# Píndoles estadístiques UEB-VHIR

Odds-ratio, riscos relatius, riscos absoluts....Endreçant les idees



Divendres 28 de Juny de 12:30 a 13:30 Sala d'Actes de Traumatologia i Rehabilitació

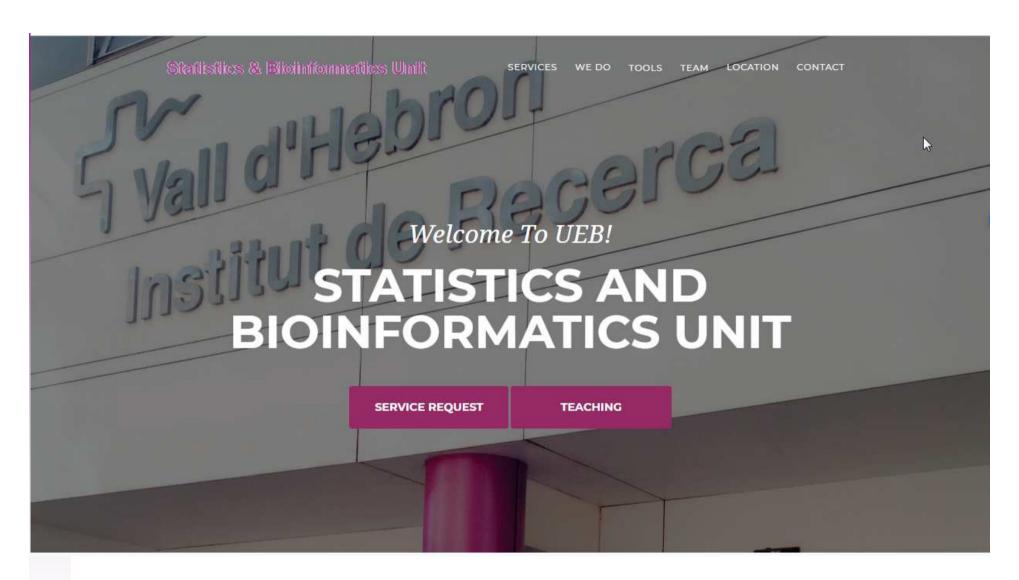
Les píndoles estadístiques son sessions divulgatives, organitzades per la Unitat d'Estadística i Bioinformàtica (UEB) del VHIR, on es presenten problemes i solucions estadístiques dirigides als professionals interessats del Campus Vall d'Hebron





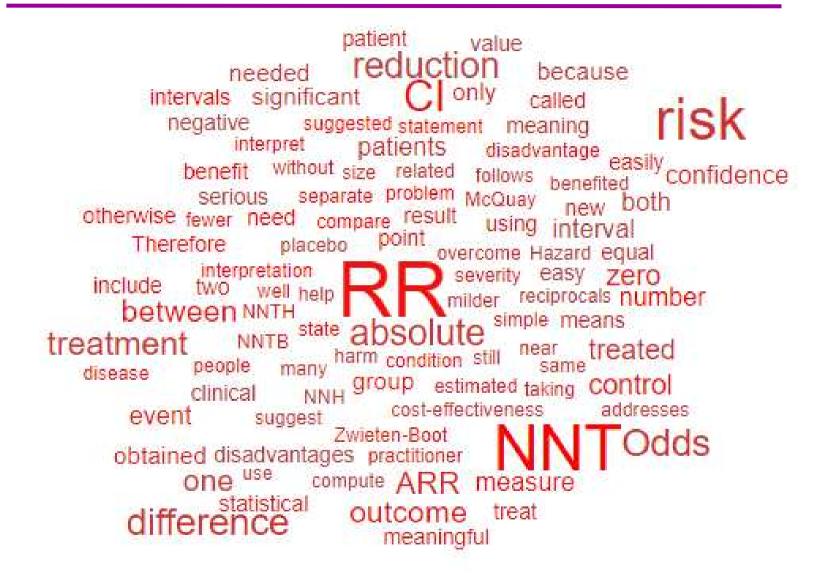






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#### Confusion in use of effect measures

