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Measures of association

DEFINITION OF BASIC TERMS

Risk: A probability that an individual will become ill or die within a specified period of time or age. It is used to denote incidence rate.

Risk factor: It can be defined as:

a. Risk marker. An attribute or an exposure that is associated with an increased risk of disease or other specific outcome.

b. Determinant. An attribute or exposure that increases the risk of disease or other specific outcome.

c. Modifiable risk factor. A determinant that can be modified by an intervention thereby reducing the risk of disease or other specific outcome.

Estimate the association between (exposure) and (disease) using the frequency measures of the two population being compared . So to aid in the calculation of measure of association , epidemiological data are often presented in the form of (2x2) table (four fold , contingency table) .

	Disease yes +	Non-disease No	
Exposed yes +(study population)	a	b	a+b
Non-exposed (control population)	c	d	C+d
	a+c	b+d	Total a+b+c+d

Incidence rate in exposed (study population) = a/ a+b .

Incidence rate in non-exposed (control population) = c/ c+d .

RR= a/a+b / c/c+d .

Mean , number of observation in which the occurrence of interest is found / total number of observation .

NOTE:- risk factor present (study population) .

Risk factor absent (control population) .

Now if , we put study and control population above the table and disease , no disease beside , what happened .

	Study(exposed)	Control (no exposed)	
disease	a	b	A+b
No disease	c	d	C+d
total	A+c	B+d	

Incidence rate in exposed (study population) = a/a+c .

Incidence rate in non- exposed (control population) = b/ b+d .

RR= a/a+c / b/b+d .

E.g, suppose the incidence of (Hepatitis –B) sero+ among those having previous blood transfusion is 5/1000/ year and those with no blood transfusion is 1/1000/ year . So what do such number give us ?
Blood transfusion ----- exposure .
Hepatitis –B ------ outcome .
So what is the magnitude of association between exposure and outcome .
The magnitude of association between exposure and outcome calculated by the (Relative Risk and Attributable Risk) , are the two most frequently used in epidemiology .

(Relative Risk) (RR)

Estimate the magnitude of association between exposure and outcome , or indicate the probability of developing the disease in the exposed relative to those unexposed .
So the exposure = risk factor .
Outcome= disease or death .
RR= Ie/ Ie- . so(Ie) incidence rate among exposed /(Ie-) incidence rate among non- exposed .

$$\text{Relative risk (RR)} = \frac{\text{Incidence rate among exposed}}{\text{Incidence rate among non exposed}}$$

Ie=a/a+b Ie- =c/c+d so RR=a/a+b/c/c+d . so RR= incidence in exposed /incidence in non-exposed (calculate from cohort study)
So by going back to the Hepatitis –B e.g .
RR= 5/1000/year / 1/1000/year= 5 times (probability of developing an outcome among the exposed compared to the non-exposed) .
If RR=1 (Mean no association between exposure and risk of disease) .
If RR> 1 (Positive association , mean increase risk among exposed).
If RR<1 (Negative association , mean decrease risk among exposed) .
(Ie> Ie-) risk factor .
(Ie < Ie-) protective factor .
So RR provides information that can be used in the judgment of causality .
RR , in study design, can be directly calculate only in a cohort study or experimental study (clinical trial) . Because incidence can not be estimated from a (case- control) study , RR can not be calculate directly from a case- control study , under some circumstances , the RR , in a case- control study can be estimated by the odds ratio (OR) .
So OR= ad/ bc .
So disease x non- disease ---------- case- control study .
Exposure x non- exposure ------ cohort study .
E.g, Data from a (cohort study) of oral contraceptive use and bacteruria among women aged (16- 49) years .

	Bacteruria Yes +	no-bacteruria No -	
OC used yes +	27	455	482
No OC used	77	1831	1908
total	104	2286	2390

Cohort study , mean incidence and start from exposure .
Ie= 27/ 482x1000= 56.02/ 1000/ year .
Ie-= 77/1908X1000=40.36/1000/year .

RR=Ie/ Ie-= 56.02/1000 / 40.36/1000 = 1.39(no unit) . so 1.39 times more is the risk of developing bacteruria in the exposed group (taking oral contraceptive pills) than not taking OC .
E.G- Data from a case-control study of current oral contraceptive use and (myocardial infarction) in premenopausal female nurses .
NOTE. When researcher used case- control study means start from diseases , and can estimate percentage .

	MI (YES)	NO (MI)	
OC used (yes)	23	304	327
(NO) OC used	133	2816	2949
total	156	3120	3276

SO, OR= ad/bc=23x2816/304x133=1.6 . those who are on OC used have a (1.6) times risk to have MI than those who do not take OC . So very important to know the type of study (cohort or case- control) study why ? Just observe the following .

EG, A hypothesis case- control study of cigarette smoking and lung cancer

	Case (yes) CA lung	Control (no) CA lung	
Smoking (yes)	70	30	100
(no) smoking	30	70	100
	100	100	200

OR= adx bc= 70x70/ 30x30=5.4.
But RR= 70/100 / 30/100 = 2.3 .

The same example above but (100 cases and 1000 control) , increase number of control (هنا جائز في الدراسه) .

	CA lung (yes) cases	(NO) CA lung control	
Smoking (yes)	70	300	370
(no) smoking	30	700	730
	100	1000	1100

OR= ad/ bc = 70x700/ 300x30= 5.4 (the same above) .
But RR= 70/370 / 30/ 730 = 4.6 Change .
So OR is more stable estimate than RR in case-control study , therefore RR is not beneficial in case-control study .

