Measure of Association

Examples of measure of association

Epidemiologists usually use relative differences to assess causal association (Table 3-1).

Table 3 – 1 Types of Measures of Association Used in Analytic Epidemiologic Studies

Type	*Examples*	*Usual application*
Absolute difference	Attributable risk in exposed	Primary prevention impact search for causes
	Population attributable risk	Primary prevention impact
	Efficacy	Impact of intervention on recurrences, case fatality, etc
	Mean differences (continuous outcomes)	Search for determinants
Relative difference	Relative risk/rate	Search for causes
	Relative odds	Search for causes

RARE DISEASE:

When the probability (risk) of developing disease is low for both the exposed and the unexposed groups, the probability odds of developing the disease approximate the probabilities.

Table 3 – 3 Hypothetical Cohort Study of the 1 – Year Incidence of Acute Myocardial Infarction in Individuals with Severe Systolic Hypertension (≥ 180 mm Hg) and Normal Systolic Blood Pressure (< 120 mm Hg)

		Myocardial Infarction			
Blood Pressure Status	Number	Present	Absent	Probability	Probability Odds $_{dis}$
Severe Hypertension	10,000	180	9820	180/10,000 = 0.0180	180/(10,000 – 180) = 180/9820 = 0.01833
Normal	10,000	30	9970	30/10,000 = 0.0030	30/(10,000 – 30) = 30/9970 = 0.00301

RR = 0.0180 / 0.0030 = 6.00

Probability OR = 0.01833/ 0.00301 = 6.09

COMMON DISEASE:

OR is biased estimation of the probabilities.

Table 3 – 4 Incidence of Local Reactions in the Vaccinated and Placebo Groups, Influenza Vaccination Trial

		Local Reaction			
Group	Number	Present	Absent	Probability	Probability Odds $_{dis}$
Vaccine	2570	650	1920	650/2570 = 0.2529	650/(2570 – 650) = 650/1920 = 0.3385
Placebo	2410	170	2240	170/2410 = 0.0705	170/(2410 – 170) = 170/2240 = 0.0759

Note : Based on data for individuals 40 years old or older in Seltser et al. To avoid rounding ambiguities in subsequent examples based on these data)Figure 3 – 4 , Tables 3 – 7 and 3 – 9), the original sample sizes in Seltzer et al's study (257 vaccinees and 241 placebo recipients) were multiplied by 10.

Source : Data from R Seltser, PE Sartwell, and JA Bell, A Controlled Test of Asian Influenza Vaccine in Population of Families, American Journal of Hygiene, Vol 75, pp 112-135,© 1962.

RR = 0.2529 / 0.0705 = 3.59

Probability OR = 0.3385/ 0.0759 = 4.46

OR_{exp} and OR_{dis}: all cases and all noncases

Table 3 – 5 Hypothetical Case-Control Study of Myocardial Infarction in Relation to Systolic Hypertension, Based on a 1- Year Complete Follow-up of the Study Population from Table 3-3

Systolic Blood Pressure Status*	Myocardial Infarction: Present	Myocardial Infarction: Absent
Severe hypertension	180 (a)	9820 (b)
Normal	30 (c)	9970 (d)
Total	210 (a + c)	19790 (b + d)

* Severe systolic hypertension ≥ 180 mm Hg, and normal systolic blood pressure < 120 mm Hg.

For the example shown in Table 3 – 5, the OR_{exp} is

$$OR_{exp} = \frac{\frac{180}{30}}{\frac{9820}{9970}} = \frac{180 \times 9970}{9820 \times 30} = 6.09 = OR_{dis}$$

OR_{exp} and OR_{dis}: all cases and 10% of noncases

If 100% of cases and example of approximately 10% of the noncases were studies, assuming no random variability, results would be identical to those obtained when including all noncases, as in table 3-5.

Table 3 – 6 Case – Control Study of the Relationship of Myocardial Infarction to Presence of Severe Systolic Hypertension Including All Cases and a 10% Sample of Noncases from Table 3 – 5

	Myocardial Infarction	
Systolic Blood Pressure Status*	Present	Absent
Severe hypertension	180 (a)	982 (b)
Normal	30 (c)	997 (d)
Total	210 (a + c)	1979 (b + d)

* Severe systolic hypertension ≥ 180 mm Hg, and normal systolic blood pressure < 120 mm Hg.

$$OR_{exp} = \frac{\frac{180}{210}}{\frac{30}{982}} = \frac{180 \times 997}{982 \times 30} = 6.09 = OR_{dis}$$

OR_{exp} and OR_{dis}: 80% of cases and 50% of noncases

Example of the fact that the OR_{exp} is the same as the OR_{dis} . This is the reason why the interpretation of the OR in case- control study is prospective.

