SHORT COMMUNICATION

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THE ODDS RATIO: A MEASURE OF STRENGTH IN CLINICAL RESEARCH AND AN ANTITHESIS TO ODDS IN GAMBLING

K.I Egbuchulem

Division of Paediatric Surgery, Department of Surgery, University College Hospital, Ibadan

INTRODUCTION

The odds ratio (OR) is a measure of association or relationship, and compares the odds of disease or an event in those exposed to the odds of disease or an event in the unexposed group.[1] Other measures of association are relative risk ratio, hazard risk, mean difference, et cetera. Odds ratios are related to the probability of a binary or categorical outcome (an outcome that is either present or absent) but not exactly related to the probability of events. Relative risk ratio is the ratio of the probabilities of outcome in both exposed and unexposed.[2]

Odds Ratio (OR) has also been defined as a numeric expression of the strength of the association between cause and an effect when both are expressed as categorical variables. In clinical medicine, odds ratios can be used to present the strength of association between risk factors and outcomes where the null value is 1.[2]

There is a difference between probability and odds. Probability is the likelihood of an event happening. However, the odds of an event represent the ratio of the probability that the event will occur and probability that the event will not occur for a given exposure/risk factor. Odds Ratio (OR) serves to determine the relationship between exposure and outcome of an event. While odds can be calculated for any event, odds ratio is always with reference to two different outcomes e.g. (cases and controls, alive or dead, et cetera). The OR can be used to evaluate whether the odds of an event are same for two groups in a study sample. The OR measures the ratio of the odds that an outcome will occur given a particular exposure or event to the odds of the outcome occurring in the absence of the exposure or event[3, 4]. When the probability is small, odds are virtually identical to the probability and will be small[2]. The smaller the OR, the lesser the effect on the outcome, and the converse is true for a larger OR[1].

For example, if the probability of developing bladder cancer in a chimney worker is 0.20 (20%), then the probability that the event will not occur is 1– 0.20 = 0.80, or 80%. The odds of a chimney worker developing bladder cancer is 0.2/0.8 = 0.25. Same probability and odds for developing bladder cancer can be calculated for a group of workers not exposed to chimney smoke. A comparison of the odds of developing bladder cancer in both groups is termed odds ratio.

Clinicians and researchers are usually interested in knowing probabilities, level of association and relationship between two or more variables, whereas gamblers think in terms of odds. Odds are useful when betting because they represent fair payouts or cash outs. If one were to bet $100 on winning a match, a payout of $300 is necessary to have an even chance of winning your money back. From the gambler's perspective, a payout smaller than $300 is unfavorable and greater than $300 is favorable. Similarly, odds with a minus sign (like -$100) indicate that you must risk more than you will win. In OR, a negative value suggests a protective effect on the intervention compared to the control. A gambler has a fallacy that a certain random event is less or more likely to occur based on previous results. However, OR is more finite, the probability that an event will occur is the fraction of times you expect to see that event in many trials[3]. The OR can also be a measure of the effect size. Formula for calculating OR = (odds of disease in exposed)/ (odds of disease in the unexposed).

Most odds ratio calculations are set up as two by two tables. Therefore, the preferred significance statistic is the Maximum Likelihood Ratio Chi-Square. However, in some instances the Fisher's Exact Probability statistics or Pearson's Chi-Square can also be used.[5]

Applications of Odds Ratio in Medical Research
1. Odd Ratios are most commonly used in case-control studies to identify risk factors for certain outcomes; however, it can be used for other study designs with few modifications such as logistic regression analysis, and cross-sectional studies.[2]

The odds ratio (OR) is one of the best tools to use when the incidence of a particular outcome is relatively low. Due to the fact that the statistic provides information that helps physicians, and their patients decide the value of a particular course of treatment, it has increasingly been used when incidence of a particular outcome is not rare.

In a case-control study, the group of exposed and unexposed individuals consists of a few cases and few controls, and they are not usually a representative sample of all exposed and unexposed persons in the population. Here, the OR compares the chances of a case being exposed to the risk factor with the odds of control being exposed. Odds ratio can be used to determine whether a particular exposure is a risk factor for the outcome of interest, and to compare how strong or weak the OR is; the magnitude of various risk factors for that outcome.[1, 4]

Example: Assuming twenty-two children from a female boarding school attended a school party and ten of them ate seafood okro. Of all the school children, seven developed allergic reactions after the meal. Now, the question arises, how do you test if the seafood okro increases the likelihood of developing an allergic reaction or not, as 10 children who did not eat the sea food okro had no complaints? To resolve this, a contingency table is drawn, and OR determined.