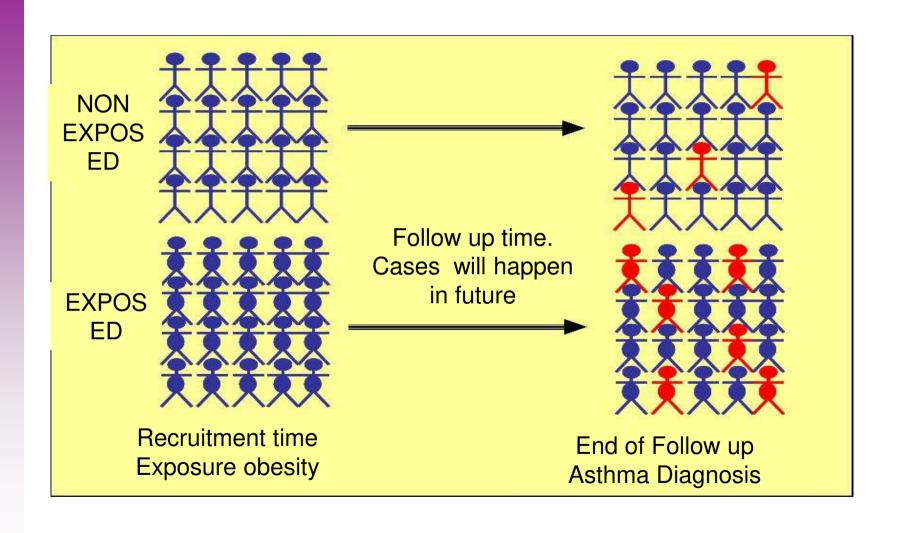


# The Question

- When a researcher want to compare two exposures or treatments with a binary outcome, several measures appear
  - RISK
  - ABSOLUTE RISK REDUCTION
  - RELATIVE RISK
  - ATRIBUTABLE RISK FRACTION
  - PREVENTABLE RISK FRACTION
  - NUMBER NEEDED TO TREAT
  - ODDS
  - ODSS RATIO
  - HAZARD
  - HAZARD RATIO

• . . . .

## Cohort or follow up Studies



#### Cumulative Incidence or Risk

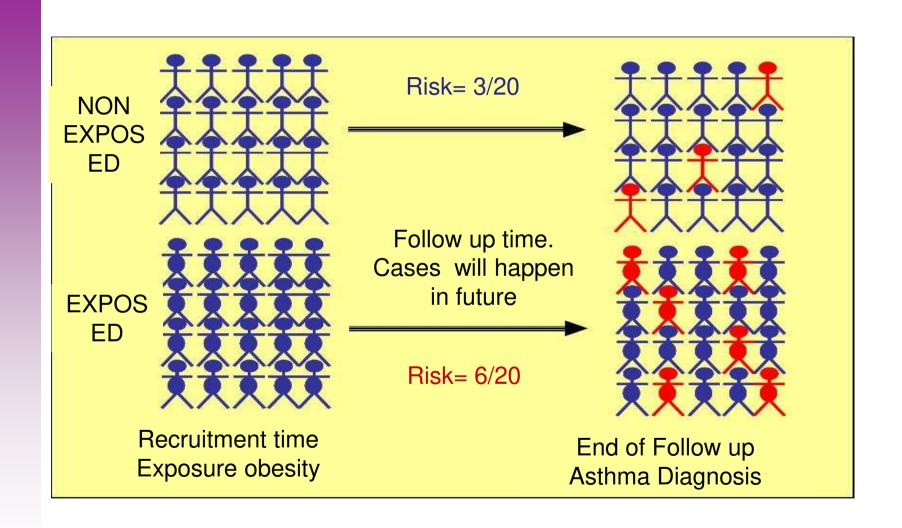
Number of new cases during a period

CI=

Number of subjects at risk at the beginning of follow-up

From a statistical view it's the conditional probability
of becoming a case during a specified period of
time given you are exposed or in treatment at the
beginning of follow up

## Cohort or follow up Studies



#### Risk

Disease
Present Absent

<u>a</u> <u>b</u>

<u>c</u> <u>d</u>

a, b, c, d are the number of subjects in each category

Risk of disease Exposed = a/(a+b)

Risk of disease No Exposed =

$$c/(c+d)$$

Exposed

Exposed

Non

#### Do not confound Risk with Prevalence

#### Prevalence<sub>t</sub>

Cases of disease in a instant or period of time t in a population. Probability one person of the population have the disease.

