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Editorial

Practical calculation of mean, pooled variance, variance, and standard deviation, in meta-analysis studies

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Meta-analysis is known as a statistical analysis that combines the results of multiple scientific studies. Meta-analysis can be performed when there are multiple scientific studies addressing the same question, with each individual study reporting measurements that are expected to have some degree of error (1). The aim then is to use approaches from statistics to derive a pooled estimate closest to the unknown common truth based on how this error is perceived (1, 2). Following the selection of a research topic, researchers need to identify the related literature on the specified subject from all data sources and subsequently extract any evidence from available scientific documents called Systematic Review (SR). The data included can be associated with levels of measurement for variables, dominant theoretical model or approach, significance level, effect size, effect or direction of a relationship, and sample size (2).

Afterward, researchers make use of the existing statistical methods such as logarithmic integration, T-score, probability integration, Z-score, P-test, counting method, and blocking to combine the results of studies. Regarding the advantages and limitations of each method, researchers select an appropriate one (3). According to Carver (1993), these tests can only represent a small and concise index or reflection of statistical significance associated with the results of a hypothesis and they fail to show the strength or intensity of relationships between variables or researchers' desired effects. Moreover, these tests can merely indicate that the relationships observed in the findings do not arise out of chance. Although statistical significance testing makes researchers not to interpret the substantial differences between small statistical populations as significant, these tests cannot prevent the consideration of significance associated with very small differences in large populations (4). As stated by Kirk (1996), "small differences in large populations can be statistically significant"(5). Critics also believe that significance levels and effect size indices should be taken into account in the analysis of findings (6). Therefore, it is of utmost importance to employ such integration methods endowed with effect sizes.

Means using a dispersion index such as standard deviation or pooled variance are types of effect sizes and in the meta-analysis studies, the effect size of the primary studies should be correctly recorded or estimated.

It should be noted that effect size is a quantitative measure by which statistical results can be combined, summarized, and homogenized. Effect size has recognized as a critical element in the meta-analysis; in fact, effect size makes met-analysis possible. Accordingly, the main purpose to employ effect sizes is to equalize different statistical findings in a numeric scale and common measure in order to provide the possibility of comparisons and combinations of statistical results of different studies (7). Besides, the effect size can have several categories, but the most common effect size equations are extracted based on three data types including means, binary data, and correlations, which

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make it possible to complete a meta-analysis. The most common effect size equations are presented in Table 1. A wide range of such equations has been also proposed by Borenstein et al. (2009) (3).

Table 1. Roadmap of formulas (3)

Effect sizes based on means
Raw (unstandardized) mean difference (D)
Based on studies with independent groups
Based on studies with matched groups or pre-post designs
Standardized mean difference (d or g)
Based on studies with independent groups
Based on studies with matched groups or pre-post designs
Response ratios (R)
Based on studies with independent groups
Effect sizes based on binary data
Risk ratio (RR)
Based on studies with independent groups
Odds ratio (OR)
Based on studies with independent groups
Risk difference (RD)
Based on studies with independent groups
Effect sizes based on correlational data
Correlation (r)
Based on studies with one group

As observed in the above classifications, effect size based on means may be related to the difference between two means in a raw form or difference between two means in a standard form or even ratio of two means. Sometimes, effect size based on means may also be associated with cross-sectional and single-group studies in which the means of the same groups will be counted as effect sizes. To perform a meta-analysis on continuous data, there is also a need for effect size based on means using a dispersion index such as variance or standard deviation to pool the data. However, in one possible case, clinical trials may only report median, range, and sample size. Otherwise, the total mean and standard deviation or pooled variance might not be reported (8). For example, in a multi-dimensional questionnaire, researchers may merely compare the means of each dimension of the questionnaire, and total mean and standard deviation or total variance may not be reported even with the presence of standard deviation for each dimension. The present study was an attempt to estimate mean and standard deviation in such studies wherein effect size is not reported or the corresponding author does not respond, based on elementary and straightforward inequalities. These estimates will be also distribution-free. The value of our approximation(s) is in giving a method for estimating the mean and the variance exactly when there is no indication of the underlying distribution of the data (8, 9)

Furthermore, an exact method of calculating the variance of a pooled data set is presented. These estimations are distribution-free, i.e., they do not assume the distribution of the underlying data. The advantages of using the exact pooled variance include that it is simple, requires no assumptions, is exact, is easily understood and remembered, is pedagogically helpful, and can yield evidence for possible consistent errors suggesting rejection of the pooling and/or investigation of the measurements.

