Meta-analyze dichotomous data: Do the calculations with Log Odds Ratios and report Risk Ratios or Risk Differences

Henk van Rhee, vanrhee@rsm.nl

Robert Suurmond, suurmond@rsm.nl

Rotterdam School of Management, Erasmus University, Department of Technology and Operations Management, Rotterdam, The Netherlands

Abstract

This paper describes a method to convert meta-analytic results in (log) Odds Ratio to either Risk Ratio or Risk Difference. It has been argued that odds ratios are mathematically superior for meta-analysis, but risk ratios and risk differences are shown to be easier to interpret. Therefore, the proposed method enables the calculation of meta-analytic results in (log) odds ratio and to transform them afterwards in risk ratio and risk difference. This transformation is based on the assumption of equal significance of the results. It is implemented *Meta-Essentials*: Workbooks for meta-analyses.

Introduction

There are several measures to describe the size of the effect for dichotomous outcomes. Three

commonly used measures are the odds ratio (OR), the risk ratio (RR), and the risk difference

(RD). The measures as used in this paper refer to: Odds ratio= $\frac{ad}{bc}$, Risk ratio= $\frac{a/(a+b)}{c/(c+d)}$,

Risk difference= $\frac{a}{a+b}$ - $\frac{c}{c+d}$, see Table 1 for notation.

Table 1: two-by-two table for dichotomous outcomes

	Outcome 1	Outcome 2
Group 1	a	b
Group 2	c	d

Scholars have argued that the odds ratio is statistically preferable for meta-analyses (Fleiss &

Berlin, 2009), but others have argued the lack of interpretability of the odds ratio (e.g. Deeks,

2002). One of the problems described in the literature is the fact that logistic regressions will

yield odds ratios, not risk ratios, but that researchers are inclined to interpret the results, in

odds ratios, as if it where risk ratios (Zhang & Yu, 1998). In general the difference between the

odds ratio and the risk ratio is only practically significant when outcomes are common, i.e. the

risk in the control group is relatively high (Cummings, 2009). Statistical criteria for selecting the

most appropriate effect size measure for meta-analyses have been described by Deeks (2002):

consistency of effect, ease of interpretation, and mathematical properties. With respect to

consistency of effect, the OR and RR are shown to produce more consistent results than the RD.

However, risk differences and risk ratios are more easily correctly interpreted and are therefore

preferred over odd ratios. When it comes to mathematical properties, scholars have argued

that the OR is symmetrical with respect to outcome and non-outcome and that the RR is not,

i.e., the OR for the reverse outcome is the inverse of the original OR (Cummings, 2009). The RR has been shown to be bounded by the control group risk, meaning that the risk ratio can never exceed the risk in the control group, specifically when the risk ratio is larger than 1 (Cummings, 2009).

However, although the OR is mathematically superior to the RR and RD, the size of the effect is hard to interpret with odds ratios; this is widely acknowledged by scholars in the field of medicine (e.g., Bland & Altman, 2000; McColl, Smith, White, Field, 1998; Sinclair & Bracken, 1994), let alone how difficult interpretation of the OR is for scholars in fields in which this effect size is relatively uncommon. Because of this, several authors propose to execute the meta-analysis in odds ratios and subsequently transform the outcomes into effect size measures that are easier to interpret like the risk ratio and the risk difference (e.g., Borenstein et al., 2009, p. 38, Fleiss & Berlin, 2009, p. 250; Localio et al., 2007). For the conversion of the combined effect size in odds ratio into risk ratios, a substitution method can be used (as will be discussed later) that also can be used for the confidence and predication interval limits. Also, analogous to this, the combined effect size in odds ratios can be converted into risk difference, but not the confidence interval limits nor the prediction interval limits. In the following sections first the method of substitution will be explained, subsequently a new method of deriving the confidence and prediction interval limits for risk differences from a meta-analyses of odds ratios will be discussed.