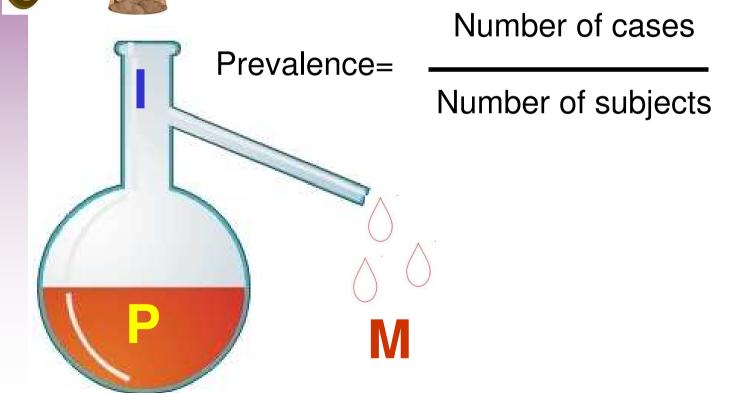
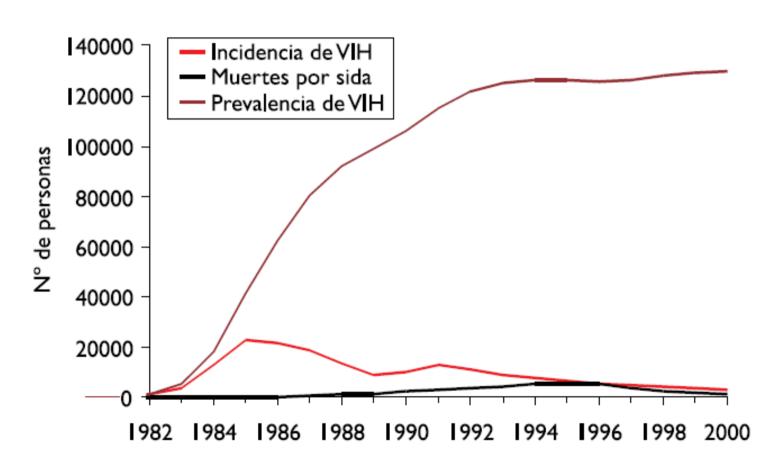


Figura 3. Simulación de la epidemia de VIH y sida en España.



## One consideration interpreting risk

 Physicians tend to consider risk in terms of the group of patients that they treat,

#### Whereas

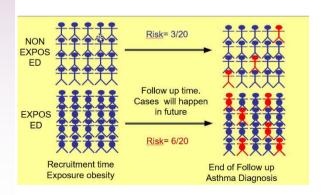
 Patients interpret risk as applying to their own individual case.

## How to compare RISK

#### Difference of Risk or Absolute Risk Reduction

ARR= Risk in exposed- Risk in non exposed

- Easy to compute and calculate confidence interval
- 0 in the confidence interval means no risk difference
- The main problem is that the same risk difference means not the same depending the underlying risk

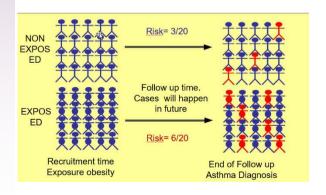


ARR=6/20-3/20=3/20

## How to compare RISK

#### Relative Risk

- Easy to compute and interpret as the excess or deffect of risk of exposed vs unexposed
- >1 means excess of risk
- <1 means deffect of risk</p>



$$RR = \frac{6/20}{3/20} = 2$$

## Relative Risk (RR)

	Disea: Present	
Exposed	<u>a</u>	<u>b</u>
Non exposed	<u>C</u>	<u>d</u>

a, b, c, d are the number of subjects in each category

Disease Risk in exposed relative to Disease risk in non exposed

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

## Which is the effect of the exposure

#### Attributable risk fraction

It is the excess of risk ought to factor exposure

Preventable risk fraction

It is the deffect of risk ought to factor exposure

Attributable Risk Fraction	RR	RR	Atributable Preventable Fraction
	1,0000	1,0000	
25% more	1,2500	0,8000	20% less
33% more	1,3333	0,7500	25% less
50% more	1,5000	0,6667	33% less
100% more	2,0000	0,5000	50% less
150% more	2,5000	0,4000	60% less
200% more	3,0000	0,3333	66% less
400% more	5,0000	0,2000	400% more

## Number needed to treat (NNT)

#### Number Needed to Treat (NNT):

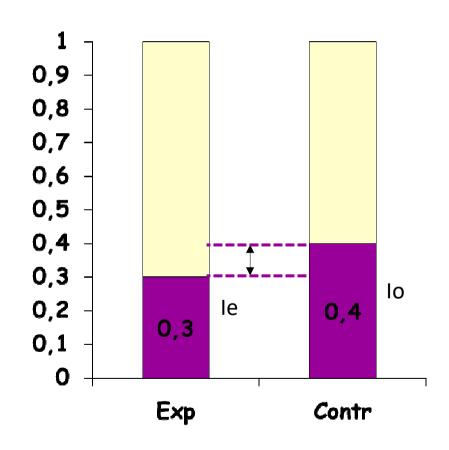
Number of persons who would have to receive an intervention for 1 to benefit.