1. Detailed calculation of pooled variance

Pooled Variance is the mean of the variances plus the variance of the means, which is a set of combined data. First, the calculation method and then the applied example is presented (9). The integrated variance will be accurately calculated in eight steps. Suppose you have numeric sets of a variable. These sets include:

$D_p = \{x_1, x_2, \ldots x_n\}$

$D_1 = \{x_1, x_2, \ldots x_j\}$ $D_2 = \{x_{j+1}, x_{j+2}, \ldots x_{j+k}\}$ $D_2 = \{x_{j+k+1}, x_{j+k+2}, \ldots x_{j+k+m}\}$

The mean or average of D_p is $a_p = \frac{1}{n}\sum_{i=1}^{n} x_i$. Means a_1 a_2, and a_3 for D_1, D_2, and D_3, are found similarly.

Then $a_p = \frac{ja_1 + ka_1 + ma_1}{n}$ = the mean of the means.

①

The sum of squares D_p is $S_p = \sum_{i=1}^{n} x_i^2$. Sums S_1, S_2, and S_3 are similarly defined for sets D_1, D_2, and D_3.

Then $S_p = S_1 + S_2 + S_3$

②

Define the variance of data set D_p to be $V_p = \frac{1}{n}\sum_{i=1}^{n}(x_i - a_p)^2$. Expanding the argument easily shows

That $v_p = \frac{S_p}{n} - a_p^2$

③

Similarly, $v_1 = \frac{S_1}{j} - a_1^2$, $v_2 = \frac{S_2}{k} - a_2^2$, and $v_3 = \frac{S_3}{m} - a_3^2$

④

Our goal is to calculate v_p from the means and variances of the constituent sets. From ②, ③, and ④, $nv_p = S_1 + S_2 + S_3 - na_p^2 = j(v_1 + a_1^2) + k(v_2 + a_2^2) + m(v_3 + a_3^2) - na_p^2$

Or $nv_p = jv_1 + kv_2 + mv_3 + ja_1^2 + ka_2^2 + ma_3^2 - na_p^2$

⑤

The mean of the variances is $a(v) = \frac{(jv_1 + kv_2 + mv_3)}{n}$

⑥

From①, the variance of the means is $v(a) = \frac{[j(a_1 - a_P)^2 + k(a_2 - a_P)^2 + m(a_3 - a_P)^2]}{n}$

Or

$nv(a) = ja_1^2 + ka_2^2 + ma_3^2 - 2a_p(ja_1 + ka_2 + ma_3) + na_p^2 = ja_1^2 + ka_2^2 + ma_3^2 - na_p^2$

⑦

Pooled variance is combining①,⑤, ⑥ and ⑦ yields $v_p = a(v) + v(a)$ QED

⑧

So the Pooled Variance is the mean of the variances plus the variance of the means (9). The importance of these calculations is very significant at the time of writing a meta-analysis study. Suppose that a meta-analysis study is performed on the questionnaire (SF-36) related to health-related quality of life. This questionnaire has two main summaries, each of which is obtained from the sum of

four dimensions and the total score of this questionnaire is the sum of eight dimensions. Now, suppose that in one of the studies introduced into a meta-analysis, you have access to the scores of eight dimensions but you do not have two summary scores and total score. Through the formulas above, we can calculate the summary scores and total score.

Example: According to the study of La Nasa et al. (2013), the mean and standard deviation of eight dimensions of health-related quality of life have been extracted from the control group with a sample size of 124 subjects and listed in Table 2 (10). Based on the information in the article, the mean and standard deviation of dimensions of PCS, MCS, and HRQOL has been calculated below.

Table 2. The mean and standard deviation of eight dimensions of health-related quality of life in the control group in the study of La Nasa et al. (2013) (10)

	PF	RP	BP	GH	PCS	VT	SF	RE	MH	MCS	HRQOL
Mean	90.42	71.45	63.29	65.24	?	64.63	83.64	74.37	73.95	?	?
(SD)	12.68	34.5	27.43	22.82	?	17.95	23.46	36.05	20.31	?	?

