

Structure of epidemiological dataset

- In a typical epidemiological study, a range of different information is collected on each participant.
- A typical dataset then has:
 - Rows (normally each participant has one row)
 - Columns (normally each variable has one column)

Inspection of data

- It is crucial that you get familiar with your dataset:
 - Structure
 - Number of individuals
 - Variables
 - Range of values
 - Definitions
 - Outliers
 - Missingness
- Always inspect the raw dataset before any analysis

Measures of association

- Risk of disease, rate of disease in different groups of population
- Comparison of risks/rates

Constructing 2-way table

For binary health outcomes (Y/N), it is possible to construct 2x2 table and to estimate either relative or absolute measures of risk

	Disease		
Exposure	Yes	No	Total
Yes	a	b	a+b
No	c	d	c+d
Total	a+c	b+d	a+b+c+d

Example

- Random sample of individuals were questioned about their occupation and their BP was measured. Based on SBP and DBP measures they were classified as hypertensive or non-hypertensive. Among 300 people in non-manual jobs, there were 72 hypertensive individuals. Among 240 people in manual jobs, there were 96 hypertensive individuals.

Constructing 2-way table

As a first step we need to organize our data in a formal way
– we construct 2-way table

	Hypertension		
	Yes	No	Total
Manual	96	144	240
Non-manual	72	228	300
Total	168	372	540

What does it mean when we speak about an association between two categorical variables?

- It means that knowing the value of one variable tells us something about the value of the other variable.
- Two variables are therefore said to be associated if the distribution of one variable varies according to the value of the other variable.

What does it mean when we speak about an association between two categorical variables?

- In our example, the two variables, occupation and hypertension, are associated if the distribution of hypertension varies between occupational groups.
- And, if distribution of hypertension is same in both occupational groups, we can say that there is no association between hypertension and occupational category - because knowing a occupational category of individual will not tell us anything about hypertension.

What does it mean when we speak about an association between two categorical variables?

- Having constructed a two-way table, the next step is to look whether the distribution of one variable differs according to the value of the other variable.
- We need to calculate either row or column percentages.
- Often, one variable can be regarded as **the response variable**, while the other is **the explanatory variable**, and this should help to decide what percentages are shown
- If the columns represent the explanatory variable, then column percentages are more appropriate, and vice versa.


Constructing 2-way table

As a second step we calculate proportion of hypertensive individuals among manual workers, non-manual workers and in the whole sample

	Hypertension		
	Yes	No	Total
Manual	96 (40.0%)	144 (60.0%)	240
Non-manual	72 (24.0%)	228 (76.0%)	300
Total	168 (31.1%)	372 (68.9%)	540

The numbers in the four categories in the 2-way table in the previous slide all called

OBSERVED NUMBERS

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- The data seem to suggest some association between hypertension and occupation (40% of manual workers with hypertension compared to 24% of non-manual workers with hypertension)
 - The calculation and examination of such percentages is an essential step in the analysis of a two-way table, and should always be done before starting formal significance tests.

Significance test for the association

- Although it seems that there is an association in the table, the question is whether this may be attributable to sampling variability
- Each of the percentages in the table is subject to sampling error, and we need to assess whether the differences between them may be due to chance
- This is done by conducting a significance test
- The null hypothesis is “***there is no association between the two variables***”

Expected numbers

- The significance test is **Chi-squared test**
- This test compares the **observed** numbers in each of four categories of contingency table with the numbers to be **expected** if there was no difference in proportion of hypertensive individuals in two occupational groups

Expected numbers

	Hypertension		
	Yes	No	Total
Manual	74.64		240
Non-manual			300
Total	168 (31.1%)	372 (68.9%)	540

- From the table above, the overall proportion of hypertensive individuals is 168/372 (31.1%).
- If the null hypothesis were true, the expected number of manual subjects with hypertension is 31.1% of 240, which is 74.64

- Expected numbers in the other cells of the table can be calculated similarly, using the general formula:

$$\text{Expected number} = \frac{\text{Row total} \times \text{Column total}}{\text{Overall total}}$$

	Hypertension		
	Yes	No	Total
Manual	74.64	165.36	240
Non-manual	93.36	206.64	300
Total	168 (31.1%)	372 (68.9%)	540

