Interpretation of Odds and Risk Ratios

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Background: Odds ratio and risk ratio are measures of association used to describe the efficacy of interventions and disease determinates; however, they are not interchangeable measures of association.

Objectives: To illustrate that interpretation of the odds ratio as a risk-based measure of efficacy can be misleading.

Animals: None.

Methods: A meta-analysis reported, the odds ratio and the risk ratio as measures of vaccine effect. Example data were obtained from a meta-analysis of the risk of infection with *Tritrichomonas fetus (T. fetus)*, in trials that assessed whole-cell killed *T. fetus* vaccination in beef heifers.

Results: When risk was used as the measure of disease frequency, the summary risk ratio was 0.82 (95% CI = 0.7–1.01), a 18% decrease in risk of infection. When odds were used as the measure of disease frequency and the summary odds ratio was 0.41 (95% CI = 0.2–0.84), a 59% decrease in odds of infection.

Conclusions and Clinical Importance: Problems arise for clinicians or authors when they interpret the odds ratio as a risk ratio. In the example provided, the efficacy of protective interventions was overestimated. In the case of disease determinates that increase the occurrence of disease, the interpretation of the odds ratio as a risk ratio would also lead to overestimation of the effect. It is important not to use the terms risk or probability of disease when the odds are the measure of disease frequency.

Key words: Cattle; Epidemiology; Parasitology; Protozoa; Statistics.

Problems arise for clinicians or authors when they interpret the odds ratio as a risk ratio, as the efficacy of protective interventions or the strength of disease determinate associations will be overestimated. Both the odds ratio and the risk ratio are valid measures of association; however, as they use different measures of disease frequency (odds versus risk), it is important they are not treated as interchangeable. Risk refers to the probability of being diseased in a specified time period. Odds refer to the ratio of the probability of being diseased to the probability of not being diseased in a specified time period. The purpose of this communication is to provide an empirical example of the different interpretations of the odds ratio and risk ratio with the aim of improving interpretation of these common measures of association.

The Example

To illustrate the different interpretations of the odds ratio and risk ratio, data from a meta-analysis on the risk of infection with *Tritrichomonas fetus (T. fetus)* in a group of trials that assessed vaccination with whole-cell killed *T. fetus* in beef heifers (Fig 1) are used. Each study in the meta-analysis is labeled and the number of events and number enrolled in vaccinated and unvaccinated groups are reported in the 4 columns of numerical data on the left-hand side. On the right-hand side is a forest plot that contains a new line of data for each study. Each box in the forest plot represents the point estimate of the effect of the vaccine, either an odds ratio or a risk ratio. The horizontal line through each box represents the 95% confidence interval for the vaccine effect. At the bottom of each forest plot is a large diamond, which is the summary effect measure, a weighted combination of the estimates from each study. The top and bottom points of the diamond represent the point estimate and the lateral points represent the bounds of the 95% confidence interval. When the vaccine has no effect the numerator and denominator in the risk ratio or odds ratio will be the same, and therefore the ratio will be one.

In the upper panel of Figure 1, risk has been used as the measure of disease frequency and the summary risk ratio is 0.82 (95% CI = 0.7–1.01). In the lower panel, odds are used as the measure of disease frequency and the summary odds ratio is 0.41 (95% CI = 0.2–0.84). A risk ratio of 0.82 signifies that the magnitude of risk of disease in the numerator is approximately 82% of the magnitude of risk of disease in the denominator (ie, that the numerator is approximately 18% lower than the denominator). Therefore, the meta-analysis results in Figure 1 suggest that vaccination proportionally reduced the risk of infection with *T. fetus* by only 18% (vaccine efficacy = 1–RR, 1–0.82), but the same studies estimated that vaccination reduced the odds of infection by 60% (1–0.4). Clearly, it would be incorrect to say vaccination reduced the risk of infection by 60%, as it is the odds that are reduced by 60%. If the end user wants to interpret and evaluate the intervention based on risk, which is far more intuitive than odds, then they must restrict their interpretation to the risk, in this situation, an 18% decrease in risk.

