Statistical algorithms for the Calculator in Review Manager 5.2

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Test values (Z and ttest scores) and p-values

What is usually described as 'distribution' in various software is the cumulative probability function, that is the function that maps a test value (t-test value or z value, here called t and z) to a probability. These functions are denoted here as pt (for the t-distribution) and pnorm (for the normal distribution associated with the z test).

The p-value can be calculated as

$$\text{pvalue}=2\left(1\text{-pt}(|t|,\text{df})\right) \quad (1)$$

$$\text{pvalue}=2\left(1\text{-pnorm}(|z|)\right) \quad (2)$$

where df are the degrees of freedom (see below on how to calculate these).

The inverse of the functions pt and pnorm (denoted qt and qnorm respectively, 'q' stands for the quantiles) maps the p-value to a value of t-test or z-test (denoted as t and z) using the following functions

$$t=\text{qt}\left(1\text{-}\frac{\text{pvalue}}{2},\text{df}\right) \quad (3)$$

$$z=\text{qnorm}\left(1\text{-}\frac{\text{pvalue}}{2}\right) \quad (4)$$

The sign of t or z in each case can be obtained from the difference between the two means (or one mean compared to zero) for continuous data and from the signs of log(OR) or log(RR) or RD for binary data.

Continuous Data

Calculations for one group (experimental or control)

Data structure

	Group size	Mean Response	Standard Deviation
Experimental	N_1	$Mean_1$	SD_1
Control	N_2	$Mean_2$	SD_2

For experimental

The following formulae are used in the calculations of various statistics

To calculate the standard error

$$SE_1 = \frac{SD_1}{\sqrt{N_1}}$$

To calculate the t-test value for comparing one mean with zero as

$$ttest_1 = \frac{Mean_1}{SE_1}$$

P-value$_1$ and ttest$_1$ can be calculated from equations (1) and (3) with df=N_1-1

$$pvalue_1 = 2(1\text{-}pt(|ttest_1|, N_1\text{-}1))$$

$$ttest_1 = qt\left(1\text{-}\frac{pvalue_1}{2}, N_1\text{-}1\right)$$

Let’s call f the ‘confidence level’. That is f = 0.90, 0.95 or 0.99 depending on what is selected by the user.

Upper and lower limits for the f % Confidence Interval (CI) are given by

$$Mean_1 \pm qt\left(\frac{1+f}{2}, N_1\text{-}1\right) SE_1$$

When N_1, Mean1 and SD_1 need to be estimated from a combination of two (sub)groups with sample sizes, means and standard deviations N_A, $Mean_A$, SD_A, N_B, $Mean_B$, SD_B
the following formulae apply

$$N_1 = N_A + N_B$$

$$Mean_1 = \frac{N_A Mean_A + N_B Mean_B}{N_A + N_B}$$

$$SD_1 = \sqrt{\frac{(N_A\text{-}1)SD_A{}^2 + (N_B\text{-}1)SD_B{}^2}{N_A + N_B\text{-}1} + u}$$

where

$$u = \frac{\frac{N_A N_B}{N_A + N_B}(Mean_A{}^2 + Mean_B{}^2 \text{-} 2Mean_A Mean_B)}{N_A + N_B\text{-}1}$$

Note: The formulae above hold only when groups A and B are independent; so it cannot be used to estimate SD_1 for change scores (combining pre and post measurements for the same group).

For control
All formulae described for **experimental** hold for $Mean_2$, SD_2, SE_2, N_2, $ttest_2$, $pvalue_2$

Calculations for Mean Difference

The calculations associated with mean difference (MD) and its standard error (SE) are described below.