Next step – compare observed and expected numbers

OBSERVED	Hypertension		
	Yes	No	Total
Manual	96	144	240
Non-manual	72	228	300
Total	168 (31.1%)	372 (68.9%)	540

EXPECTED	Hypertension		
	Yes	No	Total
Manual	74.64	165.36	240
Non-manual	93.36	206.64	300
Total	168 (31.1%)	372 (68.9%)	540

Chi-squared test (χ^2 test)

$$\chi^2 = \sum [(O - E)^2 / E]$$

- Calculate $(O-E)^2/E$ for each cell and sum over all cells

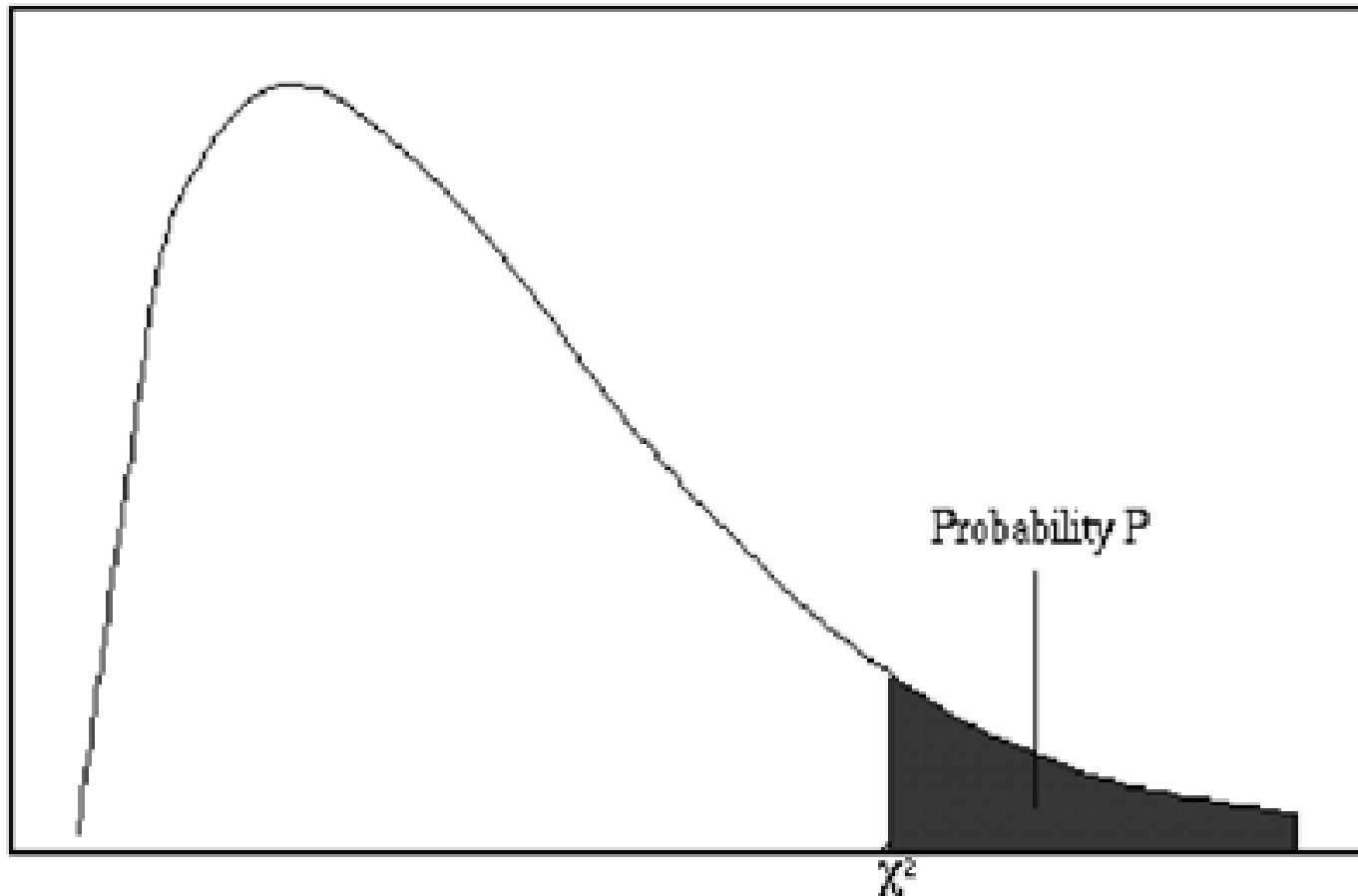
- In our example:

$$\chi^2 = [(96-74.64)^2 / 74.64 + (144-165.36)^2 / 165.36 + (72-93.36)^2 / 93.36 + (228-206.64)^2 / 206.64] = 15.97$$

