Effect Sizes Based on Binary Data (2 × 2 Tables)

INTRODUCTION

For data from a prospective study, such as a randomized trial, that was originally reported as the number of events and non-events in two groups (the classic 2 × 2 table), researchers typically compute a risk ratio, an odds ratio, and/or a risk difference. This data can be represented as cells *A, B, C*, and *D*, as shown in Table 5.1.

For example, assume a study with a sample size of 100 per group. Five patients died in the treated group, as compared with ten who died in the control group (see Table 5.2).

Table 5.1 Nomenclature for 2 × 2 table of outcome by treatment.

	Events	Non-Events	N
Treated	*A*	*B*	n_1
Control	*C*	*D*	n_2

Table 5.2 Fictional data for a 2 × 2 table.

	Dead	Alive	N
Treated	5	95	100
Control	10	90	100

From these data we might compute a risk ratio, an odds ratio, and/or a risk difference.

RISK RATIO

The risk ratio is simply the ratio of two *risks*. Here, the risk of death in the treated group is 5/100 and the risk of death in the control group is 10/100, so the ratio of the two risks is 0.50. This index has the advantage of being intuitive, in the sense that the meaning of a ratio is clear.

For risk ratios, computations are carried out on a log scale. We compute the log risk ratio, and the standard error of the log risk ratio, and will use these numbers to perform all steps in the meta-analysis. Only then will we convert the results back into the original metric. This is shown schematically in Figure 5.1.

The computational formula for the risk ratio is

$$RiskRatio = \frac{A/n_1}{C/n_2}. \tag{5.1}$$

The log risk ratio is then

$$LogRiskRatio = \ln{(RiskRatio)}, \tag{5.2}$$

with approximate variance

$$V_{LogRiskRatio} = \frac{1}{A} - \frac{1}{n_1} + \frac{1}{C} - \frac{1}{n_2}, \tag{5.3}$$
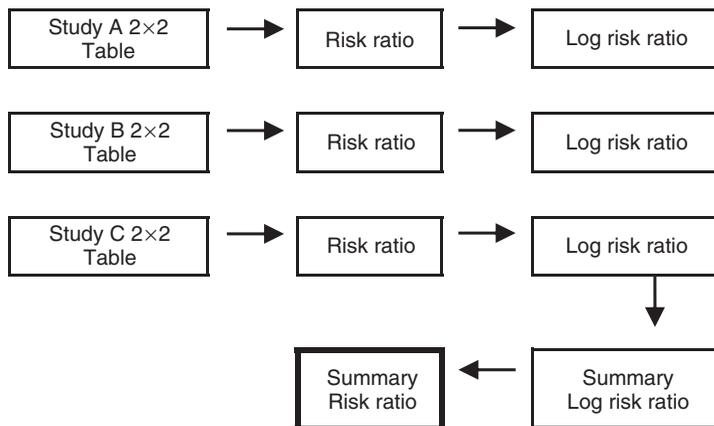
and approximate standard error

Figure 5.1 Risk ratios are analyzed in log units.

$$SE_{LogRiskRatio} = \sqrt{V_{LogRiskRatio}}. \tag{5.4}$$

Note that we do not compute a variance for the risk ratio in its original metric. Rather, we use the *log* risk ratio and its variance in the analysis to yield a summary effect, confidence limits, and so on, in log units. We then convert each of these values back to risk ratios using

$$RiskRatio = \exp(LogRiskRatio), \tag{5.5}$$

$$LL_{RiskRatio} = \exp(LL_{LogRiskRatio}), \tag{5.6}$$

and

$$UL_{RiskRatio} = \exp(UL_{LogRiskRatio}) \tag{5.7}$$

where *LL* and *UL* represent the lower and upper limits, respectively.