To calculate the t-test value for comparing two means

$$\text{ttest}=\frac{\text{MD}}{\sqrt{\frac{(\text{N}_1\text{-1})\text{SD}_1{}^2+(\text{N}_2\text{-1})\text{SD}_2{}^2}{\text{N}_1+\text{N}_2\text{-2}}\left(\frac{1}{\text{N}_1}+\frac{1}{\text{N}_2}\right)}}$$

Note that it is $N=N_1+N_2$.To calculate the p-value and ttest use equations (1) and (3) with df=N-2.

$$\text{pvalue}=2(1\text{-pt}(|\text{ttest}|,\text{N-2}))$$

$$\text{ttest}=\text{qt}\left(1\text{-}\frac{\text{pvalue}}{2},\text{N-2}\right)$$

Upper and lower limits of the f % CI are given by

$$\text{MD}\pm\text{qnorm}\left(\frac{1+\text{f}}{2}\right)\text{SE}$$

When SD_1 and SD_2 are not provided, it is possible to calculate them from

$$\text{SD}_1=\text{SD}_2=\frac{\text{SE}}{\sqrt{\frac{1}{\text{N}_1}+\frac{1}{\text{N}_2}}}$$

Note: RevMan estimates the SE of the MD as $SE=\sqrt{\frac{SD_1^2}{N_1}+\frac{SD_2^2}{N_2}}$ which is often referred to as the 'unspooled SE' in contrast to the 'pooled standard error' $\sqrt{\frac{(\text{N}_1\text{-1})\text{SD}_1{}^2+(\text{N}_2\text{-1})\text{SD}_2{}^2}{\text{N}_1+\text{N}_2\text{-2}}\left(\frac{1}{\text{N}_1}+\frac{1}{\text{N}_2}\right)}$ which is used in the t-test. This incompatibility might make the back calculation from the t-test to SE unreliable particularly when the two groups are very imbalanced and $SD_1$and SD_2 differ substantially.

Calculations for Standardized Mean Difference

The calculations associated with standardized mean difference (SMD) and its standard error (SE) are described below.

To calculate the z-test value for SMD=0

$$\text{z}=\frac{\text{SMD}}{\text{SE}}$$

The p-value and z can be calculated from formulae (2) and (4).
The f % CI are

$$\mathrm{SMD} \pm \mathrm{qnorm}\left(\frac{1+f}{2}\right)\mathrm{SE}$$

Because the SE of SMD involves only SMD and the sample size

$$\mathrm{SE} = \sqrt{\frac{N}{N_1 N_2} + \frac{\mathrm{SMD}^2}{2(N\text{-}3.94)}}$$

when z and sample size are available we can calculate SMD as

$$\mathrm{SMD} = \sqrt{\frac{z^2 2N(N\text{-}3.94)}{N_1 N_2 (2(N\text{-}3.94)\text{-}z^2)}}$$

Dichotomous data

Data structure

	Event	No event	Total
Experimental	a	b	N_1
Control	c	d	N_2

For Odds Ratio (OR), Risk Ratio (RR), Risk Difference (RD) and the standard errors SE(logOR), SE(logRR) and SE(RD) the following formulae apply:

The z tests for logOR=0, logRR=0, RD=0 can be calculated as

$$z = \frac{\mathrm{logOR}}{\mathrm{SE(logOR)}}, z = \frac{\mathrm{logRR}}{\mathrm{SE(logRR)}}, z = \frac{\mathrm{RD}}{\mathrm{SE(RD)}}$$

The p-value and the z value can be estimated from equations (2) and (4).

You can calculate the SEs if you know the p-value from.

$$z = \mathrm{qnorm}\left(1\text{-}\frac{\mathrm{pvalue}}{2}\right)$$

The f % CI for logOR, logRR and RD are

$$\mathrm{logOR} \pm \mathrm{qnorm}\left(\frac{1+f}{2}\right)\mathrm{SE(logOR)}$$
$$\mathrm{logRR} \pm \mathrm{qnorm}\left(\frac{1+f}{2}\right)\mathrm{SE(logRR)}$$
$$\mathrm{RD} \pm \mathrm{qnorm}\left(\frac{1+f}{2}\right)\mathrm{SE(RD)}$$

The f % CI for the OR and RR are calculated by exponentiation of the upper and lower limits in the first two intervals to obtain the intervals above.

The OR,RR and RD are linked through the control group risk (CGR) which is c/N_2.

It is

$$RR = \frac{OR}{1 - CGR(1 - OR)}$$
$$OR = \frac{RR(1 - CER)}{1 - CGR \times RR}$$
$$RD = CGR(RR - 1)$$

It is possible to calculate a,b,c,d from OR, RR and RD as described below.

