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## Mathematical and Statistical Modelling in Medicine

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## Testing for proportions



Testing forsingle proportion
The square contingency table
Pearson -, Yates - and Fisher exact tests

## Special distribution of a continuous variable: the normal distribution $\mathbf{N}(\mu, \sigma)$

- The density curves are symmetric, single-peaked and bell-shaped
- The 68-95-99.7 rule .

In the normal distribution with mean $\mu$ and standard deviation $\sigma$ :

- $68 \%$ of the observations fall within $\sigma$ of the mean $\mu$
- $95 \%$ of the observations fall
 within $2 \sigma$ of the mean $\mu$
- $99.7 \%$ of the observations fall within $3 \sigma$ of the mean $\mu$


## Standard normal probabilities

| x | $(\mathrm{x}):$ proportion of area to the left of x |
| :--- | :--- |
| -4 | 0.0003 |
| -3 | 0.0013 |
| -2.58 | 0.0049 |
| -2.33 | 0.0099 |
| -2 | 0.0228 |
| -1.96 | 0.0250 |
| -1.65 | 0.0495 |
| -1 | 0.1587 |
| 0 | 0.5 |
| 1 | 0.8413 |
| 1.65 | 0.9505 |
| 1.96 | 0.975 |
| 2 | 0.9772 |
| 2.33 | 0.9901 |
| 2.58 | 0.9951 |
| 3 | 0.9987 |
| 4 | 0.99997 |



## The use of the normal curve table



## Example

- Find the area under a standard normal curve between $x=-1.96$ and $x=1.96$.
- Solution.
- $\mathrm{P}(-1.96<\mathrm{X}<1.96)=\mathrm{P}(\mathrm{X}<1.96)-\mathrm{P}(\mathrm{X}<-1.96)=0.95$
- $\Phi(-1.65)=0.025, \Phi(1.96)=0.975$. We find the area by subtracting. Thus, the area between is 0.975 $0.025=0.95$


## PROPORTIONS

## Comparing a single proportion

- In a country hospital were 515 Cesarean section (CS) in 2146 live birth in 2001. Compare this proportion to the national proportion $22 \%$. Does proportion of CS in this hospital differ from the national one?
- $\mathrm{H}_{0}: \mathrm{p}=22 \%$
- $\mathrm{H}_{\mathrm{A}}: \mathrm{p} \neq 22 \%$

$$
z=\frac{\hat{p}_{1}-p}{\sqrt{\frac{p(1-p)}{n}}}=\frac{(515 / 2146)-0.22}{\sqrt{\frac{0.22 \cdot 0.78}{2146}}}=\frac{0.24-0.22}{0.0089}=2.234
$$

## Decision

- As the calculaterd |z| score was greater than 1.96, thus Nullhypothesis is rejected, and the alternative hypothesis is accepted, namely the diffence is significant


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Testing for independence

## Chi-squre test: 2 by 2 tables

|  | Risk factor |  | Total |
| :--- | :--- | :--- | :--- |
|  | Yes | No |  |
| Group 1 | $k_{11}$ | $k_{12}$ | $k_{1+}$ |
| Group 2 | $k_{21}$ | $k_{22}$ | $k_{2+}$ |
| Total | $k_{+1}$ | $k_{+2}$ | $n$ |

## Chi-square test for $\mathbf{2 x 2}$ tables

- Formula of the test statistic

$$
\chi_{p}{ }^{2}=\frac{n\left(k_{11} k_{22}-k_{12} k_{21}\right)^{2}}{k_{+1} k_{+2} k_{1+} k_{2+}}, \mathrm{df}=1 ;
$$

- Frank Yates, an English statistician, suggested a correction for continuity that adjusts the formula for Pearson's chisquare test by subtracting 0.5 from the difference between each observed value and its expected value in a $2 \times 2$ contingency table. This reduces the chi-square value obtained and thus increases its $p$-value.

$$
\chi^{2}=\frac{n\left(k_{11} k_{22}-k_{12} k_{21} \mid-n / 2\right)^{2}}{k_{+1} k_{+2} k_{1+} k_{2+}}, \mathrm{df}=1 ; \text { Yates }
$$

## Example

- We are going to compare the proportions of two different treatments' output. Our data are tabulated as below.
- $\mathrm{H}_{0}$ : the outcome is independent of treatment in the population.
outcome
Treatment

| A |
| :--- |
| B |


| Death | Survival | Total |
| :--- | :--- | :---: |
| Total | 13 | 45 |
| 8 | 42 | 50 |
| 50 |  |  |

$$
\chi_{p}{ }^{2}=\frac{n\left(k_{11} k_{22}-k_{12} k_{21}\right)^{2}}{k_{+1} k_{+2} k_{1+} k_{2+}}=\frac{100(5 * 42-8 * 45)^{2}}{50 * 50 * 13 * 87}=0.79, \mathrm{df}=1 ;
$$