Problems arise if the odds ratio is misinterpreted as a risk ratio. For protective interventions such as illustrated here, incorrectly interpreting the odds ratio as a

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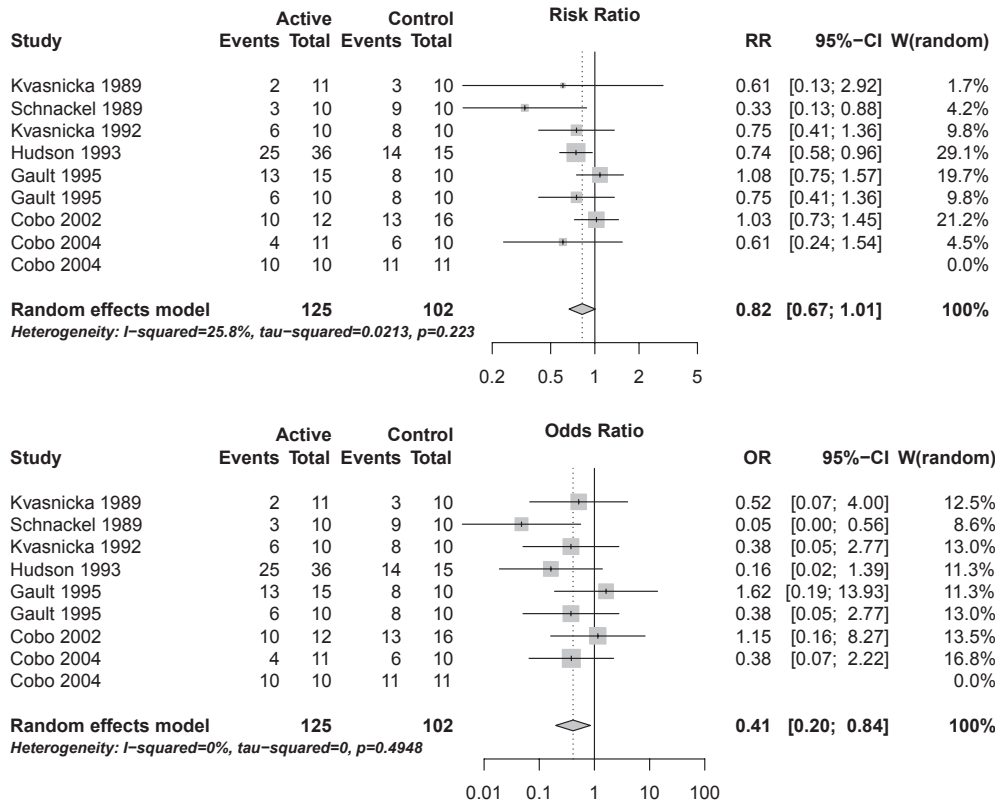
Fig 1. Forest plot and meta-analysis using the same data. The upper panel uses the risk as the measure of disease frequency and the risk ratio as the measure of vaccine efficacy. The lower panel uses the odds as the measure of disease frequency and the risk ratio as the measure of vaccine efficacy.

risk ratio will always lead to an overestimation of the protective effect. Although our example relies upon a clinical trial with a protective intervention, the issue of misinterpretation will occur for any hypothesis testing studies were the odds ratio and risk ratio are valid measures of the association. If the study addresses a disease determinate that increases disease occurrence, then the odds and risk ratios would be greater than one. The impact of misinterpretation of the odds ratio as a risk would be the same, overestimation of the risk of disease associated with exposure. This happens because the difference between the odds ratio and risk ratio increases as the baseline risk of disease increases.

Why Does This Happen?