Interpretations of ORs: What does value of odds ratio mean? [1]

1. OR of 1: There is no difference between the groups; i.e., there would be no association between the exposure and the outcome.
2. OR of >1: Suggests that the odds of exposure/ intervention are positively associated with the adverse outcome/treatment target compared to the odds of not being exposed.
3. OR of <1 Suggests that the odds of exposure are negatively associated with the adverse outcomes compared to the odds of not being exposed. This means the exposure gives a protective effect.

Strength of the OR:

- 1.0 – 1.49 weak positive
- 1.5 – 2.99 moderate positive
- $\geq$ 3 is strong positive.

The converse will be true for negative OR.
Patients may decide to accept or forego a particular treatment option (painful or costly treatments) if they understand what their odds are for a particular outcome of care if they choose one course, the opportunity cost of not choosing the other, and the risks of choosing the alternate course of action.

2. Testing the significance of the Odds ratio
Odds ratios are commonly used to express the strength of associations from logistic regression when predicting an outcome[2]. Since the OR is calculated based on sample data, there is need to test for the significance of the observed value comparing it with a hypothetical value.

Variables	Food allergy	No allergy	Total
Ate sea food	5 a	5 b	10
Did not eat	2 c	10 d	12
Total	7	15	22

OR: Odds of developing food allergy = a/c = 5/2 = 2.5,
Odds of not developing food allergy = b/d = 5/10 = 0.5,
OR = (a/c)/(b/d) = 2.5/0.5 = 5.0 (A strong positive OR)
In this example, those who ate the seafood (exposure) were 5 times more likely (OR = 5.0) to develop allergy (outcome), compared to those who did not eat the seafood okro.

Researchers often analyze a binary outcome using multivariate logistic regression. One potential limitation of logistic regression is that the results are not directly interpretable as either probabilities or relative risk ratios. However, the results from a logistic regression are converted easily into odds ratios because logistic regression estimates a parameter, known as the log odds, which is the natural logarithm of the odds ratio[1], while the main parameter reported in a linear regression is the regression coefficient.

Crude or unadjusted OR is seen in univariate or single/independent logistic regression, while the adjusted OR indicates that the risk factor is independently associated with the dependent variables. Adjusted OR is seen in multivariate analysis, and results when several independent variables are combined to run a logistic regression. Testing the significance of the OR can be done with available online calculators e.g. MedCalc: https://www.medcalc.org/calc/oddsw_ratio.php, and softwares such as STATA, SPSS, and R, can estimate OR easily. The level of significance can also be tested using the Chi-square test[5,6]. Importantly, along with OR, this online calculator provides value of 95% CI, Z statistic, and significance level.[6]

The null value for OR is 1.0, unlike mean difference which is 0, and odds ratios typically are reported in a table with confidence interval (CIs). If the 95% CI for an odds ratio does not include 1.0, then the odds ratio is considered to be statistically significant at the 5% level. e.g. 0.23 - 0.56, 2.67-5.87[7]. Confidence interval for OR is not significant when the interval includes 1.0. e.g. 0.67-4.66. Basically, the precision of the OR is estimated by the 95% CI. The 95% CI is often used as a proxy for the presence of statistical significance if it does not overlap the null value (e.g., OR = 1).[8] One of the important parts of understanding scientific research is effective analysis and interpretation, and OR is one such statistical tool that adds value to CI.

What are the Limitations of Odds Ratios?

Some considerations have to be made when interpreting results with odds ratios.

1. First, the interpretation of odds ratios is framed in terms of odds, not in terms of probabilities. Odds ratios are often mistaken for relative risk ratios or mean difference. [1] Although for rare outcomes odds ratios approximate relative risk ratios. When the outcomes are not rare, odds ratios always overestimate relative risk ratios, a problem that becomes more acute as the baseline prevalence rate of the outcome exceeds 10%. Odds ratios cannot be calculated directly from relative risk ratios. For example, an odds ratio of 3.0 also could correspond to a probability of an event occurring 60% for men and 43% for women, or to a probability of 70% for boys and 57% for girls.

2. Secondly, the magnitude of the odds ratio from a logistic regression is scaled by an arbitrary factor equal to the square root of the variance of the unexplained part of binary outcome.[4] This arbitrary scaling factor changes when more or better explanatory variables are added to the logistic regression model because the added variables explain more of the total variation and reduce the unexplained variance.[1] Therefore, adding more independent principal variables to the model will increase the odds ratio of the variable of interest (e.g., treatment) due to division by a smaller scaling factor.[4]

CONCLUSION

Odds ratio is the odds of the event in one group that is exposed, divided by the odds in another group not exposed. The great value of the odds ratio is that it is simple to calculate, very easy to interpret, and it is also useful in epidemiological studies when the data are retrospective.

Conflict of Interest Statement

The authors affirm that they have no conflict of interests to declare.

The odds ratio provides information that both clinicians and their patients can use for decision-making, as it is sometimes helpful in clinical situations to be able to provide the patient with information on the odds of one outcome versus another.

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