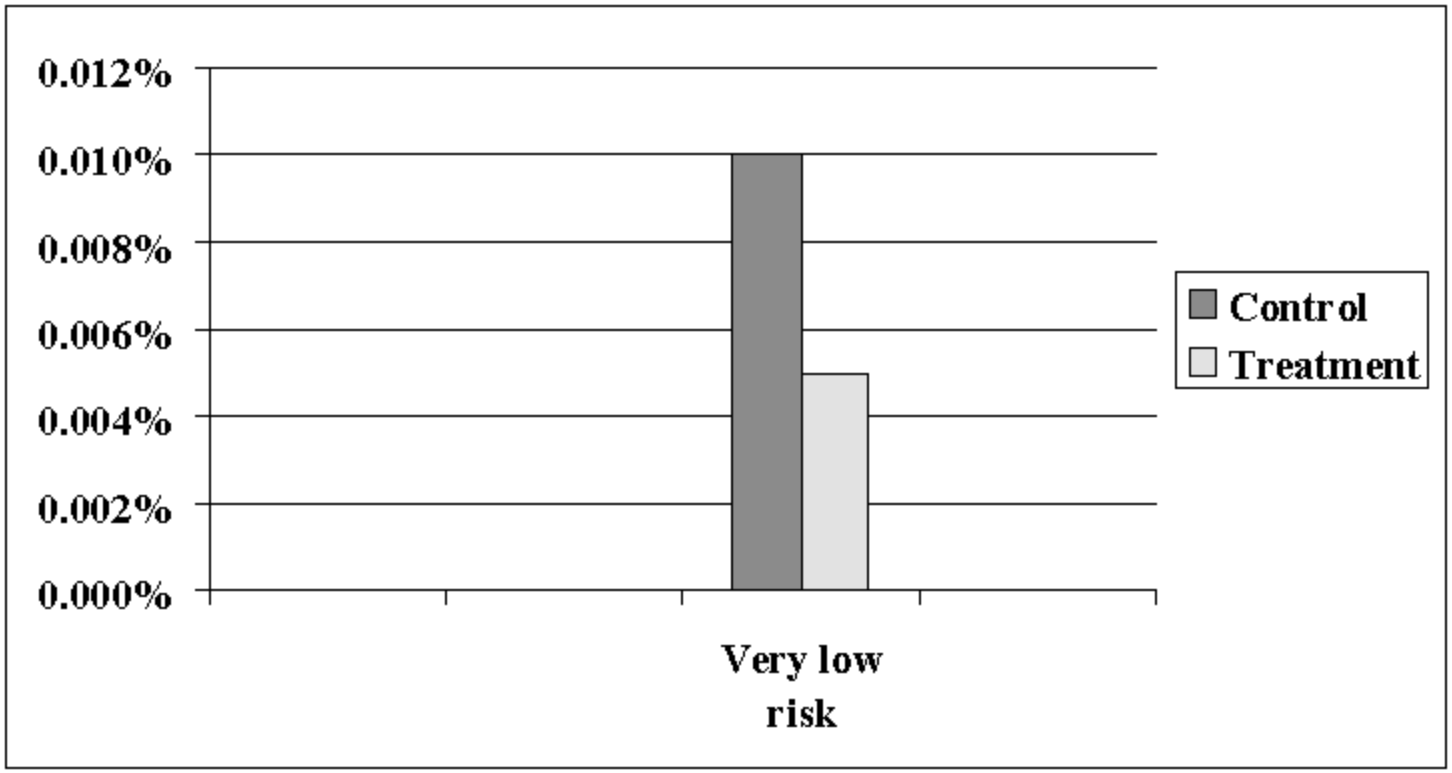
RR = 0.4 / 0.8 = 0.5 **RD = 0.8 – 0.4 = 0.4** **NNT = 1 / 0.4 = 2.5**

How large is the treatment effect: relative and absolute risk



RR = 0.1 / 0.2 = 0.5 RD = 0.2 – 0.1 = 0.1 NNT = 1 / 0.1 = 10

How large is the treatment effect: relative and absolute risk



RR = 0.00005/ 0.00010 = 0.5 RD = 0.0001 – 0.00005 = 0.00005

NNT = 1 / 0.00005 = 20,000