Converting odds ratios into risk ratios

A method which has become known as the method of substitution can be used to convert odds ratios into risk ratios (Daly, 1998; Zhang & Yu, 1998). This method can be used to convert the combined effect size and the limits of both the confidence interval and the prediction interval, using the following formula:

$$Risk\ ratio\ = \frac{Odds\ ratio}{(1 - Assumed\ control\ risk) + (Assumed\ control\ risk \times Odds\ ratio)}$$

It relies on the assumed control group risk, commonly the median of control group risk in the studies that are being meta-analyzed is used for this (Fleis & Berlin, 2009).

Please note that caution is warranted for applying the substitution method to convert the combined effect size of a meta-analysis if the individual studies' baseline risks are high and odds ratios are large, since this might result in confidence and prediction intervals that are too narrow (McNutt et al., 2003; Localio et al., 2007).

Converting odds ratios into risk differences

The method of substitution can also be used convert the meta-analyzed point estimate of the odds ratio into risk difference.

$$\text{Risk difference} = \text{Assumed control risk -} \frac{\text{Odds ratio} \times \text{Assumed control risk}}{\text{1 - Assumed control risk} + \text{Odds ratio} \times \text{Assumed control risk}}$$

$$= \text{Risk ratio} \times \text{Assumed control risk - Assumed control risk}$$

As is shown in the final line of the formula, the risk difference can be easily derived from the combined effect size in risk ratio. However, the method cannot be applied to the confidence interval limits nor to the prediction interval limits of odds ratios because the scales are different; odds ratios and risk differences are not equally distributed. Therefore, we propose a new method for the derivation of confidence and prediction interval limits of risk differences that have the same probability as the limits of the odds ratio, given the (substituted) combined effect size. The first assumption of this method is that the likelihood of a certain value can be expressed by a z-value that is expressed as a standard normal distribution. The z-value reflects the distance between the summary effect size and the null hypothesis. Since this z-value is measured on the standard normal distribution, it is assumed equal for both log odds ratio and risk difference. Therefore, first the z-value is calculated for the confidence interval limits of the odds ratio with use statistics of the combined effect size that are generally available when meta-analyzing binary data:

$$z_{\ln(\text{Odds Ratio})} = \frac{\text{Combined effect size}_{\ln(\text{Odds Ratio})}}{\text{Standard error}_{\ln(\text{Odds Ratio})}}$$

The z-value of the risk difference would usually be calculated as follows:

$$z_{\text{Risk Difference}} = \frac{\text{Combined effect size}_{\text{Risk Difference}}}{\text{Standard error}_{\text{Risk Difference}}}$$

Simple substitution gives:

$$\text{Standard error}_{\text{Risk Difference}} = \frac{\text{Combined effect size}_{\text{Risk Difference}}}{z_{\text{Risk Difference}}}$$

However, since the *z*-value of the risk difference is unknown, we use the *z*-value of the log odds ratio under the assumption that these are equal:

$$z_{Risk\ Difference} = z_{\ln(Odds\ Ratio)}$$

Thus:

$$\text{Standard error}_{\text{Risk difference}} = \frac{\text{Combined effect size}_{\text{Risk Difference}}}{z_{\text{Risk Difference}}}$$

$$= \frac{\text{Combined effect size}_{\text{Risk Difference}}}{z_{\ln(\text{Odds Ratio})}}$$

Then, we calculate the confidence interval limits as usual with use of the earlier substituted combined effect size and the derived standard error:

$$CI\ Limit\ RD = CES\ RD \pm t_{\alpha,df} \times SE_{RD}$$

Where $t_{\alpha,df}$ is the critical *t*-value for α = (1-confidence level) and *df* is the degrees of freedom, calculated as the number of studies in the meta-analysis minus 1 (*k*-1).