Second (Attributable risk) (AR) .
Also called (risk difference , excess risk , and rate difference) .
It is provide information about the absolute effect of the exposure , i.e – the excess risk of disease among the exposed compared to the non-exposed .
AR= Ie-(Ie-) = a/a+b- c/c+d
AR=Incidence rate exposed- Incidence rate in non-exposed , calculate in (cohort study) . Back to hepatitis –b e.g .

AR= 5/1000/year – 1/1000/year= 4/1000/year . (absolute measure , effect of the exposure) . The value of AR indicate the number of cases of the disease among the exposed that can be attribute to the exposure itself .
OR, The number of cases of the disease among the exposed that could be eliminated if the exposure was eliminated .
Now returned back to Bacteriuria and OC table , so
AR=Ie-(Ie-)= 56.02/1000/year- 40.36/1000/year=15.66/1000/year .
So 15.66/ 1000/year ---- 1566/100000/year are attributable to OC use among the group who are exposed .
Note :- AR is only calculated from cohort study and can not calculated from case-control study . The value of RR dose not necessarily give an idea about the AR , if I have a higher RR dose not mean the AR is high and vice- versa .
Not:- if AR=0 (ZERO) , exposure has no relation .
If AR> 0 , exposure has relation to the out come .
If AR<0 , exposure is protective . e.g (vitamin supplementation)or (good personal hygiene) or (vaccination) .

E.G:- Annual mortality rate per 100000 , one exposure and two outcome.

	CA LUNG	CHD	
Cig, smoking	140	669	
Non-smoking	10	413	
RR	14	1.6	
AR	130/100000/year	256/100000/year	

Her give us direct incidence .
This is a cohort study the exposure is smoking , the outcome is either lung cancer or CHD .
RR= Ie/ Ie-= 140/ 10 = 14 in CA lung .
RR= Ie-Ie- = 669/ 413=1.6 in CHD .
SO 14 mean a person who smokers will have a 14 times chance to die from lung ca than non- smoker . 1.6 times chance to die from CHD than a non- smoker .
So 1.6 times chance to die from CHD than a non- smoker .
But , AR=Ie-(Ie-), smoking leading to lung CA , 140-10=130/100000/year
Smoking leading to CHD , 669-413=256/100000/year .
So more smokers die due to CHD than from lung CA . If I wanted to do a public health program to decreases death rates due to smoking , I would choose death due to CHD , because CHD has a higher incidence , according to the table , so financial and personal would be distributed on preventing death of smokers due to CHD .

THIRD, Attributable risk percent (AR%) .
Estimates the proportion of the disease , among the exposed that is attributable to the exposure . Gives an idea about the proportion of the disease in the exposed that could be prevented by eliminating the exposure .

$$\text{Percentage reduction} = \frac{\text{IR among exposed} - \text{IR among non exposed}}{\text{IR among exposed}} \times 100$$

AR%=AR/Iex100%.
AR%=Ie-(Ie-)/ Iex100% . (calculated in cohort study) .
But in case- control study , AR%=OR-1/ORX100% .

FOURTH , Population attributable risk. (PAR) .
PAR predicts the reduction in risk achievable if a risk is removed from a population . Estimates the excess rate of disease in the total study population of exposed and non-exposed individuals that is attributable to the exposure or helps to determine which exposure have the most relevance affect to the health of a community . It is calculated by multiplying AR by prevalence of exposure to the risk factor .
PAR= ARX Proportion of population exposed (prevalence of exposure).
(prevalence of exposure in the total population , from an external source , or that of the study population if it representative the general population .
E.G:-Consider a cohort study of decompression illness (DCI) , taken in one year , with 500 divers with a variation in heart anatomy known as a patent foramen ovale (PFO) controlled against 500 divers without a (PFO) . The result are summarized as follows .

	DCI(disease)	No(DCI) NO disease	total
PFO(Exposed)	2	498	500
No PFO(Non-exposed)	1	499	500

OR .

	PFO(exposed)	No PFO(non-exposed)(control)	
DIC	2	1	
No DIC	498	499	
TOTAL	500	500	

It is widely believed that a POF , or any other right –to-left circulatory shunt , increases the risk of DIC . Some 30% of individuals within the general population have a POF , and some surveys have shown that a similar proportion of divers have a POF . Culculated
a- RR.
b-AR.
c-AR% .
d-PAR .
NOTE :-
1- When the disease is rare so a/a+b =a/b and c/c+d = c/d , therefore the odds ratio closely approximates the RR if the disease is rare . when there is chronic disease , but low prevalence (less than 10%) OR=RR .

E.G :- In a study about lung CA in smokers , (90) cases of lung CA , were diagnosis in smokers in a population of (100000) person . these figures were compared to only (7) cases of lung CA among non-smokers . This study was performed in a population known to be of low smoking prevalence , where the prevalence of smoking was only (2%) calculated :- a- RR , b-AR , c-AR% , d-PAR .

Q/4 . What is risk ?

Risk --- probability of an event to occur . (this event is either dangerous or not) .

Q/5. What is the difference between a risk and a rate ?

Rate mathematical expression between 2 variables , so it is the only measure that represent the risk . Any rate must have three measures . 1- It is a proportion 2- Time factor 3- Population at risk .