#### Number Needed to Harm(NNH):

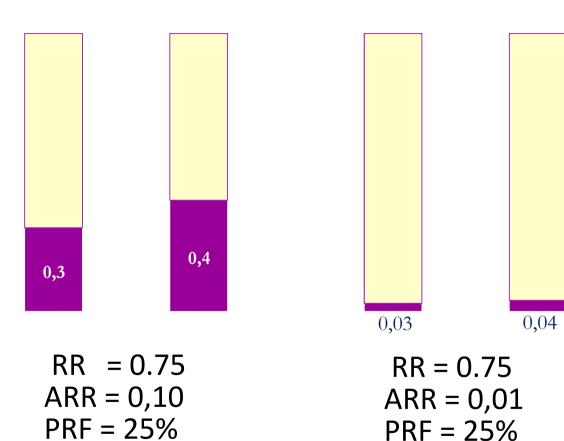
Number of persons who would have to receive an intervention for 1 to be experience a adverse event.

NNT= 1 /ARR=1

#### **Effect measures in Clinical Trial**



#### Effect measures in Clinical Trial



NNT = 10

PRF = 25%

NNT = 100

# Caution

Relation or excess of risk among exposed does not mean

#### How Common Is Attention-Deficit/ Hyperactivity Disorder?

#### Incidence in a Population-Based Birth Cohort in Rochester, Minn

William J. Barbaresi, MD; Slavica K. Katusic, MD; Robert C. Colligan, PhD; V. Shane Pankratz, PhD; Amy L. Weaver, MS; Kevin J. Weber, PhD; David A. Mrazek, MD; Steven J. Jacobsen, MD, PhD

Table 5. Cumulative Incidence of AD/HD in the 1976-1982 Birth Cohort\*

	Cumulative Incidence of AD/HD by Age 19 Years, % (95% CI)	Mean ± SD Age at Which Research Criteria Were Fulfilled, y	M/F Relative Risk (95% CI)
Definite AD/HD			
Overall	7.5 (6.5-8.4)	$10.2 \pm 3.5$	3.1 (2.3-4.0)
Males	10.8 (9.3-12.3)	$10.0 \pm 3.4$	, ,
Females	3.9 (2.8-5.1)	10.8 ± 3.8	
Definite AD/HD plus probable AD/HD	, ,		
Overall	9.4 (8.3-10.4)	10.4 ± 3.6	3.0 (2.3-3.8)
Males	13.3 (11.7-15.0)	10.2 ± 3.4	, ,
Females	5.1 (3.8-6.4)	11.2 ± 4.0	
Definite AD/HD plus probable AD/HD plus questionable AD/HD	,		
Overall	16.0 (14.7-17.3)	$10.6 \pm 3.5$	2.3 (2.0-2.8)
Males	21.1 (19.1-23.0)	$10.3 \pm 3.3$	, ,
Females	10.5 (8.8-12.2)	11.1 ± 3.8	

<sup>\*</sup>AD/HD indicates attention-deficit/hyperactivity disorder; CI, confidence interval.

#### Other measure of risk: Odds

"Odds" is often known as the ratio of money that may be won versus the amount of money bet

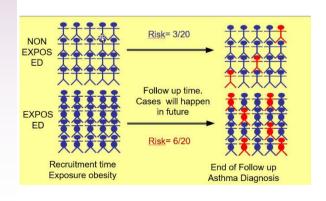
In Statistics, is the probability of being case vs the probability of being no case

ODSS= Number of cases

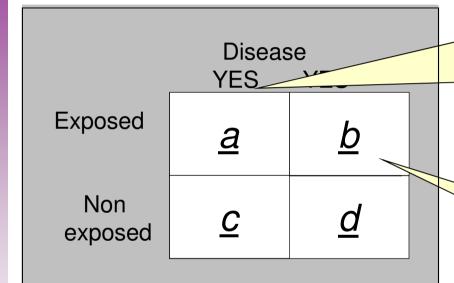
Number of no cases

Odds Exposed=6/14

Odds no exposed= 3/17



#### **ODDS**



Odds of disease in exposed a/b

a, b, c, d number of subjects in each cell

Odds of disease in non exposed c/d

# Odds vs Risk

Risk Odds

# Odds vs Risk

Cases	Non cases	Risk	Odds	
1	999	0,0010	0,0010	
10	990	0,0100	0,0101	
100	900	0,1000	0,1111	
200	800	0,2000	0,2500	
300	700	0,3000	0,4286	
400	600	0,4000	0,6667	
500	500	0,5000	1,0000	
600	400	0,6000	1,5000	
700	300	0,7000	2,3333	
800	200	0,8000	4,0000	
900	100	0,9000	9,0000	
990	10	0,9900	99,0000	
999	1	0,9990	999,0000	