Consider hypothetical data from three populations (Table 1). The 1st 2 sets of data present data from a study of a protective intervention as might occur in a vaccine trial. In a vaccine trial the effect of the protective intervention could be reported as either the risk ratio or the odds ratio as both can be calculated from the trial data. The odds ratio is obtained by dividing the odds of disease in 1 group by the odds of disease in another. The risk ratio is obtained by dividing the risk of disease in 1 group by the risk of disease in another. The odds are the ratio of 2 simple proportions (Table 2: Formula 1). The risk is a simple

proportion (Table 2: Formula 2). Notice that the risk of disease is only part of the formula for the odds; ie, the numerator of the odds is the risk of disease.

Using the data from Table 1 to illustrate the difference, the odds of disease in the vaccinated animals are 0.25 (Table 2: Formula 1) while the risk of disease in the vaccinated animals is 0.20 or 20%. The difficulty or confusion arises if clinicians or authors incorrectly conclude there is a 25% risk of disease in the vaccinated animals in Table 1, rather than a 0.25 odds of disease in the vaccinates. This difficulty in translation is further compounded when summary measures of association such as the odds ratio or risk ratio are used. In Table 1, the odds ratio is 0.375, meaning the odds of disease were 62.5% lower in the vaccinated animals compared to the unvaccinated animals (Table 2: Formula 3). However, the risk ratio of 0.5 means the risk of disease was 50% lower in the vaccinated animals compared to the unvaccinated animals (Table 2: Formula 4). The difference of 12.5% might not seem important, but since the application of these ratios is dependent upon the baseline level of disease the difference in the odds ratio and risk ratio can become large.

The difference between the odds ratio and the risk ratio increases as the baseline level of disease increases, as shown in Table 1. When the baseline prevalence of disease in the control group changes from 40% to 4%, the risk ratio does not change; however, the odds ratio does and becomes more similar to the risk ratio as the

Table 1. Hypothetical disease populations with high and low baseline risk populations.

	Disease Present	Disease Absent	Odds	Risk
High baseline risk population for a protective factor (40%)				
Vaccinated	20	80	20 ÷ 80 = 0.25[a]	20 ÷ 100 = 0.20[b]
Not vaccinated	40	60	40 ÷ 60 = 0.33[a]	40 ÷ 100 = 0.40[b]
Relative measure of association			Odds ratio = 0.25 ÷ 0.33 = 0.37[c]	Risk ratio = 0.2 ÷ 0.4 = 0.50[d]
Low baseline risk population for a protective factor (4%)				
Vaccinated	2	98	2 ÷ 98 = 0.02[a]	2 ÷ 100 = 0.02[b]
Not vaccinated	4	96	4 ÷ 96 = 0.042[a]	4 ÷ 100 = 0.04[b]
Relative measure of association			Odds ratio = 0.02 ÷ 0.041 = 0.48[c]	Risk ratio = 0.02 ÷ 0.04 = 0.50[d]
High baseline risk population for a factor that increases disease (40%)				
Exposure present	80	20	80 ÷ 20 = 4[a]	80 ÷ 100 = 0.80[b]
Exposure absent	60	40	60 ÷ 40 = 1.5[a]	60 ÷ 100 = 0.60[b]
Relative measure of association			Odds ratio = 4 ÷ 1.5 = 2.67[c]	Risk ratio = 0.8 ÷ 0.6 = 1.33[d]

[a]Formula 1 for odds.
[b]Formula 2 for risk.
[c]Formula 3 for odds ratio.
[d]Formula 4 for risk ratio.

Table 2. Table of formulas used for calculation of odds, odds ratio, risk, risk ratio, and absolute risk.