- If χ^2 value is large then (O-E) is, in general, large and data do not support $H_0 =$ **association**
- If χ^2 value is small then (O-E) is, in general, small and data do support $H_0 =$ **no association**
- Large values of χ^2 suggest that the data are **inconsistent** with the null hypothesis, and therefore that there is an association between the two variables.

Obtaining p-value

- Under H_0 : χ^2 distribution



Obtaining p-value

- The P-value is obtained by referring the calculated value of χ^2 to tables of the chi-squared distribution.
- The P-value in this case corresponds to the value shown as α in the tables.
- The degrees of freedom are given by the formula:

$$d.f. = (r - 1) \times (c - 1)$$

- r = number of rows, c = number of columns

Table I. Critical Values of χ^2

<i>df</i>	LEVEL OF SIGNIFICANCE FOR TWO-TAILED TEST					
	.20	.10	.05	.02	.01	.001
1	1.64	2.71	3.84	5.41	6.64	10.83
2	3.22	4.60	5.99	7.82	9.21	13.82
3	4.64	6.25	7.82	9.84	11.34	16.27
4	5.99	7.78	9.49	11.67	13.28	18.46
5	7.29	9.24	11.07	13.39	15.09	20.52
6	8.56	10.64	12.59	15.03	16.81	22.46
7	9.80	12.02	14.07	16.62	18.48	24.32
8	11.03	13.36	15.51	18.17	20.09	26.12
9	12.24	14.68	16.92	19.68	21.67	27.88
10	13.44	15.99	18.31	21.16	23.21	29.59
11	14.63	17.28	19.68	22.62	24.72	31.26
12	15.81	18.55	21.03	24.05	26.22	32.91
13	16.98	19.81	22.36	25.47	27.69	34.53
14	18.15	21.06	23.68	26.87	29.14	36.12
15	19.31	22.31	25.00	28.26	30.58	37.70
16	20.46	23.54	26.30	29.63	32.00	39.29
17	21.62	24.77	27.59	31.00	33.41	40.75
18	22.76	25.99	28.87	32.35	34.80	42.31
19	23.90	27.20	30.14	33.69	36.19	43.82
20	25.04	28.41	31.41	35.02	37.57	45.32
21	26.17	29.62	32.67	36.34	38.93	46.80
22	27.30	30.81	33.92	37.66	40.29	48.27
23	28.43	32.01	35.17	38.97	41.64	49.73
24	29.55	33.20	36.42	40.27	42.98	51.18
25	30.68	34.38	37.65	41.57	44.31	52.62
26	31.80	35.56	38.88	42.86	45.64	54.05
27	32.91	36.74	40.11	44.14	46.96	55.48
28	34.03	37.92	41.34	45.42	48.28	56.89
29	35.14	39.09	42.69	46.69	49.59	58.30
30	36.25	40.26	43.77	47.96	50.89	59.70
32	38.47	42.59	46.19	50.49	53.49	62.49
34	40.68	44.90	48.60	53.00	56.06	65.25
36	42.88	47.21	51.00	55.49	58.62	67.99
38	45.08	49.51	53.38	57.97	61.16	70.70
40	47.27	51.81	55.76	60.44	63.69	73.40
44	51.64	56.37	60.48	65.34	68.71	78.75
48	55.99	60.91	65.17	70.20	73.68	84.04
52	60.33	65.42	69.83	75.02	78.62	89.27
56	64.66	69.92	74.47	79.82	83.51	94.46
60	68.97	74.40	79.08	84.58	88.38	99.61

Back to our example:

$$\chi^2 = 15.97$$

Table 2x2

d.f.=1

and from the table

$P < 0.001$

Quick formula

There is a quick formula for calculating chi-squared test for 2x2 table

			Total
	a	b	e
	c	d	f
Total	g	h	N

If we use following notation:

