Measures of association

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Measures of association

They convey the degree of association between a **determinant** and a **parameter of occurrence**.

They are obtained by comparing the parameter of occurrence in different determinant categories with the parameter of occurrence in a reference category.

For instance, the incidence of hepatic cirrhosis among HBsAg positive people will be compared with the incidence among HBsAg negative people.

Measures of association

ABSOLUTE MEASURES

Risk Difference (RD)

«Rischio Attribuibile» (RA) in Italian

$RD = I_1 - I_0$

Risk difference = difference between incidence among the exposed and incidence among the unexposed

Important for public health

RELATIVE MEASURES

Relative Risk (RR), Rate Ratio or Hazard Ratio (RR)

“Rischio Relativo” in Italian

$RR = I_1 / I_0$

Relative risk = ratio of incidence among the exposed and incidence among the unexposed

Important to address causes (etiology) of diseases

	non-smokers	smokers
Lung cancer	0.1 / 1000 person*years	1.4 / 1000 person*years
Myocardial ischemia	4.13 / 1000 person*years	6.69 / 1000 person*years

	Risk difference	Relative risk
Lung cancer	1.3 / 1000 person*years	14
Myocardial ischemia	2.56 / 1000 person*years	1.62

The cause-effect relation between cigarette smoke and lung cancer is much stronger than the cause-effect relation between smoke and myocardial ischemia (RR:14 vs 1.62).

However the association between smoke and myocardial ischemia is more important from a public health perspective (RD: 2.56/1000 vs 1.3/1000 person*years).

$$\frac{1.4}{\cancel{1000\ py}} * \frac{\cancel{1000\ pa}}{0.1} = 1.4 / 0.1 = 14$$

Measures of association

ABSOLUTE MEASURES

RELATIVE MEASURES

Etiologic fraction

$(I_1 - I_0) / I_1$

To compute etiologic fraction:

1) Compute the difference between incidence among exposed and incidence among unexposed.
2) Divide the difference by incidence among exposed.

Important to address causes (etiology) of diseases.

	non-smokers	smokers
Lung cancer	**0.1 / 1000 person*years**	**1.4 / 1000 person*years**
Myocardial ischemia	**4.13 / 1000 person*years**	**6.69 / 1000 person*years**

	Etiologic fraction
Lung cancer	$\frac{1.4/1000 \text{ p.y.} - 0{,}1/1000 \text{ p.y.}}{1.4 / 1000 \text{ p.y.}}$ **= 0.929 = 92.9 %**
Myocardial ischemia	$\frac{6.69/1000 \text{ p.y.} - 4.13/1000 \text{ p.y.}}{6.69 / 1000 \text{ p.y.}}$ **= 0.383 = 38.3 %**

92.9% of smokers with lung cancer would not have had the disease, if they hadn't smoked.

38.3% of smokers with myocardial ischemia would not have had the disease, if they hadn't smoked.

EXERCISE: The incidence of bronchial carcinoma in people aged 45-54 years is addressed.

incidence in smokers (I_1) = 67.0 / 100,000 person*years

Incidence in non-smokers (I_0) = 5.8 / 100,000 person*years

$$\text{Risk difference (RD)} = I_1 - I_0 = \frac{67}{100{,}000 \text{ py}} - \frac{5.8}{100{,}000 \text{ py}} = \frac{61.2}{100{,}000 \text{ person*years}}$$

$$\text{Relative risk (RR)} = I_1 / I_0 = \frac{67 / 100{,}000 \text{ person*years}}{5.8 / 100{,}000 \text{ person*years}} = 11.55$$

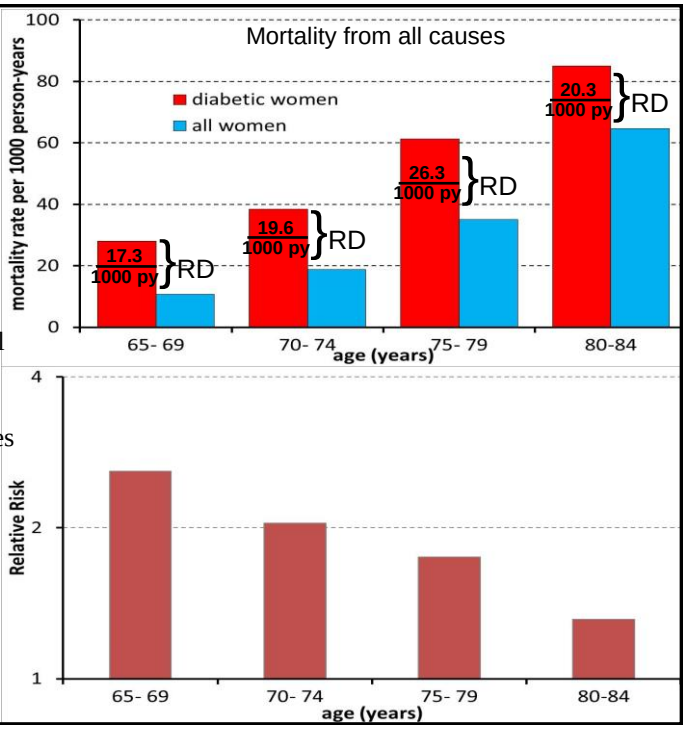
$$\text{Etiologic fraction} = (I_1 - I_0) / I_1 = \frac{67 / 100\,000 \text{ py} - 5.8 / 100{,}000 \text{ py}}{67 / 100{,}000 \text{ person*years}} = \frac{61{,}2 \text{ py}}{67 \text{ py}} = 0.91$$

Smoke is associated with 61.2 additional cases of bronchial carcinoma per 100,000 smokers every year (RD). This figure allows to evaluate the impact of smoke on the onset of bronchial carcinoma from a Public Health perspective.