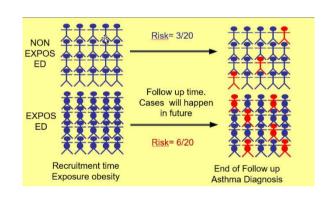
## **Odds Interpretation**

- Difficult to interpret if you are not used to bets
- It can be calculated in cross-sectional and case/control studies (not need follow up)
- It is similar to Risk if incidence/prevalence is low



#### **Odds Ratio**

#### **Odds Ratio**

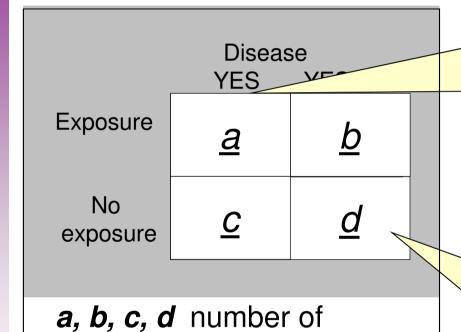


Odds Exposed=6/14

Odds no exposed= 3/17

OR = 6/14 / 3/17 = 6\*17/14\*3 = 2.43

#### **ODDS** Ratio



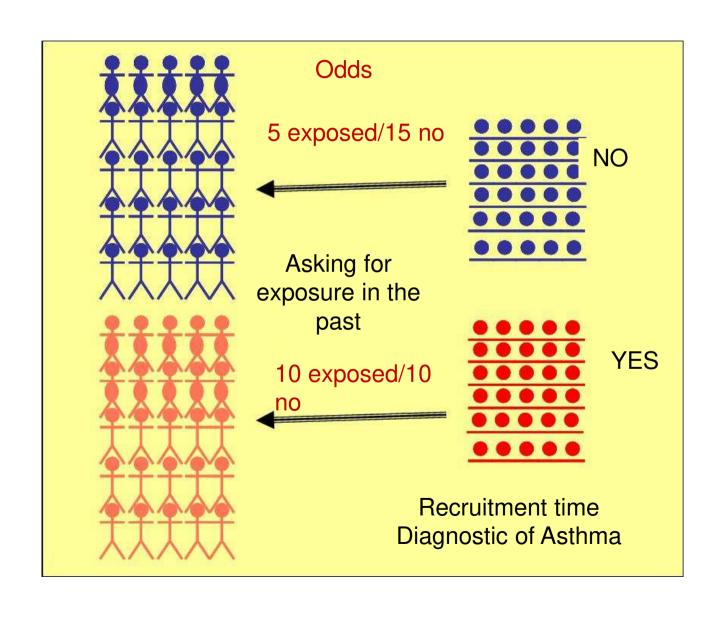
subjects in each cell

Odds of disease in exposed a/b

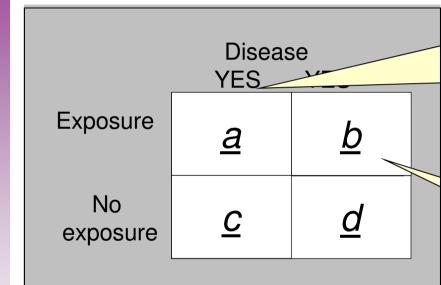
Odds of disease in non exposed c/d

$$\frac{\frac{a}{b}}{\frac{c}{d}} = \frac{ad}{bc}$$

#### **Case-Control Studies**



#### **ODDS**

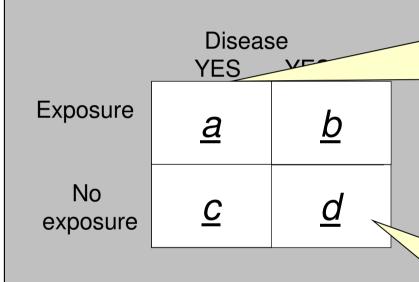


a, b, c, d number of subjects in each cell

Odds of exposure in disease a/c

Odds of exposure in healthy b/d

#### **ODDS** Ratio



a, b, c, d number of subjects in each cell

Odds of exposure in disease a/C

Odds of exposure in healthy b/d

$$\frac{\frac{a}{c}}{\frac{b}{d}} = \frac{ad}{bc}$$

OR=(10/10)/(5/15)=3

# Example



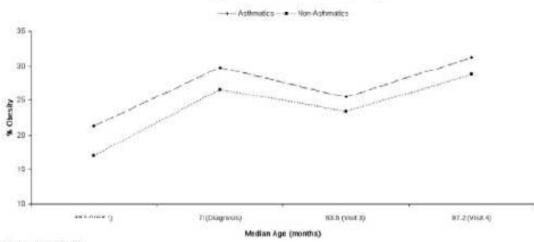


Table 2. Data for Asthma According to BMI Status in a Longitudinal Model

Model	Odds ratio (95% confidence interval) for cases*	value
Age-adjusted model	1.30 (0.64 2.65)	.46
Model further adjusted for atopic dermatitis	1.20 (0.55 2.60)	.65
Model further adjusted for food and other allergies	1.18 (0.54 2.58)	.69
Model further adjusted for allergic rhinitis	0.92 (0.40 2.15)	.86

Abbreviation: BMI, body mass index.

ercentage overweight and risk of overweight of cases and ling to age and visit number.