   In the running example the risk ratio is

$$RiskRatio = \frac{5/100}{10/100} = 0.5000.$$

The log is

$$LogRiskRatio = \ln(0.5000) = -0.6932,$$

with variance

$$V_{LogRiskRatio} = \frac{1}{5} - \frac{1}{100} + \frac{1}{10} - \frac{1}{100} = 0.2800,$$

and standard error

$$SE_{LogRiskRatio} = \sqrt{0.280} = 0.5292.$$

Note 1. The log transformation is needed to maintain symmetry in the analysis. Assume that one study reports that the risk is twice as high in Group A while another reports that it is twice as high in Group B. Assuming equal weights, these studies should balance each other, with a combined effect showing equal risks (a risk ratio of 1.0). However, on the ratio scale these correspond to risk ratios of 0.50 and 2.00, which would yield a mean of 1.25. By working with log values we can avoid this problem. In log units the two estimates are -0.693 and $+0.693$, which yield a mean of 0.00. We convert this back to a risk ratio of 1.00, which is the correct value for this data.

   Note 2. Although we defined the risk ratio in this example as

$$RiskRatio = \frac{5/100}{10/100} = 0.5000$$

(which gives the risk ratio of dying) we could alternatively have focused on the *risk* of staying alive, given by

$$RiskRatio = \frac{95/100}{90/100} = 1.0556.$$

The 'risk' of staying alive is *not* the inverse of the risk of dying (that is, 1.056 is not the inverse of 0.50), and therefore this should be considered a different measure of effect size.

ODDS RATIO

Where the risk ratio is the ratio of two *risks*, the odds ratio is the ratio of two *odds*. Here, the odds of death in the treated group would be 5/95, or 0.0526 (since probability of death in the treated group is 5/100 and the probability of life is 95/100), while the odds of death in the control group would be 10/90, or 0.1111. The ratio of the two odds would then be 0.0526/0.1111, or 0.4737.

Many people find this effect size measure less intuitive than the risk ratio, but the odds ratio has statistical properties that often make it the best choice for a meta-analysis. When the risk of the event is low, the odds ratio will be similar to the risk ratio.

For odds ratios, computations are carried out on a log scale (for the same reason as for risk ratios). We compute the log odds ratio, and the standard error of the log odds ratio, and will use these numbers to perform all steps in the meta-analysis. Only then will we convert the results back into the original metric. This is shown schematically in Figure 5.2.

The computational formula for the odds ratio is

$$OddsRatio = \frac{AD}{BC}. \tag{5.8}$$

The log odds ratio is then

$$LogOddsRatio = \ln(OddsRatio), \tag{5.9}$$

with approximate variance

$$V_{LogOddsRatio} = \frac{1}{A} + \frac{1}{B} + \frac{1}{C} + \frac{1}{D} \tag{5.10}$$
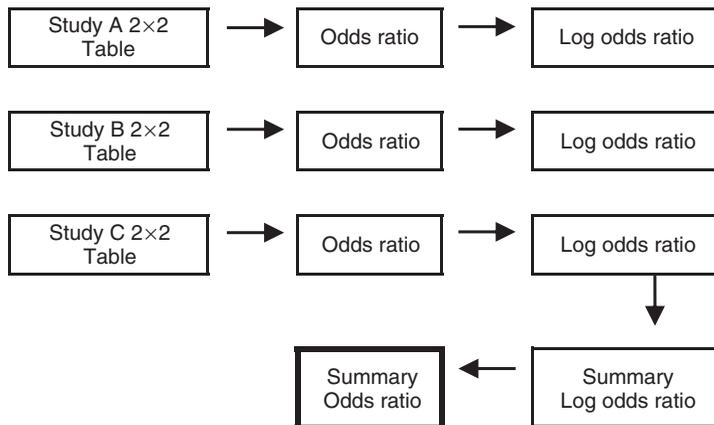

Figure 5.2 Odds ratios are analyzed in log units.

and approximate standard error

$$SE_{LogOddsRatio} = \sqrt{V_{LogOddsRatio}}. \tag{5.11}$$

Note that we do not compute a variance for the odds ratio. Rather, the log odds ratio and its variance are used in the analysis to yield a summary effect, confidence limits, and so on, in log units. We then convert each of these values back to odds ratios using

$$OddsRatio = \exp(LogOddsRatio), \tag{5.12}$$

$$LL_{OddsRatio} = \exp(LL_{LogOddsRatio}), \tag{5.13}$$

and

$$UL_{OddsRatio} = \exp(UL_{LogOddsRatio}), \tag{5.14}$$

where LL and UL represent the lower and upper limits, respectively.

