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Cohort studies

General concept

- A sample of the population is selected (cohort)
- Information is obtained to determine which persons have been exposed to a particular etiological agents that is suspected of being related to a disease
- Exposed and unexposed individuals are followed for a period of time (follow-up) to observe who develops the disease

Is exposure related to the disease?

- Incidence rate for the development of the disease are calculated among exposed and unexposed subjects
- If the incidence rate of the disease is greater among the persons exposed than among the ones unexposed, an association is said to exist between the exposure and the disease

What is an incidence rate?

- Number of new cases of a disease occurring in a population during a specified period of time
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- Number of persons in the population during that period of time

How to organize the data?

	Disease +	Disease -	Total
Exposure +	a	b	a + b
Exposure -	c	d	c + d
Total	a + c	b + d	a + b + c + d

Malaria and gender study

	Malaria +	Malaria -	Total
Males	95	55	150
Females	60	87	147
Total	155	142	297

Incidence rates of malaria

- Incidence rate = cases/number of subjects
- Incidence rate in males $95/150 = 0.63$
- Incidence rate in females $60/147 = 0.41$
- The incidence rate is greater in males than in females
- Males appear to be at higher risk of malaria
- We can say that there is an association between gender and malaria

How strong is the association?

- The relative risk measures the strength of the association
- Incidence rate in exposed / incidence rate in unexposed
- In our example $0.63/0.41 = 1.5$

How to interpret relative risk?

- If relative risk is $= 1$ there is no association between exposure and disease (the incidence rate in the exposed is the same as in the unexposed)
- If relative risk is > 1 the exposure is associated with the disease, the larger the relative risk the stronger the association
- If relative risk is < 1 , the exposure is protective

Back to the malaria study

- Relative risk = 1.5
- What can we say about the association between malaria and gender?

Is the association true?

- Think about potential confounders!
- An apparent association between an exposure and disease may actually be due to another variable (confounder)
- A confounder:
 - is a risk factor for the study disease
 - is associated with the study exposure

Which variable could confound the association between malaria and gender?

- If somebody works outdoor is more likely to be exposed to mosquito bites (occupation is related to the disease)
- Men are more likely to work outdoor than females (occupation is related to the exposure)
- Thus, occupation may be a confounder

How to disentangle confounding?

- Stratify the data in multiple 2 x 2 tables to calculate the stratum specific relative risk
- Use statistical techniques to mathematically model the risk of developing the disease, adjusted for the effects of possible confounding factors (example: logistic regression)

Let's stratify by occupation

Outdoor occupation

	Malaria +	Malaria -	Total	Incidence
Males	70	10	80	$70/80 =$ 0.87
Females	10	2	12	$10/12 =$ 0.83
Total	80	12	92	

$$\text{Relative risk} = 0.87/0.83 = \mathbf{1.04}$$

Let's stratify by occupation

Indoor occupation

	Malaria +	Malaria -	Total	Incidence
Males	25	45	70	$25/70 =$ 0.36
Females	50	85	135	$10/12 =$ 0.37
Total	75	130	205	

$$\text{Relative risk} = 0.36/0.37 = \mathbf{0.97}$$

What do we learn from stratification?

- There are more cases of malaria in people working outdoor than indoor (look at the incidence rates)
- More males are working outdoor
- The stratum specific relative risks are similar to each other (~ 1) and different from the crude relative risk (1.5) suggesting that occupation is a confounder of the observed association between male gender and malaria

Two types of cohort studies

- **Concurrent:** the investigator begins with a group of individuals and follows them for a number of years
- **Non concurrent:** the period of observation starts sometime in the past and the investigator traces the subjects by various means to the present

A major source of difficulty

- Maintaining the follow up of the individuals in the cohort
- It is important to trace as many subjects as possible
- Try to get information on the individuals lost to follow up and look if they are somehow different from the individuals who stay in the cohort

Advantages

- Complete description of individuals' experiences subsequent to exposure
- Clear temporal sequence of exposure and disease
- Rare exposures can be studied
- Assessment of multiple outcomes
- Assessment of different levels of exposure
- Ethically easier

Disadvantages

- Large numbers needed for rare diseases
- Long term follow-up may be necessary when the latency is long
- Can be expensive
- Exposure status can change during the course of the study

Important concepts

- How cohort studies differ from case control studies and randomized clinical trials
- Incidence rate
- Relative risk
- Confounding