Sampling method and data are shown in figure 3-4 and table 3-7.

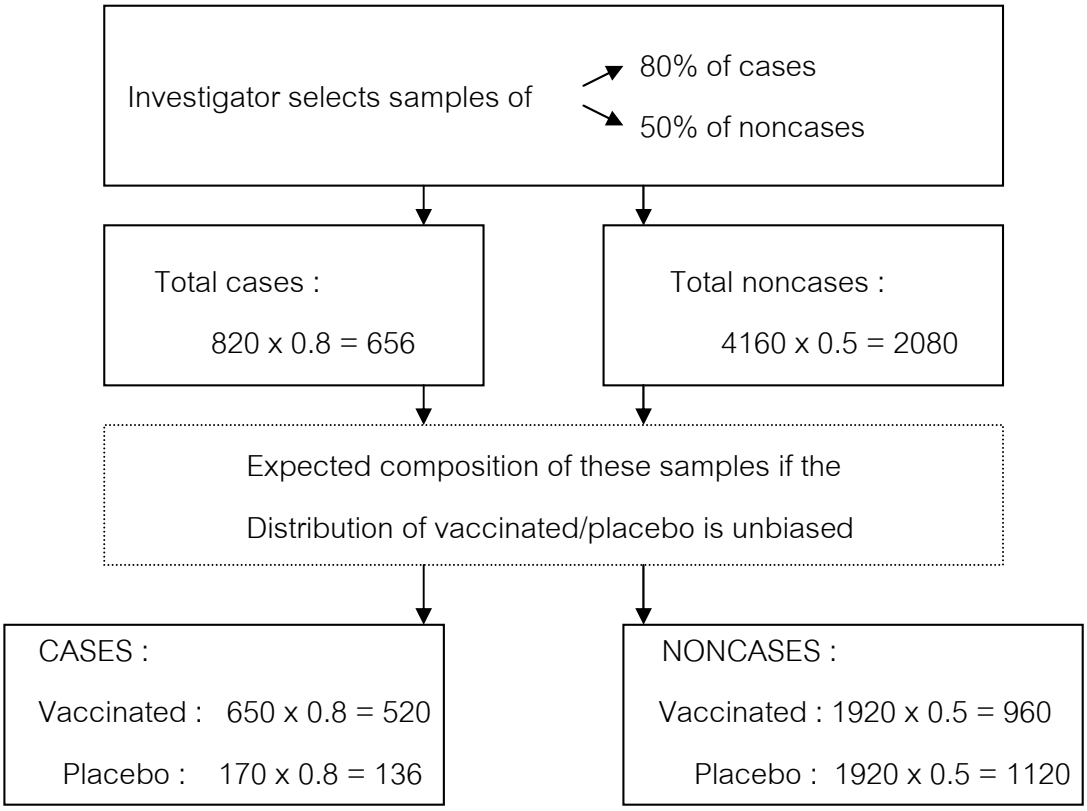

Figure 3 – 4 Selection of 80% of total cases and 50% of noncases in a case-control study from the study population shown in Table 3 – 4 . Expected composition is assuming no random variability. Source : Data from R Seltser, PE Sartwell, and JA Bell, A Controlled Test of Asian Influenza Vaccine in a Population of Families, American Journal of Hygiene, Vol 75, pp 112-135, © 1962.

Table 3–7 Case – Control Study of the Relationship Between Occurrence of Local Reaction and Previous Influenza Immunization

Vaccination	*Cases of Local Reaction*	*Controls Without Local Reaction*
Yes	520	960
No	136	1120
Total	820 x 0.8 = 656	4160 x 0.5 = 2080

Note : Based on a perfectly representative sample of 80% of the cases and 50% of the controls from the study population shown in Table 3-4 (see Figure 3 – 4).