Physical Function (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Function (SF), Role Emotional (RE), Mental Health (MH), Mental Component Summary (MCS) , Physical Component Summary (PCS)

First, initial mean values should be multiplied by the sample size, in the present example, since the mean values are related to the dimensions of a tool, therefore, the mean of each primary dimension must be multiplied by the constant sample size (124) and the numbers obtained are summed then, divided by the number obtained from the product of the number of dimensions and the sample size. So since it should be multiplied and divided into a constant number, this step can be summarized as follows.

The mean of the means

$$a_{PCS} = \frac{124(90.42)+124(71.45)+124(63.29)+124(65.24)}{124+124+124+124} = 72.6$$

$$a_{PCS} = \frac{90.42+71.45+63.29+65.24}{4} = 72.6$$

$$a_{MCS} = \frac{64.63+83.64+74.37+73.95}{4} = 74.15$$

$$a_{HRQOL} = \frac{90.42+71.45+63.29+65.24+90.42+71.45+63.29+65.24}{8} = 73.37$$

The variance

Given that the standard deviation of each dimension is available, the variance can be calculated using the formula=POWER (number, power) in Excel. The variance of eight dimensions of quality of life has been listed in Table 3.

Table 3. Calculation of variance based on the standard deviation of health-related quality of life in the study of La Nasa et al. (2013) (10)

	PF	RP	BP	GH	PCS	VT	SF	RE	MH	MCS	QOL
SD	12.68	34.5	27.43	22.82	?	17.95	23.46	36.05	20.31	?	?
V	160.8	1190.25	752.40	520.75	?	322.20	550.37	1299.60	412.5	?	?

The mean of the variances

$j = k = m = f$

$$a(v_{PCS}) = \frac{(jv_{PF}+kv_{RP}+mv_{BP}+fv_{GH})}{(j+k+m+f)} \qquad a(v_{PCS}) = \frac{160.8+1190.25+752.4+520.75}{4} = 656.05$$

$$a(v_{MCS}) = \frac{(jv_{VT}+kv_{SF}+mv_{RE}+fv_{MH})}{(j+k+m+f)} \qquad a(v_{MCS}) = \frac{322.2+550.37+1299.6+412.5}{4} = 646.17$$

$$a(v_{HRQOL}) = \frac{v_{PCS}+v_{MCS}}{2} \qquad a(v_{HRQOL}) = \frac{656.05+646.17}{2} = 651.11$$

The variance of the means

$j = k = m = f$

$$v(a_{PCS}) = \frac{[j(a_{PF}-a_{PCS})^2+k(a_{RP}-a_{PCS})^2+m(a_{BP}-a_{PCS})^2+f(a_{GH}-a_{PCS})^2]}{(j+k+m+f)}$$

$$v(a_{PCS}) = \frac{317.55+1.32+86.68+54.17}{4} = 114.93$$

$$v(a_{MCS}) = \frac{[j(a_{VT}-a_{MCS})^2+k(a_{SF}-a_{MCS})^2+m(a_{RE}-a_{MCS})^2+f(a_{MH}-a_{MCS})^2]}{(j+k+m+f)}$$

$$v(a_{MCS}) = \frac{90.63+90.1+0.05+0.04}{4} = 45.20$$

$$v(a_{HRQOL}) = \frac{[j(a_{PF}-a_{HRQOL})^2+k(a_{RP}-a_{HRQOL})^2+m(a_{BP}-a_{HRQOL})^2+f(a_{GH}-a_{HRQOL})^2+j(a_{VT}-a_{HRQOL})^2+k(a_{SF}-a_{HRQOL}}{(j+k+m+f+j+k+m+f)}$$

$$v(a_{HRQOL}) = \frac{306.25+3.7+101.6+66.1+76.4+105.47+1+0.34}{8} = 82.61$$

Pooled variance

$$v_{P_{PCS}} = a(v_{PCS}) + v(a_{PCS}) \qquad v_{P_{PCS}} = 656.05 + 114.93 = 770.98$$

$$SD_{P_{PCS}} = 27.77$$

$$v_{P_{MCS}} = a(v_{MCS}) + v(a_{MCS})$$

$$v_{P_{HRQOL}} = a(v_{HRQOL}) + v(a_{HRQOL}) \qquad v_{P_{HRQOL}} = 651.11 + 82.61 = 733.72$$

$$SD_{P_{HRQOL}} = 27.08$$

Finally, Excel can be used to calculate SD from the formula = SQRT (number)(11).