<sup>\*</sup> The reference group was controls (odd ratio of 1 for all).

## Why use Odds Ratio?

- Provide an estimate( and confidence interval) or effect measure of the relationship between a binary outcome and an exposure or treatment variable
- The effects of other variables can be controlled using a logistic regression. The OR is the natural way of represent results for this regression model
- Can be used in case-control and cross-sectional models

#### **Example Logistic Regression Case-Control Study**

Table 1
Distribution of studied variables in cases and controls

	Case		Control		OR <sup>a</sup>	95% Confid	95% Confidence interval	
	$\overline{N}$	%	$\overline{N}$	%				
Influenza vaccine	168	58.5	318	61.0	0.91	0.68	1.23	
Pneumococcal vaccine	112	41.9	169	34.3	1.34	0.98	1.84	

Table 2
Effectiveness of the influenza vaccination in preventing emergency admission for pneumonia, adjusted analysis

	Odds ratio of being case	95% Confidence interval		P-value	
Vaccinated for influenza	0.52	0.34	0.80	0.003	
Pneumococcal vaccination	1.52	1.01	2.29	0.047	
Co-morbidity					
Heart disease	1.59	1.08	2.35	0.020	
COPD	2.97	1.84	4.78	< 0.001	
Asthma	2.34	0.94	5.83	0.068	
Smoking habit					
Ex-smoker	0.70	0.34	1.42	0.318	
Recent ex-smoker	0.28	0.09	0.87	0.027	
Smoker	0.27	0.11	0.66	0.004	
Visits to the doctor during the last 3	3 months				
1–2 times	3.49	0.87	13.99	0.078	
3–6 times	3.97	1.03	15.29	0.045	
More than 6	4.09	0.98	17.05	0.053	
Barthel <60	3.71	0.84	16.37	0.083	

Puig-Barberà, J., Diez-Domingo, J., Pérez Hoyos, S., Belenguer Varea, Á., & González Vidal, D. (2004). Effectiveness of the MF59-adjuvanted influenza vaccine in preventing emergency admissions for pneumonia in the elderly over 64 years of age. Vaccine, 23(3), 283–289.

#### Problems with the use of Odds Ratio?

- Difficult to understand for users. Two times more risk is understable, but not two times more of odds
- Odds Ratio are often missinterpreted as meaning the same as relative risk. It is not true. It depends on the disase magnitude.
- Only if frequency of disease is very low (rare disease) figures of odds ratio are similar to relative risk, in other case OR overestimate RR.
- However, the rank and the sense of the relation is the same for both effect measures.
- Several methods have been proposed for relate OR and RR but are confusing and have been criticized.

Table 2. Divergence of Odds Ratios From Relative Risks as the Probability of an Event in a Comparison Group (Nonmembers of the National Psoriasis Foundation) Increases\*

Example	Probability of a Yes Outcome		Odds of a Yes Outcome		Members Compared With Nonmembers	
	Among Nonmembers	Among Members	Among Nonmembers	Among Members	Relative Risk of a Yes Outcome	Odds Ratio of a Yes Outcome
1	0.0001	0.0003	0.0001	0.0003	3	3.0006
2	0.001	0.003	0.002	0.003	3	3.01
3	0.01	0.03	0.01	0.03	3	3.06
4	0.02	0.06	0.02	0.06	3	3.13
5	0.05	0.15	0.05	0.18	3	3.35
6	0.1	0.3	0.11	0.43	3	3.86
7	0.15	0.45	0.18	0.82	3	4.64
8	0.2	0.6	0.25	1.5	3	6.0
9	0.25	0.75	0.33	3.0	3	9.0
10	0.3	0.9	0.43	9.0	3	21.0
11	0.33	0.99	0.49	99.0	3	201.0

<sup>\*</sup>In all of these hypothetical cases, the probability of a yes outcome is lower among nonmembers than among members. Members are 3 times more likely than nonmembers to have a yes outcome. Therefore, the relative risk of a yes outcome is always 3. As the probabilities of a yes outcome proportionately increase among members and nonmembers, the odds ratios increase dramatically and increasingly diverge from the (constant) relative risks.