1. From OR, SE (the standard error of logOR), N_1, N_2, CGR.

Calculate first c_1, c_2 as

$$-\frac{\beta \pm \sqrt{\beta^2 - 4\alpha\gamma}}{2\alpha} = \begin{cases} c_1 \\ c_2 \end{cases},$$

where
$$\alpha = (1 - OR)^2 + N_1 SE^2 OR,$$
$$\beta = -m_2[2(1 - OR) + N_1 SE^2 OR],$$
$$\gamma = N_2(N_2 + ORN_1).$$

To decide c={c_1 or c_2} consider

- If any of (c_1, c_2) is negative then c is the positive
- If both (c_1, c_2) are positive integers then consider the $cutoff_c$ value

$$\mathrm{cutoff_c} = \begin{cases} \dfrac{-(N_1OR + N_2) + \sqrt{OR(N_1OR + N_2)(N_1 + N_2OR)}}{OR^2 - 1}, & OR \neq 1 \\ \dfrac{N_2}{2}, & OR = 1 \end{cases}$$

If $\frac{\mathrm{cutoff_c}}{N_2} > CGR$ then c=min{c_1,c_2} , else c=max{c_1,c_2}

Then calculate a, b, d as

$$a = \frac{cN_1OR}{N_2 - c(1 - OR)}, \quad b = N_1 - a, \quad d = N_2 - c\,.$$

2. From RR, SE (the standard error of logRR), N_1, N_2

Calculate $c = \frac{N_2 + N_{1RR}}{N_1RR(SE^2 + \frac{N_1 + N_2}{N_1N_2})}$ then

$$a = c\frac{N_1 RR}{N_2},\ b = N_1 - a,\ d = N_2 - c$$

3. From RD, SE (the standard error of RD), N_1, N_2, CGR.

Calculate first c_1, c_2 as

$$-\frac{\beta \pm \sqrt{\beta^2 - 4\alpha\gamma}}{2\alpha} = \begin{cases} c_1 \\ c_2 \end{cases},$$

where
$$\alpha = N_1{}^2 N_2 + N_1{}^3$$
$$\beta = -N_2\left(N_1{}^2 N_2 + N_1{}^3\right) + 2N_1{}^2 N_2{}^2 RD$$
$$\gamma = -N_1{}^2 N_2{}^3\left(RD(1 - RD)\right) - N_1{}^3 N_2{}^3 SE^2$$

To decide c={c_1 or c_2} consider

- If any of (c_1, c_2) is negative then c is the positive
- If both (c_1, c_2) are positive integers then consider the $cutoff_c$ value

$$\text{cutoff}_c = \begin{cases} 0.5 - \dfrac{N_2 RD}{N_1 + N_2}, & OR \neq 1 \\ \dfrac{N_2}{2}, & OR = 1 \end{cases}$$

If $\frac{\text{cutoff}_c}{N_2} > CGR$ then c=min{c_1,c_2} , else c=max{c_1,c_2}

Then calculate a, b, d as

$$a = c\frac{N_1}{N_2} + N_1 RD,\ \ b = N_1 - a,\ \ d = N_2 - c\ .$$

Inverse Variance Data

The calculations associated with a normally distributed quantity θ and its standard error (SE) are described below.

The variance of θ is calculated as the square of SE.

To calculate the z-test value for θ =0

$$z = \frac{\theta}{SE}$$

The p-value and z can be calculated from formulae (2) and (4).
The f % CI for θ are

$$\theta \pm \mathrm{qnorm}\left(\frac{1+f}{2}\right)\mathrm{SE}$$

When the inverse variance data are specified for Mean Difference or Standardized Mean Difference, the formulae described under Continuous data are used. When the inverse variance data are specified for OR, RR or RD the formulae described under Dichotomous data are used.

Note on the calculator: All fields are internally calculated with double precision. All fields with white background represent a rounded value. A rounded value of 5 can be anything between 4.500 to 5.499. With this in mind it is not possible to copy a value from a calculated field and then paste it into the same field again without (maybe) altering other values.

References

Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to Meta-analysis. John Wiley & Sons, 2009.
Di Pietrantonj C. Four-fold table cell frequencies imputation in meta-analysis. Stat Med. 2006 Jul 15;25(13):2299-322.