2. Estimation of mean and standard deviation based on Median and Range

When you are planning to enter a study into the meta-analysis, but the mean and standard deviation of the variable is not included in the study, the mean and standard deviation can be estimated according to Median, Range and Sample Size and based on the formulas in Table 4 (8).

m = Median

a = the smallest value (minimum)

b = the largest value (maximum)

n = the size of the sample.

Table 4. The best estimating formula for an unknown distribution (8)

Sample size	n ≤ 15	15 <n ≤ 25	25 <n ≤ 70	70 <n
Estimate mean	$\bar{x} \approx \frac{a+2m+b}{4}$	$\bar{x} \approx \frac{a+2m+b}{4}$	Median	Median
Estimate standard deviation	$S^2 \approx \frac{1}{12}\left[\frac{(a-2m+b)^2}{4} + (b-a)^2\right]$	$\frac{\text{Range}}{4}$	$\frac{\text{Range}}{4}$	$\frac{\text{Range}}{6}$

Example: The study conducted by Messina et al. (2008) has investigated the quality of life associated with the health of thalassemia patients, which has reported the values of (Median age: 45 years), (Range: 18-73), and (Sample size: 124) (12). Given the fact that the sample size is above 70, the median age estimate and the standard deviation will be estimated as $\frac{\text{Range}}{6}$.

Estimate Mean ≈ Median ≈ 45 years

Estimate Standard Deviation ≈ $\frac{\text{Range}}{6}$ ≈ $\frac{73-18}{6}$ ≈ 9.16

Example: The study of Amani et al. (2015) has examined the quality of life-related to the health of thalassemic patients and the values of (Median age: 20 years), (Range: 2-42), (Mean: 20.32), (Standard Deviation: 8.47) and (Sample size: 43) have been obtained (13). Given the sample size is (25≤n≤70) below is the estimation of the mean and standard deviation, which shows that the difference is negligible.

Estimate Mean ≈ Median ≈ 20 years

Estimate Standard Deviation ≈ $\frac{\text{Range}}{4}$ ≈ $\frac{42-2}{64}$ ≈ 10

EXAMPLE: Stensrud et al. (2012) carried out a 12-week (Exercise Therapy) program in a pilot study on middle-aged patients with degenerative meniscus tears with one year of screening. The BMI, kg/m2 belonging to the 10-second participants who participated in the pilot, is extracted from the paper and is listed in Table 5 (14). Based on the data, the actual values are obtained as follows.

Standard Deviation: 3.37
Mean: 26.9
Range: 20.3-33.1
Median BMI: 26.9 kg/m2

Table 5. BMI, kg / m2 belonging to 10 second participants who participated in the pilot study of Stensrud et al. (2012) (14)

Participants	11	12	13	14	15	16	17	18	19	20
BMI, kg / m2	26.6	25.1	24.5	28.1	26.7	27.1	30	20.3	27.4	**33.1**

Because only 10-second subjects are considered, so the sample size is (15<n). Below is the estimation of the mean and standard deviation, which shows that the difference is negligible.

Estimate Mean $\bar{x} \approx \frac{a+2m+b}{4} \approx \frac{20.3+53.8+33.1}{4} \approx 26.8$

Estimate variance

$S^2 \approx \frac{1}{12}\left[\frac{(a-2m+b)^2}{4} + (b-a)^2\right] \approx \frac{1}{12}\left[\frac{(20.3-53.8+33.1)^2}{4} + (12.8^2\right] \approx 13.66$

Estimate Standard Deviation $\approx \sqrt{13.66} \approx 3.69$

Conclusion

Using these formulas, we hope to help meta-analysts use clinical trials in their analysis, even when not all of the information is available and/or reported.

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