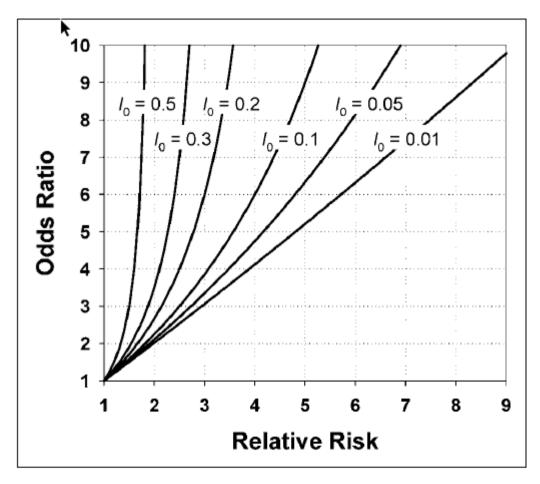


Figure 1 Relationship between Odds Ratio and Relative Risk for various incidence rates

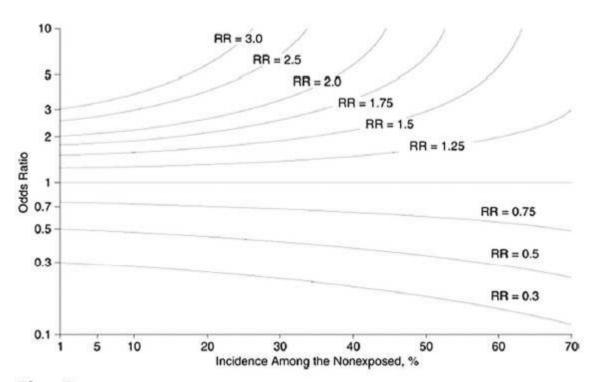
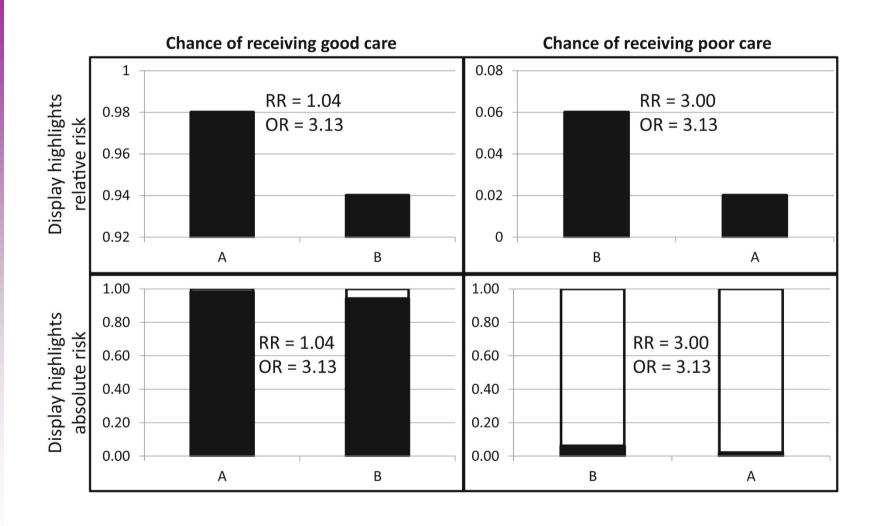


Fig. 2 The relationship between risk ratio (RR) and odds ratio by incidence of the outcome. Adapted from Zhang and Yu.8

Odds Ratios and Risk Ratios: What's the Difference and Why Does It Matter? Anthony J. Viera. *Southern Medical Journal* • Volume 101, Number 7, July 2008



Math Matters: How Misinterpretation of Odds Ratios and Risk Ratios May Influence Conclusions R. Christopher Sheldrick, PhD, Paul J. Chung, MD, MS, Robert M. Jacobson, MD. Academic Pediatrics 2017 17, 1-3DOI: (10.1016/j.acap.2016.10.008)

# Hazard rate $\lambda(t)=h(t)$

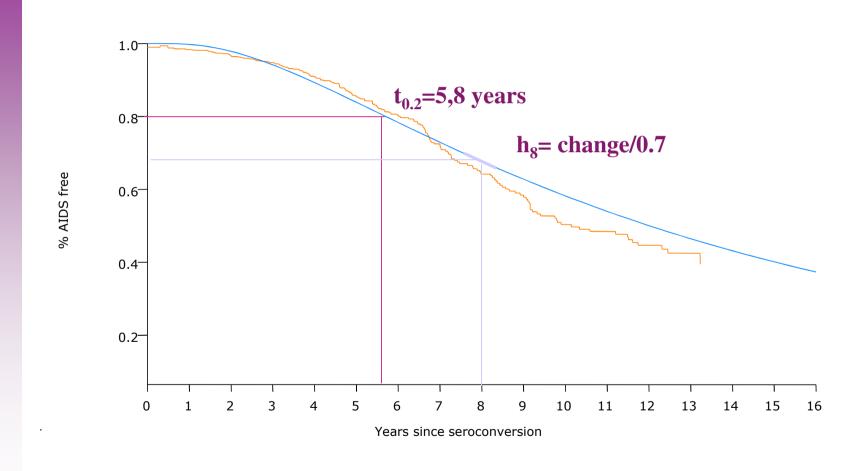
Instantaneous probability of death in an infinitesimal interval knowing to be alive at the beginning

