Measures of Association

Dr. M.M. Mweu,

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Measures of Association

- Are used to assess the magnitude/strength of the relationship between an exposure and the disease
- They reflect the increase in frequency of d'se in one pop in comparison with another
- Measures of statistical significance (e.g. Chi-square) are used to demonstrate whether an association between the exposure & disease exists
- Given a study design, d'se frequency can be expressed as:
  - Incidence risk (cohort study design)
  - Incidence rate (cohort study design)
  - Prevalence (cross-sectional study design)
  - Odds (Cohort (odds of d'se), Cross sectional and Case-control designs (odds of exposure)
- The strength of an association is expressed using a "relative" measure based on ratio of 2 estimates of d'se frequency

Measures of Association

- There are 3 common ratio measures of association: *Risk ratio (RR), incidence rate ratio (IR)* and *odds ratio (OR)*
- The appropriate measure depends on the study design and its corresponding measure of d'se frequency

Risk ratio (relative risk)

- Ratio of the incidence risk of d'se in exposed group to risk of d'se in unexposed group

	Diseased	Non-diseased	
Exposed	a	b	(a+b)
Unexposed	c	d	(c+d)
	(a+c)	(b+d)	a+b+c+d=n

$$RR = \frac{p(D+|E+)}{p(D+|E-)} = \frac{a}{a+b} / \frac{c}{c+d}$$

- Computed in cohort studies (sometimes in cross-sectional studies especially when d'se risk is small – otherwise prevalence ratio)

Risk ratio (relative risk)

- Cannot be computed in case-control studies
- *RR* ranges from 0 to infinity. Value of 1 means no association betwn exposure & d'se
  - $RR < 1$ exposure is protective (e.g. vaccines)
  - $RR = 1$ exposure has no effect (i.e. null value)
  - $RR > 1$ exposure is positively associated with d'se

Example

	Ocular melanoma +	Ocular melanoma -	
Fair skin	38	4962	5000
Dark skin	2	998	1000
	40	5960	6000

$$RR = \frac{38}{5000} / \frac{2}{1000} = 3.8$$ (*fair-skinned people have roughly 4 times higher risk of ocular melanoma than dark-skinned people*)

- Prevalence ratio (PR) is computed in the same way as *RR*

Rate ratio

- Ratio of d'se frequency (incidence rate) in exposed group to rate in unexposed group

	No. of cases	Person-time at risk
Exposed	a_1	t_1
Unexposed	a_0	t_0
	a	t

$$IR = \frac{a_1}{t_1} / \frac{a_0}{t_0}$$

- Calculated in cohort studies (when incidence rates are used)
- Ranges from 0 to infinity
- As in *RR*, $IR = 1$ (no association); $IR < 1$ (protective assoc); $IR > 1$ (positive assoc)

Rate ratio

Example

	No. of CHD cases	Person-years at risk	Rate per 1000 person-years
Post-menopause	26	6848	3.8
Pre-menopause	6	8384	0.7

$$IR = \frac{3.8}{0.7} = 5.4$$

- Interpreted as: *Post-menopausal women have a rate of CHD roughly five-and-a-half times higher than that of pre-menopausal women*

Odds ratio

- Is the odds of disease in the exposed group divided by odds of d'se in the unexposed group (cohort studies):

$$OR = \frac{odds\,(D+|E+)}{odds\,(D+|E-)} = \frac{a}{b} / \frac{c}{d} = \frac{ad}{bc}$$

- In case-control studies it is odds of exposure in d'sed group divided by odds of exposure in non-d'sed group:

$$OR = \frac{odds\,(E+|D+)}{odds\,(E+|D-} = \frac{a}{c} / \frac{b}{d} = \frac{ad}{cb}$$ (note that *OR* is <u>similar</u> in both cases)

- Based on Ocular melanoma example the $OR = \frac{38}{2} / \frac{4962}{998} = 3.82$

<u>Interpretation:</u> Odds of ocular melanoma is about 4 times higher in those with fair skin than in those with dark skin