In the running example

$$OddsRatio = \frac{5 \times 90}{95 \times 10} = 0.4737,$$

and

$$LogOddsRatio = \ln(0.4737) = -0.7472,$$

with variance

$$V_{LogOddsRatio} = \frac{1}{5} + \frac{1}{95} + \frac{1}{10} + \frac{1}{90} = 0.3216$$

and standard error

$$SE_{LogOddsRatio} = \sqrt{0.3216} = 0.5671.$$

Note. When working with the odds ratio or risk ratio we can place either the Treated group or the Control group in the numerator, as long we apply this consistently across all studies. If we put the Treated group in the denominator the log odds ratio would change signs (from -0.7472 to $+0.7472$) and the odds ratio would change to its inverse (from 0.4737 to 2.1110). The same thing happens to the odds ratio if we swap Dead and Alive within each group. However, this is *not* the case for the risk ratio.

RISK DIFFERENCE

The risk difference is the *difference* between two risks. Here, the risk in the treated group is 0.05 and the risk in the control group is 0.10, so the risk difference is -0.05.

Unlike the case for risk ratios and for odds ratios, computations for risk differences are carried out in raw units rather than log units.

The risk difference is defined as

$$RiskDiff = \left(\frac{A}{n_1}\right) - \left(\frac{C}{n_2}\right) \tag{5.15}$$

with approximate variance

$$V_{RiskDiff} = \frac{AB}{n_1^3} + \frac{CD}{n_2^3} \qquad (5.16)$$

and approximate standard error

$$SE_{RiskDiff} = \sqrt{V_{RiskDiff}}. \qquad (5.17)$$

In the running example

$$RiskDiff = \left(\frac{5}{100}\right) - \left(\frac{10}{100}\right) = -0.0500$$

with variance

$$V_{RiskDiff} = \frac{5 \times 95}{100^3} + \frac{10 \times 90}{100^3} = 0.0014$$

and standard error

$$SE_{RiskDiff} = \sqrt{0.00138} = 0.0371.$$

CHOOSING AN EFFECT SIZE INDEX

In selecting among the risk ratio, odds ratio, and risk difference the researcher needs to consider both substantive and technical factors.

The risk ratio and odds ratio are relative measures, and therefore tend to be relatively insensitive to differences in baseline events. By contrast, the risk difference is an absolute measure and as such is very sensitive to the baseline risk. If we wanted to test a compound and believed that it reduced the risk of an event by 20 % regardless of the baseline risk, then by using a ratio index we would expect to see the same effect size across studies even if the baseline risk varied from study to study. The risk difference, by contrast, would be higher in studies with a higher base rate.

At the same time, if we wanted to convey the clinical impact of the treatment, the risk difference might be the better measure. Suppose we perform a meta-analysis to assess the risk of adverse events for treated versus control groups. The risk is 1/1000 for treated patients versus 1/2000 for control patients, for a risk ratio of 2.00. At the same time, the risk difference is 0.0010 versus 0.0005 for a risk difference of 0.0005. These two numbers (2.00 and 0.0005) are both correct, but measure different things.

Because the ratios are less sensitive to baseline risk while the risk difference is sometimes more clinically meaningful, some suggest using the risk ratio (or odds ratio) to perform the meta-analysis and compute a summary risk (or odds) ratio. Then, they can use this to predict the risk difference for any given baseline risk.

SUMMARY POINTS

- We can compute the risk of an event (such as the risk of death) in each group (for example, treated versus control). The ratio of these risks then serves as an effect size (the risk ratio).
- We can compute the odds of an event (such as ratio of dying to living) in each group (for example, treated versus control). The ratio of these odds then serves as the odds ratio.
- We can compute the risk of an event (such as the risk of death) in each group (for example, treated versus control). The difference in these risks then serves as an effect size (the risk difference).
- To work with the risk ratio or odds ratio we transform all values to log values, perform the analyses, and then convert the results back to ratio values for presentation. To work with the risk difference we work with the raw values.