## Decision

- Here Pearson $\chi^{2}=0.796<\chi_{\text {bade }}^{2}=3.841$ thus we accept the null hypothesis that the two variables are independent
- SPSS $p$-value ( $=0.372$ ) is greater than $\alpha=0.05$ so thus we accept also the null hypothesis that the two variables are independent

Chi-Square Tests

|  | Value | df | Asymp. Sig. (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Pearson Chi-Square | ,796 ${ }^{\circ}$ | 1 | \% ,372 |  |  |
| Continuity Correction ${ }^{\text {a }}$ | ,354 | 1 | ,552 |  |  |
| Likelihood Ratio | ,802 | 1 | ,370 |  |  |
| Fisher's Exact Test |  |  |  | ,554 | ,277 |
| Linear-by-Linear Association | ,788 | 1 | ,375 |  |  |
| N of Valid Cases | 100 |  |  |  |  |

a. Computed only for a $2 \times 2$ table
b. 0 cells $(, 0 \%)$ have expected count less than 5 . The minimum expected count is 6,50 .

## Notes

- Both variables are dichotomous
- The Chi-squares give only an estimate of the true Chi-square and associated probability value, an estimate which might not be very good in the case of the marginals being very uneven or with a small value (~less than five) in one of the cells
- In that case the Fisher Exact is a good alternative for the Chi-square. However, with a large number of cases the Chi-square is preferred as the Fisher is difficult to calculate.


## Fisher's-exact test

Calculation of the p -value is based on the permutational distribution of the test Statistic (without using chi-square formula).

## Display of data

|  | Disease status |  |  |
| :--- | :---: | :---: | :---: |
|  | Disease | No | Total |
| Exposed | a | b | $\mathrm{a}+\mathrm{b}$ |
| Non-exposed | c | d | $\mathrm{c}+\mathrm{d}$ |
| Total | $\mathrm{a}+\mathrm{c}$ | $\mathrm{b}+\mathrm{d}$ | n |

## Fisher-exact test

- The procedure, ascribed to Sir Ronald Fisher, works by first using probability theory to calculate the probability of observed table, given fixed marginal totals.
- Note :0!=1

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

## Example

|  | Disease status |  |  |
| :--- | :---: | :---: | :---: |
|  | Yes | No | Total |
| Exposed | 2 | 3 | 5 |
| Non-exposed | 4 | 0 | 4 |
| Total | 6 | 3 | 9 |


|  | Value | df | Asymp. Sig. (2-sided) | Exact Sig. (2-sided) | Exact Sig. (1-sided) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Pearson Chi-Square | 3,600 ${ }^{\circ}$ | 1 | ,058 |  |  |
| Continuity Correction ${ }^{\text {² }}$ | 1,406 | 1 | ,236 |  |  |
| Likelihood Ratio | 4,727 | 1 | ,030 |  |  |
| Fisher's Exact Test |  |  |  | ,167 | ,119 |
| Linear-by-Linear Association | 3,200 | 1 | ,074 |  |  |
| N of Valid Cases | 9 |  |  |  |  |

a. Computed only for a $2 \times 2$ table
b. 4 cells $(100,0 \%)$ have expected count less than 5 . The minimum expected count is 1,33.

## Original table

## Observed probabilities

|  | Disease | Status |
| :--- | :---: | :---: |
|  | Yes | No |
| Exposed | 2 | 3 |
| Non-exposed | 4 | 0 |

Possible re-arrangements

|  | Disease | Status |
| :--- | :---: | :---: |
|  | Yes | No |
| Exposed | 3 | 2 |
| Non-exposed | 3 | 1 |
|  |  | $\mathrm{p}=0,4762$ |
| Exposed | 4 | 1 |
| Non-exposed | 2 | 2 |
|  |  | $\mathrm{p}=0,3571$ |
| Exposed | 5 | 0 |
| Non-exposed | 1 | 3 |
|  |  | $\mathrm{P}=0,0476$ |

$$
p_{\text {obs }}=\frac{5!4!6!3!}{9!2!3!4!0!}=\frac{12441600}{104509440}=0,1190
$$

Fisher's p-value $=0,119+0,0476=0,167$

Fisher showed that to generate a significance level, we need consider only the cases where the marginal totals are the same as in the observed table, and among those, only the cases where the arrangement is as extreme as the observed arrangement, or more so.

