Toubasi AA, Al-Sayegh TN, Rayyan R. Methods of Converting Effect Measures Used in Meta-analysis: A Narrative Review and A Practical Guide. *High Yield Medical Reviews*. Published online June 1, 2023. doi:10.59707/hymrRJKR4024

Online first

Methods of Converting Effect Measures Used in Meta-analysis: A Narrative Review and A Practical Guide

Ahmad A. Toubasi[1], Thuraya N. Al-Sayegh[1], Rama Rayyan[1]

[1] School of Medicine, University of Jordan

Keywords: meta-analysis, effect measures, narrative, author's guide

https://doi.org/10.59707/hymrRJKR4024

High Yield Medical Reviews

The publication of meta-analyses has grown exponentially over the past 20 years. Well-designed and reported meta-analyses to provide valuable information to clinicians and policymakers. However, researchers face several hurdles in the process of conducting meta-analyses. The analysis process is one of these obstacles, particularly when the included studies report their outcomes using different outcome measures. This study aims to provide authors and researchers with a guide that can help them overcome the struggle of incorporating different outcome measures into the analysis. This article also intends to serve as an author's guide to the key methods used to convert effect measures, the assumptions required for that, and the hierarchy for using these methods.

INTRODUCTION

A meta-analysis is simply a review article that is performed according to predefined steps and synthesizes its results quantitatively.[1] The publication of meta-analyses has gained a huge interest among researchers, especially in medicine. When the term "meta-analysis" was searched on PubMed between 1966 and 2000, only 9,876 results were retrieved, compared to 256,072 results between 2000 and 2022. This implies that over the past 20 years, "meta-analysis" has been mentioned more than 25 times more frequently. A meta-analysis is a robust study design that uses evidence from published and unpublished studies to estimate the pooled effects of interventions on clinical outcomes. All meta-analyses require solid methods of systematic reviews, as any meta-analysis must be preceded by a systematic review.[1] Therefore, conducting a meta-analysis requires careful planning and design and includes protocol writing, research question development, systematic search, study selection, data extraction, quality of evidence assessment, data synthesis and analysis, and manuscript writing.[2] The Cochrane collaboration always develops a protocol before conducting a study.[2] In addition, several journals require protocols to be registered in registries such as PROSPERO, but these registries only allow registration before data collection is completed (https://www.crd.york.ac.uk/prospero/).

Systematic reviews and meta-analyses are a crucial part of the literature as they guide researchers and policymakers about the direction of the impact of interventions, the potential harms associated with those interventions, and the magnitude of those potential harms and effects. Hence, they are important in establishing complex statements and clinical practice guidelines.[2]

The problem for most researchers in conducting meta-analysis stems from the fact that it requires advanced skills in data analysis. Although it might be simple when studies similarly report measures of effect, it can be very complicated when different studies report their outcomes using other measures of impact. Handling data and converting it to a unified effect measure poses a significant challenge for researchers, as it needs a good knowledge of conversion equations and assumptions. This review aims to provide a concise summary of the approaches to data unification so that it can be analyzed using the software.

CONTINUOUS OUTCOMES

Continuous data are usually reported as a mean and standard deviation or as a median associated with a range or interquartile range (IQR). First, it is essential to note that the mean alone, or median alone, without any measure of data dispersion, is incompatible with the pooled analysis. Second, the effect measures of the meta-analysis for continuous outcomes are mean difference, weighted mean difference, and standardized mean difference. Analysis software converts the means and standard deviations into these effect measures. Therefore, the researcher should convert all effect measures reported by included studies into means and standard deviations.

Let us assume that mean=x, median=m, higher end of range=b, lower end of range=a, range=r, quartile=q, and sample size=n. If the data from a survey are normally distributed, the mean equals the median, which is the major equation used to convert the mean to the median. So, the researchers can use this equation whenever they find evidence of data normality in the included study. Another method was described by Hozo et al. for studies with a sample size of less than 25, which is the mean equals (a + b + m*2) divided by 4.[3] However, Hozo emphasized that the best mean estimate is the median when the sample size is greater than 25, and the data are normally distributed.

Table 1. Summary of Methods Used for Continuous Outcomes.

Continuous Outcomes			
Author	Input	Output	Equation
Hozo et al	Median	Mean	X=m
Hozo et al	Median and Range	Mean	(a + b + m*2)/4
Wan et al	Median and IQR	Mean	X= (Q1+Q3+m)/3
Luo et al	Median, Sample size and Range	Mean	X=(4/4+n^0.75)*(a+b /2) + (n^0.75/ 4+n^0.75)*m
Luo et al	Median, Sample size and IQR	Mean	X=(0.7+0.39/n)*(q1+q3/2)+(0.3-0.39/n)*m
Hozo et al	Range	Standard Deviation	STDV=r/4
Hozo et al	Range and Median	Standard Deviation	STDV=((((a-2*m+b)^2)/4)+(r^2)/12))
Cochrane Collaboration	IQR	Standard Deviation	STDV=IQR/1.35
Wan et al	IQR	Standard Deviation	STDV=IQR/2*inverse ((0.75*n-0.125)/(n+0.25))

mean=x, median=m, IQR: Interquartile range, higher end of range=b, lower end of range=a, range=r, quartile=q and sample size=n.