For the prediction interval limits (Higgins et al, 2009), we would normally calculate the between studies variance (T^2) and then proceed as normal, multiplying the square root of both the standard error and the between studies variance by a critical *t*-value as above. However, we can also express the distance between the prediction interval limits in log odds ratios and the combined effect size in terms of standard errors (which we derived earlier). Therefore we need to calculate a new value for the standardized difference between the prediction interval limits and the combined effect size:

$$z_{PI,\ln(Odds\ Ratio)} = \frac{\left| CESCombined\ effect\ size_{\ln(Odds\ Ratio)} - PI\ Limit_{\ln(Odds\ Ratio)} \right|}{Standard\ error_{\ln(Odds\ Ratio)}}$$

If we assume:

$$z_{PI,Risk\ Difference} = z_{PI,\ln(Odds\ Ratio)}$$

Then:

$$PI\ Limit_{Risk\ Difference}$$

$$= Combined\ effect\ size_{Risk\ Difference} \pm z_{PI,\ln(Odds\ Ratio)}$$

$$\times Standard\ error_{Risk\ Difference}$$

This prediction interval limits are point estimates with the same probability as the ones in odds ratio, given the point estimate of the combined effect size. Thus the prediction interval has the same power to reject the null-hypothesis of zero effect as the one in odds ratio. Note however that this is not a substitution method.

Discussion

This paper proposes a new method for the execution of meta-analysis for dichotomous outcomes. Scholars have argued that the meta-analysis of odds ratios statistically preferable, while presentation in other effect size measures, risk ratios or risk differences, would help to interpret the clinical relevance of the outcomes. The proposed method makes use of the substitution method argued by Zhang and Yu (1998) and extends the work to deal with the conversion of odds ratios into risk differences as well. We propose a method making use of the distance between the summary effect and the null hypothesis (z-value) under the standard

normal distribution. This distance can be calculated for the meta-analysis in log odds ratios and then used to estimate the confidence and prediction interval limits of the risk difference.

The methods discussed in this paper have been implemented in the *Meta-Essentials*: Workbooks for meta-analyses (Van Rhee, Suurmond, & Hak, 2015).

References

Bland, J. M., & Altman, D. G. (2000). The odds ratio. *BMJ*, 320(7247), 1468.

Borenstein, M., Hedges, L. V., Higgins, J. P., & Rothstein, H. R. (2009). *Introduction to meta-analysis*. John Wiley & Sons.

Cummings, P. (2009). The relative merits of risk ratios and odds ratios. *Archives of pediatrics & adolescent medicine*, 163(5), 438-445.

Daly, L. E. (1998). Confidence limits made easy: interval estimation using a substitution method. *American Journal of Epidemiology*, 147(8), 783-790.

Deeks, J. J. (2002). Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes. *Statistics in medicine*, 21(11), 1575-1600.

Fleiss, J. L., & Berlin, J. A. (2009). Effect sizes for dichotomous data. In H. Cooper, L. V. Hedges & J. C. Valentine (Eds.), *The handbook of research synthesis and meta-analysis* (Second Ed.) (pp. 237-253). New York, NY: Russell Sage Foundation

Higgins, J., Thompson, S. G., & Spiegelhalter, D. J. (2009). A re-evaluation of random-effects meta-analysis. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 172(1), 137-159.

Localio, A. R., Margolis, D. J., & Berlin, J. A. (2007). Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. *Journal of clinical epidemiology*, 60(9), 874-882.

McColl, A., Smith, H., White, P., & Field, J. (1998). General practitioners' perceptions of the route to evidence based medicine: a questionnaire survey. *BMJ*, 316(7128), 361-365.

McNutt, L. A., Wu, C., Xue, X., & Hafner, J. P. (2003). Estimating the relative risk in cohort studies and clinical trials of common outcomes. *American journal of epidemiology*, 157(10), 940-943.

Sinclair, J. C., & Bracken, M. B. (1994). Clinically useful measures of effect in binary analyses of randomized trials. *Journal of clinical epidemiology*, 47(8), 881-889.

Van Rhee, H.J., Suurmond, R., & Hak, T. (2015). User manual for *Meta-Essentials*: Workbooks for meta-analyses (Version 1.0) Rotterdam, The Netherlands: Erasmus Research Institute of Management. Retrieved from www.erim.eur.nl/research-support/meta-essentials

Zhang, J., & Yu, K.F. (1998). What's the relative risk?: A method of correcting the odds ratio in cohort studies of common outcomes. *Jama*, 280(19), 1690-1691.