The risk of bronchial carcinoma is 11 times higher in smokers than in non-smokers (RR). This figure suggests that a strong association exists between smoke and bronchial carcinoma, probably reflecting a cause-effect relation.

91.3% of smokers with bronchial carcinoma would not have had the disease if they had not smoked (etiologic fraction).

In many epidemiological settings, RA remains constant while RR decreases, as age increases



Odds

The horse Varenne has 20% chances to win a race.

The horse Varenne → 20% chances to win

The horse Varenne → 80% chances to lose

Odds of winning = 20 / 80 = 1 / 4 = 0.25

Hence Varenne is given 4 to 1

If you bet 1000 € on Varenne winning one hundred times,
you should win 4,000 € twenty times, 80,000 € overall,
you should lose 1000 € eighty times, 80,000 € overall,
so that losses are balanced by wins.

ODDS RATIO (OR) – 1

(in Italian «rapporto crociato», an indirect estimate of Relative Risk)

EXAMPLE:

A smoker has 40% chances to be hypertensive at an age of 60 years.

A non-smokers has 20% chances to be hypertensive when 60 years old.

1) Probability (p) → p (hypertension / smoker) = 40 / 100 = 0.4 = 40%

1) Probability (p) → p(hypertension / non-smoker) = 20/100 = 0.2 = 20%

2) Odds (ω) = $\frac{p}{1-p}$ → odds of hypertension in smokers = 40 / 60 = 0.67 = 67%

2) Odds (ω) = $\frac{p}{1-p}$ → odds of hypertension in non-smokers = 20/80 = 0.25=25%

3) Odds Ratio (O.R.) = $\frac{\frac{p_1}{1-p_1}}{\frac{p_0}{1-p_0}}$

odds ratio of hypertension in smokers with respect to non-smokers = 0.67 / 0.25 = 2.67

ODDS RATIO (OR) – 2

EXAMPLE: Risk factors for pleural mesothelioma are investigated:

1) All patients suffering from pleural mesothelioma (cases) are identified, and their exposure to asbestos (risk factor) is assessed.
2) Two controls are selected for each case, i.e. two individuals with the same characteristics (same age, sex, site of residence, profession, …).
3) Controls exposed to asbestos are identified.
4) Results are summarized through a 2*2 contingency table 2*2.

	cases (M+)	controls (M-)	
exposed (E+)	30	10	40
unexposed (E-)	20	90	110
	50	100	150

ODDS RATIO (OR) – 3

1) Let's compute the Relative Risk

It is not possible as incidence or prevalence among exposed and unexposed are unknown. The ratio of diseased to healthy people (cases / controls) is artificially established by the Researcher.

2) Ahi que aremos ? (Ahi, what shall we do?)

3) Let's devise a new measure of association, the Odds Ratio!

a) The odds of exposure is computed among cases

p(E+ / M+) = 30/50 p(E- / M+) = 20/50 $\text{odds} = \frac{30/50}{20/50} = \frac{30}{20}$

b) … and among controls

p(E+ / M-) = 10/100 p(E- / M-) = 90/100 $\text{odds} = \frac{10/100}{90/100} = \frac{10}{90}$

c) The Odds Ratio is computed

$$OR = \frac{\text{odds in cases}}{\text{odds in controls}} = \frac{30/20}{10/90} = \frac{30 * 90}{20 * 10} = \frac{27}{2} = 13.5$$

N.B. The Odds Ratio of exposure is equivalent to the Odds Ratio of disease in case-control study.

The Odds Ratio is close to the Relative Risk when p (probability) is low. In this case, 1-p ≈ 1 and hence the odds p/(1-p) ≈ p/1 = p.

The Odds Ratio is a measure somewhat difficult to understand, and should be abandoned according to some Authors.

However the Odds Ratio is necessary:

1) to evaluate case-control studies;

2) to express the results of a logistic regression model.

EXAMPLE

Randomized Clinical Trial: Helsinki Heart Study

Treatments: Group A: 2,051 patients treated with Gemfibrozil
Group B: 2,030 patients treated with placebo

Primary end-point: Cumulative incidence of myocardial infarction (fatal or not fatal) during a five-year follow-up

Results

Treatment	Number of events	Cumulative incidence	Patients without the event under study
Gemfibrozil	56	2.73% (56/2051)	97.27% (1995/2051)
Placebo	84	4.14% (84/2030)	95.86% (1946/2030)

Trial results

Measures of association	
ARR = Absolute Risk Reduction (*Differenza assoluta tra i rischi*)	4.14 – 2.73 = 1.41 %
RR = Relative Risk $_{\text{gemfibrozil versus placebo}}$ (*Rischio Relativo*)	2.73 / 4.14 = 0.659
RRR = Relative Risk Reduction (*Riduzione relativa del rischio*)	1.41/4.14 = 0.341 = 34.1%
Odds Ratio (OR) (*Rapporto crociato*)	(56*1946) / (84*1995) = 0.650
Number Needed to Treat (NNT) (patients to treat in order to prevent an event)	1/ 0.0141 = 70.9 ≈ 71

ODDS RATIO

	Gemfibrozil	Placebo
Probability of infarction= p(infarction)	0.0273 (56/2051)	0.0414 (84/2030)
1 – p(infarction)	1 – 0.0273 = 0.9727	1 – 0.0414 = 0.9586
Odds= p(infarction) / [1-p(infarction)]	0.0273/ 0.9727 =0.0281	0.0414/ 0.9586 =0.0432
Odds Ratio	0.0281 / 0.0432 = 0.650	