Formula 1

$$\text{Odds of disease in vaccinates} = \frac{\text{Probability of disease}}{\text{Probability of non disease}} = \frac{20}{100} \Big/ \frac{80}{100} = \frac{20}{80} = 0.25$$

Formula 2

$$\text{Risk of disease in vaccinates} = \text{Probability of disease} = \frac{20}{100} = 0.20$$

Formula 3

$$\text{Odds ratio} = \frac{\text{Odds of disease in vaccinates}}{\text{Odds of disease in non vaccinates}} = \frac{20}{80} \Big/ \frac{40}{60} = \frac{20 \times 60}{40 \times 80} = 0.375$$

Formula 4

$$\text{Risk ratio} = \frac{\text{Risk of disease in vaccinates}}{\text{Risk of disease in non vaccinates}} = \frac{20}{100} \Big/ \frac{40}{100} = \frac{20 \times 100}{40 \times 100} = 0.5$$

Formula 5
Absolute risk of disease per 100 animals in vaccinates = Assumed control risk per 100 non vaccinates × risk ratio
$$= 78 \times 0.82 = 64 \text{ diseased animals per 100 vaccinates}$$
$$= 0.64$$

Formula 6

$$\text{Risk ratio} = \frac{\text{Odds ratio}}{1 - \text{Assumed control risk in non vaccinates} \times (1 - \text{Odds ratio})}$$

disease becomes rarer. This is because, when the disease is rare, the denominators of the odds and the risk are very similar. For example, in Table 1 when the baseline risk is 4%, the odds of disease in vaccinated animals is given by 2 ÷ 98, whereas the risk of disease in vaccinated animals is given by 2 ÷ 100.

The third set of data in Table 1 contains hypothetical data where the factor being studied increases the occurrence of disease. The odds ratio is 2.67, whereas the risk ratio is 1.3. Incorrect interpretation of the odds ratio as suggesting a 167% increase in risk ratio is clearly an overestimate of the increased risk, which is 30%.

Why Is Interpretation Difficult?

Difficulty interpreting odds and the odds ratio is common among clinicians and researchers; and numerous publications are available with a detailed discussion of the appropriate interpretation of the odds ratio.[1–3] As suggested by Prasad et al, "Probably, no one (with the possible exception of certain statisticians) intuitively understands the ratio of odds".[4] The issue is that most people, including clinicians, think in terms of probability (risk) rather than odds.

Solution and Conclusion

The solution is for authors to use risk-based measures of disease, which are not difficult to interpret. When prospective trials are conducted with binary outcomes, calculation of risk is possible.[3] However, for meta-analysis, clinical trials, or observational studies that require adjustment for covariates, the odds ratio might be preferred because it has desirable mathematical properties. If meta-analysis, clinical trials, or observational studies are conducted using odds ratio, it is possible to convert it back to the risk ratio, provided a sensible assumed risk of disease in the control group can be specified (Table 2: Formula 6).[5,6] When clinicians are unsure of the assumed risk of disease to use, a low, moderate, and high risk estimate can be used to obtain several risk ratios. Such an approach would facilitate interpretation and clarify the impact of uncertainty about the most appropriate assumed risk of disease.

Some groups recommend translating the relative measures such as the odds ratio and risk ratio to absolute risk differences to further facilitate translation of the research findings for clinicians.[7] To do this, it is necessary to specify a sensible assumed risk of disease in the control group. For example, using the data from Figure 1, a sensible assumed risk of the infection in the control group may be 80/102 (78%), which can be converted to 78 cases in 100 unvaccinated animals. Using the summary risk ratio of 0.82, this would translate to an expectation of 64 (78 cases times 0.82) infected animals infected animals (95% CI = 55–79) in 100 vaccinated animals (Table 2: Formula 5). If authors begin with the odds ratio, Formula 6 in Table 2 can be used to convert this to the risk ratio. The assumed control risk can be a median or mean risk, though it should be justified.[6] Again, if there is uncertainty about the sensible assumed risk, a low, moderate, and high estimate might be used.

The non equivalence of the risk ratio and odds ratio does not indicate that either is wrong or both estimates are entirely valid ways of describing an intervention effect. Clinicians and authors must avoid the easy error of interpreting the odds as a risk or probability. In particular, it is important not to use the terms risk or probability of disease when the odds are the measure of disease frequency.

Acknowledgment

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