Source : Data from R Seltser, PE Sartwell, and JA Bell, A Controlled Test of Asian Influenza Vaccine in a Population of Families, *American Journal of Hygiene,* Vol 75, pp 112-135 , © 1962.

$$OR_{exp} = \frac{\left[\frac{520}{136}\right]}{\left[\frac{960}{1120}\right]} = 4.46 = OR_{dis}$$

CASE-CONTROL STUDY:

1. Unmatched case-control design

No need for rarity assumption when

1.1 Control are the total study population at baseline (not only the noncase).

$$OR_{exp} = \frac{\text{Odds}_{\text{exp cases}}}{\text{Odds}_{\text{exp total population}}} = \frac{\left(\frac{a}{c}\right)}{\left(\frac{a+b}{c+d}\right)} = \frac{\left(\frac{a}{a+b}\right)}{\left(\frac{c}{c+d}\right)} = RR$$

Example of control group is from the total study population at baseline.

Table 3-8 Cross – Tabulation of a Defined Population by Exposure and Disease Development

Exposure	*Cases*	*Noncases*	*Total Population (Cases + Noncases)*
Present	a	b	a + b
Absent	c	d	c + d

OR_{exp} is an unbiased estimation of RR

$$OR_{exp} = \frac{\text{Odds}_{\text{exp cases}}}{\text{Odds}_{\text{exp pop}}} = \frac{\left(\frac{650}{170}\right)}{\left(\frac{2570}{2410}\right)} = \frac{\left(\frac{650}{2570}\right)}{\left(\frac{170}{2410}\right)} = \frac{q+}{q-} \qquad 3.59 = RR$$

1.2 Case-cohort study design

Example of a sample of cases and a sample of control group (from the total study population).

Table 3 –9 Case – Cohort Study of the Relationship of Previous Vaccination to Local Reaction

Previous Vaccination	Cases of Local Reaction	Cohort Sample
Yes	260	514
No	68	482
Total	328	996

Note : Based on a random sample of the study population in Table 3-4 , with sampling fractions of 40% for the cases and 20% for the cohort.

Source : Data from R Seltser, PE Sartwell, and JA Bell, A Controlled Test of Asian Influenza Vaccine in a Population of Families, *American Journal of Hygiene,* Vol 75, pp 112 – 135, © 1962.

Based on case-cohort study, RR can be estimated directly and need not to rely on rarity assumption. In addition, Pop AR can be estimated.

$$OR_{exp} = \frac{\frac{260}{68}}{\frac{514}{482}} = 3.59 = RR$$

Summary of the Influence of Control Selection

Table 3-10 Summary of the Influence of Control Selection on the Parameter Estimated by the Odds Ratio of Exposure in Case – Control Studies Within a Defined Cohort

Design	*Population Frame for Control Selection*	*Exposure Odds Ratio Estimates*
Case –cohort	Total cohort at baseline	Cumulative incidence ratio (relative risk)
	(Total cohort at baseline minus cases that develop during follow-up)	(Probability odds ratio)
Nested case-control	Population at approximate times when cases occur During follow-up	Rate (density) ratio
	(Population during follow-up minus cases)	(Density odds ratio)

Calculation of the OR when there are more than two exposure categories.

Table 3 –11 Distribution of Cases of Craniosynostosis and Normal Controls According to Maternal Age

Maternal Age (Years) (1)	*Cases* (2)	*Controls* (3)	*Odds of Specified Maternal Age vs Reference in Cases* (4)	*Odds of Specified Maternal Age vs Reference in Controls* (5)	*Odds Ratio* (6) = (4)/(5)
<20	12	89	12 / 12	89 / 89	1.00*
20 – 24	47	242	47/ 12	242 / 89	1.44
25 – 29	56	255	56/ 12	255 / 89	1.63
>29	58	173	58/12	173 /89	2.49

* Reference category.

Source : Data from BW Alderman et al, An Epidemiologic Study of Craniosynostosis : Risk Indicators for the Occurrence of Craniosynostosis in Colorado, American Journal of Epidemiology, Vol 128 , pp 431-438,

Step for a calculation of the OR_{exp}

You should approach history of exposure rather than cross-product. concept to avoid confusion of 2x2 table arrangement. .

Exposure	*Controls*	*Cases*
Yes	“a”	“b”
No	“c”	“d”

$$OR_{exp} = \frac{\text{Odds}_{\text{exp cases}}}{\text{Odds}_{\text{exp controls}}}$$