The equation described by Wan et al. is another method if the study provides only the IQR, median, and sample.[4] Wan reported that the mean equals Q1+Q3+m divided by 3. Several drawbacks were reported in the literature on the Hozo et al. and Wan et al. methods, including low accuracy in estimating the sample variance and insufficient use of the information about the sample size.[3] In addition, Luo et al. proposed a method of conversion to improve the estimation, as opposed to Hozo's and Wan's methods.[5] The method's equation was X=(4/4+n^0.75)*(a+b /2) +(n^0.75/ 4+n^0.75)*m. On the other hand, if the included study reported the IQR instead of the range, the following equation could be used X=(0.7+0.39/n)*(q1+q3/2)+(0.3-0.39/n)*m.[5] **Table 1** summarizes the methods used for converting the median to the mean.

Regarding standard deviation, Hozo et al. described that standard deviation equals range divided by four if the data were normally distributed.[3] Yet, if the sample size of the included study was less than 15, the standard deviation equals the square root of ((((a-2*m+b)^2)/4)+(r^2)/12)).[3] Moreover, Wan et al. described a method in case only the IQR was provided by the included study (IQR/2*inverse ((0.75*n-0.125)/(n+0.25))).[4] The Cochrane collaboration also reported a method for converting IQR to standard deviation, proposing that standard deviation equals IQR divided by 1.35.[6] **Table 1** summarizes the methods used for converting measures of dispersion.

BINARY OUTCOMES

Most analysis software pool data for binary variables using multiple effect measures, including odds ratio (OR), relative risk (RR), and hazard ratio, and their related 95% Confidence Intervals (95%CI). As a result, researchers should convert all the data from the included studies to one of these effect measures.

Multiple methods can be used for this aim, depending on the scenario. First, if data were raw and only the number of events for each exposure group is reported, RR or OR and their 95% confidence intervals can be used. Several online websites calculate these measures easily using the classical Altman et al. equation and the assumption for adding 0.5 if any zeros were encountered in any group.[7-9] Although using the events to calculate OR or RR is an option, this has some limitations. These include the unavailability of the raw data in the included studies and that calculating an effect measure based on the number of events yields a crude effect measure that is not adjusted to any confounding variables. Therefore, researchers should be careful when distinguishing between the adjusted effect measure taken from the study and the calculated effect measure, which is a crude measure. A summary of methods used for binary outcomes is provided in **Table 2**.

Furthermore, to overcome these limitations, several assumptions were made to convert RR to OR and vice versa. The simplest way is RR=OR when the disease prevalence is rare (less than 10%).[10-12] However, when the disease prevalence is high OR overestimates the RR, nevertheless, many equations can be used instead when the disease prevalence is large. These equations depend primarily on the control event rate. Sinclair et al. described that RR=OR/(1+control event rate)*(OR-1).[13,14] Another equation was described by Zhang et al. and Yu et al. as they stated that OR/ RR=(OR-1)*(Probability of disease+1).[15,16] However, although there is no other way to convert OR to RR or vice versa, many authors criticize these equations. They claim that they overestimate effect measures and narrow the confidence interval.[17,18] Another option is to either access the original data and perform regression analysis or simply utilize events to calculate the crude effect measure, which could be confounded by many other variables. Consequently, researchers can continue to use these equations if they are aware and cautious with their interpretation.

Table 2. Summary of Methods Used for Binary Outcomes.

Binary Outcomes			
Author	Input	Output	Equation
Egger et al	RR	OR	RR=OR
Sinclair et al	RR	OR	RR=OR/(1+control event rate)*(OR-1)
Zhang et al and Yu et al	RR	OR	OR/RR=(OR-1)*(Probability of disease+1)

RR: Relative Risk and OR: Odds Ratio.

When converting hazard ratios to other effect measures, it is essential to highlight that the hazard ratio is a measure of the speed of events while OR is the probability of an event occurring without taking hazards into consideration.[19,20] So, researchers have one of two solutions, calculating the OR or RR using the frequency of events by creating a 2*2 contingency table or calculating the hazard ratio from all the included studies. The latter requires the included studies to report the observed and the expected number of events in each group. Tierney et al. demonstrated detailed guidance on how to calculate hazard ratios if the aforementioned data were reported by the included studies.[21]

DISCUSSION

So far, we have presented how to process the data extracted from the included studies, as well as summarized the assumptions and equations for converting effect measures in order to help researchers easily address the dilemma of articles reporting different effect measures. These conversion methods can be used in observational and interventional studies.