Quicker formula for calculating chi-squared test is

$$X^2 = \frac{N * (ad - bc)^2}{efgh}$$

d.f.=1

Larger tables (r x c tables)

$$X^2 = \sum \frac{(O - E)^2}{E}$$

$$\text{d.f.} = (r-1) \times (c-1)$$

- Valid if less than 20% of expected numbers are under 5 and none is less than 1
- If low expected numbers – combine either rows or columns to overcome this problem

How to calculate expected number in particular cell

$$\text{Expected number} = \frac{\text{Row total} \times \text{Column total}}{\text{Overall total}}$$

Interpretation of chi-square test results:

Chi-squared tests in STATA

- We try to evaluate whether there is an association between current smoking and age
- We have age grouped into 4 groups (30-39, 40-49, 50-59, 60-69)
- Smoking (variable smok) was coded 1=current smokers, 0=non-smokers

Let's check proportion of smokers in each age category

```
. tab smok agegroup, col
```

		30-39	40-49	50-59	60-69	Total
1=yes	0=no	30	40	50	60	
0		337	357	490	491	1,675
		54.71	56.31	72.38	78.81	65.69
1		279	277	187	132	875
		45.29	43.69	27.62	21.19	34.31
Total		616	634	677	623	2,550
		100.00	100.00	100.00	100.00	100.00

Chi-squared test

```
. tab smok agegroup, col chi
```

		30-39	40-49	50-59	60-69	Total
1=yes 0=no		30	40	50	60	
0		337	357	490	491	1,675
		54.71	56.31	72.38	78.81	65.69
1		279	277	187	132	875
		45.29	43.69	27.62	21.19	34.31
Total		616	634	677	623	2,550
		100.00	100.00	100.00	100.00	100.00

Pearson chi2(3) = 118.7458 Pr = 0.000

Degrees of freedom

Chi-squared test value

p<0.001

Measures of effect

- So far, χ^2 test – testing whether there is an association between two proportions using a 2x2 (or 2xn) table
- We are often interested in the relative difference between two proportions rather than the actual difference
- The effect estimates that we present are then ratios: there are three main measures we will use:
 - Rate ratio
 - Risk ratio
 - Odds ratio

Relative measures of effect (relative risk)

We have **2 groups** of individuals:

- An **exposed** group (group with risk factor of interest) and **unexposed** group (without such factor of interest)
- We are interested in comparing the amount of disease (mortality or other health outcome) in the exposed group to that in the unexposed group

Risk/rate

- Measures the strengths of association between the risk factor and disease
- Incidence rate or Risk in exposed (r_1)
- Incidence rate or Risk in unexposed (r_0)

Risk ratio

- we calculate the risk ratio (RR) as:

$$RR = r_1 / r_0$$

Risk difference

- the absolute difference between two risks (or rates)

$$RD = r_1 - r_0$$


Example: cohort study of oral contraceptive use and heart attack

	Myocardial infarction		Total
	Yes	No	
OC use			
Yes	25	400	425
No	75	1500	1575
Total	100	1900	2000

Risk (exposed) = $25/425=0.059$

Risk (unexposed) = $75/1575=0.048$

Relative risk = $0.059/0.048 = 1.23$

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- We can also have different strata of exposure. We may calculate ratio measures for each strata – we compare measure of frequency in each level with measure of frequency in the baseline (unexposed) level.
 - *Example: Death rates from CHD in smokers and non-smokers by age*

Age	Smokers rate	Non-smokers rate	Rate ratio
35-44	0.61	0.11	5.5
45-54	2.40	1.12	2.1
55-64	7.20	4.90	1.5
65-74	14.69	10.83	1.4
75-84	19.18	21.20	0.9
85+	35.93	32.66	1.1
ALL AGES	4.29	3.30	1.3

What can you say about this table?

Age	Smokers rate	Non-smokers rate	Rate ratio
35-44	0.61	0.11	5.5
45-54	2.40	1.12	2.1
55-64	7.20	4.90	1.5
65-74	14.69	10.83	1.4
75-84	19.18	21.20	0.9
85+	35.93	32.66	1.1
ALL AGES	4.29	3.30	1.3

The rate ratio decreases with increasing age. It may suggest that the effect of smoking on the rate of CHD is higher in younger ages.