- OR is only measure applicable to case-control studies
- $OR = 1$ signifies no association; $OR > 1$ & < 1 signify increased & reduced (protection) risk of d'se

Odds ratio

- **NB:** When d'se occurs infrequently in pop (i.e. prevalence/ incidence risk $< 5\%$, OR is approx. equal to RR & IR (as in melanoma example)

Measures of Effect

- Effect/impact of a risk factor on a d'se is expressed using an absolute measure which is the *difference betwn 2 measures of d'se frequency*
- They express the no. of cases an exposure *causes/prevents*
- Can be computed for the exposed group or for the population
- Only calculated if an association already exists betwn exposure & outcome

Measures of effect in the exposed group

- Even when an exposure is strongly associated with d'se (e.g. smoking & lung cancer), there's always some d'se in the non-exposed pop (lung cancer in non-smokers)
- Incidence in non-exposed pop viewed as *"baseline" level of risk* for individuals if the *exposure were completely absent* from pop

Measures of Effect in the exposed group

- To therefore evaluate effect of exposure on d'se frequency in exposed subjects we compute absolute difference in risk between exposed & unexposed groups (**attributable risk**) & proportion of d'se in exposed group that is attributable to exposure (**attributable fraction**)
- They both estimate *how much of the disease* in exposed group is *due to the risk factor* of interest
- Both measures assume that all d'se is due to the exposure i.e. absence of confounding

Attributable risk (*AR*) (Risk Difference/Rate difference)

- Is the risk/rate of d'se in exposed group minus the risk/rate of d'se in unexposed group

$$RD = p(D+|E+) - p(D+|E-) \ \{\text{in case of risk difference}\}$$

$$\frac{a}{a+b} - \frac{c}{c+d}$$

Attributable risk (Risk Difference/Rate Difference)

It indicates the increase in the probability of d'se in exposed group beyond the baseline risk that results from the exposure

- As for incidence rate difference (ID):

$$ID = \frac{a_1}{t_1} - \frac{a_0}{t_0}$$

Interpreted as:

- $RD\ or\ ID < 0$ exposure is protective
- $RD\ or\ ID = 0$ exposure has no effect
- $RD\ or\ ID > 0$ exposure is positively associated with d'se

Attributable fraction (AF)(Risk/Rate difference percent)

- Expresses the proportion of d'se in exposed individuals that is due to the exposure *assuming the relationship is causal*
- Alternatively, it is the proportion of d'se in the exposed group that would be *avoided if the exposure were removed*
- Can be calculated from incidence data (exp/non-exp) or from RR

Attributable fraction (Risk/Rate difference percent)

$$AF = \{(\frac{a}{a+b} - \frac{c}{c+d})\}/(\frac{a}{a+b})$$

$$= \frac{RR-1}{RR}$$

$$\cong \frac{OR-1}{OR}$$ (Approximate AF for case-control studies)

- Values range from 0 (no effect of exposure) to 1 (no d'se in unexposed hence all d'se due to exposure)

Vaccine efficacy

- Is one form of AF, with unvaccinated equivalent to being "factor positive" i.e. exposed

Example

- A study measured the risk of HIV infection among children born to HIV-infected mothers according to whether the babies were breastfed or not. Among breastfed children of HIV-infected mothers, the risk of HIV infection was 280 infections per 1000 children. Among non-breastfed – 150 infection per 1000

Attributable fraction (Risk/Rate difference percent)

$$AR = 280 \text{ per } 1000 - 150 \text{ per } 1000$$

$$= 130 \; infections \; per \; 1000 \; children$$

Interpretation: 130 infections per 1000 children occurring among breastfed children are attributable to breastfeeding OR breastfeeding is responsible for infection of 130 of every 1000 children born to, and breastfed by, HIV-infected mothers

$$AF = \frac{\frac{280}{1000} - \frac{150}{1000}}{\frac{280}{1000}}$$

$$= 0.46 \; or \; 46\%$$

Interpretation: 46% of HIV infections in breastfed children is attributable to breastfeeding OR breastfeeding was responsible for 46% of HIV infections among children born to, and breastfed by, HIV-infected mothers