$$C$$
 $t$ 
 $t+\Delta t$ 

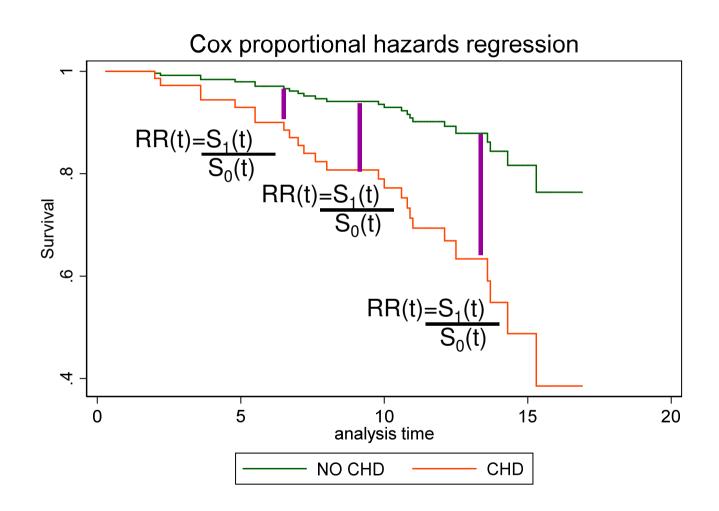
 $\lambda$  (t)=lim $\Delta$ t $\rightarrow$ 0 Prob(die in en (t,t+ $\Delta$ t)/alive at)/ $\Delta$ t =f(t)/S(t)

It is the speed of fall of the survival curve

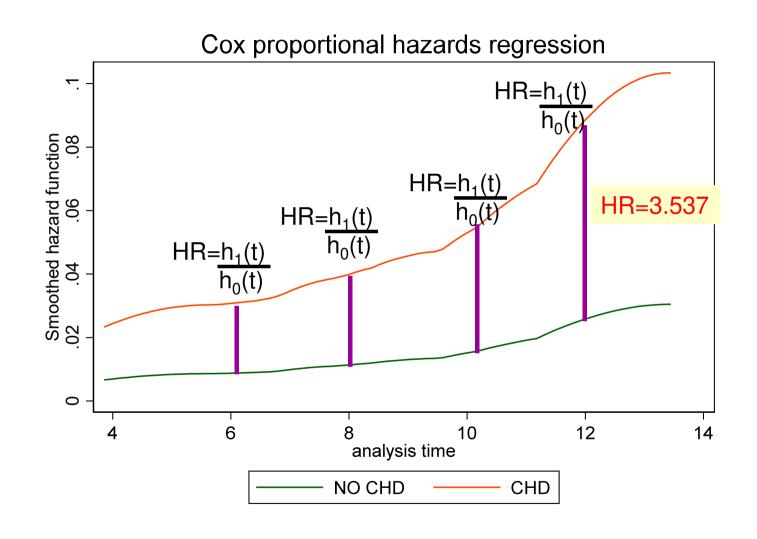
# Hazard rate $\lambda(t)=h(t)$



# Example survival curves



# Hazard rate $\lambda(t)=h(t)$ & Hazard Ratio (HR)



## Hazard Ratio (HR) vs Relative Risk (RR)

- HR is depending on time, but in a Cox model, HR is fixed an not dependent on time, is *fixed*.
- HR is a ratio of rates, RR is a ratio of probabilities
- So, HR is not an estimation of RR
- The direction of the relation is the same for both
- HR=2 must be interpreted as: The instantaneous rate at any time during follow up is twice for the exposed group
- The RR at any time of experience the event is not twice for the exposed group
- RR is not constant among time

## Summary

- Risk is the conditional probability of an event given an exposure
- Relative Risk is a measure of the effect of an exposure
- RR>1 means excess and RR<1 means less</li>
- OR is the ratio of ODDS, but it is only aproximate to RR for a low frequency event
- HR is used in survival analysis and it is not a R
- Be careful interpreting Effect measures



Any Question?