Now, the main issue lies in the hierarchy of these methods to be used. The direct methods of calculating the effect measures using a 2*2 contingency table are preferred as they do not require any assumptions. This can be followed by the conversion equations if the number of events is not mentioned or if we need to obtain an adjusted effect measure. Of the equations mentioned for continuous variables, the one reported by Lou et al. is considered the most accurate.[5] As for binary outcomes, there are no studies comparing the above equations; thus, using any is considered a relatively valid method for the analysis.

Although conversion methods are reliable, their use may introduce problems in analysis. For example, some studies may not have reported the data required for the use of conversion equations. This results in the exclusion of some studies from the analysis, which leads to publication bias or selective outcome reporting bias.

In conclusion, researchers may encounter difficulties due to variations in the reporting of effect measures among the papers included in meta-analyses. Several methods are available to researchers to convert effect measures into a consistent format that allows pooling them in the analysis. Even though direct approaches are always preferred, conversion equations are employed when there is no available data to apply them in order to avoid the studies' exclusion from the analysis.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ACKNOWLEDGMENT

None.

FUNDING

The authors have no funding to declare.

Submitted: February 28, 2023 AST, Accepted: March 18, 2023 AST

REFERENCES

1. Lee YH. An overview of meta-analysis for clinicians. *Korean J Intern Med*. 2018;33(2):277-283. doi:10.3904/kjim.2016.195

2. Hernandez AV, Marti KM, Roman YM. Meta-analysis. *Chest*. 2020;158(1):S97-S102. doi:10.1016/j.chest.2020.03.003

3. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5(1):1-10. doi:10.1186/1471-2288-5-13

4. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14(1):1-13. doi:10.1186/1471-2288-14-135

5. Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res*. 2018;27(6):1785-1805. doi:10.1177/0962280216669183

6. Higgins JPT, Deeks JJ. Selecting Studies and Collecting Data. *Cochrane Handbook for Systematic Reviews of Interventions*. 2008:151-185. doi:10.1002/9780470712184.ch7

7. Altman DG, Deeks JJ, Sackett DL. Odds ratios should be avoided when events are common. *BMJ*. 1998;317(7168):1318. doi:10.1136/bmj.317.7168.1318

8. Pagano M, Gauvreau K. Principles of biostatistics. In: *Belmont*. Brooks/Cole; 2000.

9. Deeks JJ, Higgins JPT. Statistical algorithms in review manager 5. *Statistical Methods Group of The Cochrane Collaboration*. 2010;1(11).

10. Egger M, Smith GD. Principles of and Procedures for Systematic Reviews. In: *Systematic Reviews in Health Care*. John Wiley & Sons, Ltd; 2001:23-42. doi:10.1002/9780470693926.ch2

11. Woodward M. *Epidemiology: Study Design and Data Analysis*. Chapman & Hall/CRC; 1999.

12. Rothman KJ. Analysis of crude data. Modern epidemiology. Published online 1986.

13. Prasad K, Jaeschke R, Wyer P, Keitz S, Guyatt G, Evidence-Based Medicine Teaching Tips Working Group. Tips for teachers of evidence-based medicine: understanding odds ratios and their relationship to risk ratios. *J Gen Intern Med*. 2008;23(5):635-640. doi:10.1007/s11606-007-0453-4

14. Sinclair JC, Bracken MB. Clinically useful measures of effect in binary analyses of randomized trials. *J Clin Epidemiol*. 1994;47(8):881-889. doi:10.1016/0895-4356(94)90191-0

15. Shrier I, Steele R. Understanding the relationship between risks and odds ratios. *Clinical Journal of Sport Medicine*. 2006;16(2):107-110. doi:10.1097/00042752-200603000-00004

16. Zhang J, Yu KF. What's the relative risk?: A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998;280(19):1690-1691. doi:10.1001/jama.280.19.1690

17. Greenland S. Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. *Am J Epidemiol*. 2004;160(4):301-305. doi:10.1093/aje/kwh221

18. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol*. 2003;157(10):940-943. doi:10.1093/aje/kwg074

19. Parmar MKB, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. *Statist Med*. 1998;17(24):2815-2834. doi:10.1002/(sici)1097-0258(19981230)17:24

20. Williamson PR, Smith CT, Hutton JL, Marson AG. Aggregate data meta-analysis with time-to-event outcomes. *Statist Med*. 2002;21(22):3337-3351. doi:10.1002/sim.1303

21. Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials*. 2007;8(1):1-16. doi:10.1186/1745-6215-8-16