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RESEARCH ARTICLE

FALLACY OF USING ODDS RATIO AS A MEASURE OF ASSOCIATION IN PROSPECTIVE STUDIES

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ABSTRACT

Many prospective studies report Odds Ratio as measure of association between exposure and outcome, even though Risk Ratio / Rate Ratio can be directly measured in these studies. We reviewed the relationship between Odds Ratio and Risk Ratio in prospective studies and problems associated with the use of Odds Ratio as measure of association in them. Odds approximates probability and Odds Ratio approximates Risk Ratio only when probability of outcome is small (<10%). If association between exposure and outcome is positive, Odds Ratio will be higher than Risk Ratio and if that association is negative, Odds Ratio will be lower than Risk Ratio. Difference between Odds Ratio and Risk Ratio will increase with increasing outcome probability. Odds Ratio reported from a prospective study can be misinterpreted as relative risk, when in fact it can be quite different from risk ratio or rate ratio. We should avoid using Odds Ratio as measure of association in cohort studies and RCTs as it tends to exaggerate the magnitude of association between exposure and outcome. Even while reporting results of prospective studies from multi variable analysis, authors should calculate and report adjusted Risk ratio / Rate Ratio rather than Odds Ratio.

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INTRODUCTION

Odds Ratio is a widely used measure of association in epidemiological studies. It has well known relevance in case – control studies where other measures of association like Risk Ratio cannot be calculated due to limitation of its study design (Knol et al., 2012). Odds Ratio is also popular while presenting results from multi variable analysis, as regression coefficient obtained from logistic regression analysis can be easily converted to Odds Ratio (Di Lorenzo et al., 2014). However, in many prospective studies, association between exposure and dichotomous outcome is being reported in terms of Odds Ratio rather than Risk Ratio or Rate Ratio (Knol et al., 2011; Kim et al., 2012; Balasubramanian et al., 2015). This paper aims to highlight problems associated with using Odds Ratio as a measure of association and its relation with Risk Ratio in prospective studies.

Relation between Probability and Odds

Before we try to comprehend relation between Risk Ratio and Odds Ratio, we need to understand probability and odds relationship.

If P is the probability (risk) of occurrence of an outcome and (1-P) is the probability of that outcome not occurring, then Odds of that outcome will be = $P / 1-P$. Now, if P is very small, then we can ignore P in denominator and we can consider

Odds ~ Probability

However, if probability is large, then odds will be quite different from probability, as depicted in Table 1. This table also shows that with increase in probability, the difference between probability and odds will progressively increase, odds being always higher than probability. Probability is bounded by values of 0 and 1 whereas odds can have values from 0 to infinity (Pandis N. Risk, 2012).

Relation between Odds Ratio and Risk Ratio

If P1 is probability (risk) of outcome in individuals with exposure and P0 is probability (risk) of outcome amongst individuals without exposure, then

$$\begin{aligned} \text{Risk ratio} &= \frac{\text{Cumulative Incidence (risk) of outcome among exposed}}{\text{Cumulative Incidence (risk) of outcome among non exposed}} \\ &= P1 / P0 \end{aligned}$$

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Table 1. Relation between Probability and Odds at Different Values of Probability

Probability	Odds	Odds/Probability
0.01	0.0101	1.01
0.10	0.11	1.11
0.20	0.25	1.25
0.30	0.43	1.43
0.40	0.67	1.67
0.50	1.00	2.00
0.60	1.50	2.50
0.70	2.33	3.33
0.80	4.00	5.00
0.90	9.00	10.00
0.99	99.00	100.00

Odds Ratio can be Risk Odds Ratio or Exposure Odds Ratio in prospective studies.

$$\text{Risk Odds Ratio} = \frac{\text{Odds of outcome among exposed}}{\text{Odds of outcome among non exposed}}$$

$$\text{Exposure Odds Ratio} = \frac{\text{Odds of exposure among those with outcome}}{\text{Odds of exposure among those without outcome}}$$

Although conceptually distinct, Risk Odds Ratio and Exposure Odds Ratio are algebraically identical (Schoenbach and Rosamond, 2000). So, we will use Risk Odds Ratio as Odds Ratio for our comparison with Risk Ratio in this paper.

$$\text{Odds ratio} = \frac{P1 / (1-P1)}{P0 / (1-P0)}$$

However, in case probability of outcome is not low, we cannot ignore its value in the denominator. Hence, odds will not be closer to probability, which in turn mean Odds Ratio will not be a good estimate of Risk Ratio. Value of Odds Ratio in relation to Risk Ratio will depend on direction of association between exposure and outcome. If association between exposure and outcome is positive, Odds Ratio will be higher than Risk Ratio and in case, association between exposure and outcome is negative, Odds Ratio will be smaller than Risk Ratio i.e.

Odds Ratio will in fact, always exaggerate the effect of exposure on outcome as Odds Ratio will always be further away from null value of 1, in comparison to Risk Ratio (Ospina *et al.*, 2012; Andrade, 2015). Moreover, for the same value of Risk Ratio, Odds Ratio and difference between RR and OR will increase with increase in probability, when association between exposure and outcome is positive (Table 2). Similarly, in case association between exposure and outcome is negative, Odds Ratio will decrease and difference between RR and OR will increase with increase in probability of outcome (Table 3).

“if $P1 > P0$, then $OR > RR$, and
if $P1 < P0$, then $OR < RR$ ”

Use of Odds ratio as measure of association

In case control studies, Risk Ratio or Prevalence Ratio cannot be measured because incidence or prevalence of outcome cannot be measured.

Table 2. Relation between Risk Ratio and Odds Ratio for different values of probabilities when association between exposure and outcome is positive (RR =2)

Risk in Group 1 (Exposure Present)	Risk in Group 2 (Exposure absent)	Risk Ratio (RR)	Odds Ratio (OR)	OR/RR	Relative difference (%) $\frac{(OR-RR) \times 100}{OR}$
0.01	0.005	2	2.01	1.01	0.50
0.10	0.05	2	2.11	1.06	5.26
0.20	0.10	2	2.25	1.13	11.11
0.30	0.15	2	2.43	1.21	17.65
0.40	0.20	2	2.67	1.33	25.00
0.50	0.25	2	3.00	1.50	33.33
0.60	0.30	2	3.50	1.75	42.86
0.70	0.35	2	4.33	2.17	53.85
0.80	0.40	2	6.00	3.00	66.67
0.90	0.45	2	11.00	5.50	81.82
0.99	0.495	2	101.00	50.50	98.02

Table 3. Relation between Risk Ratio and Odds Ratio for different values of probabilities when association between exposure and outcome is negative (RR=0.5)

Risk in Group 1 (Exposure Present)	Risk in Group 2 (Exposure absent)	Risk Ratio (RR)	Odds Ratio (OR)	OR/RR	Relative difference (%) $\frac{(OR-RR) \times 100}{OR}$
0.005	0.01	0.5	0.497	0.99	- 0.51
0.05	0.10	0.5	0.47	0.95	- 5.56
0.10	0.20	0.5	0.44	0.89	- 12.50
0.15	0.30	0.5	0.41	0.82	- 21.43
0.20	0.40	0.5	0.38	0.75	- 33.33
0.25	0.50	0.5	0.33	0.67	- 50.00
0.30	0.60	0.5	0.29	0.57	- 75.00
0.35	0.70	0.5	0.23	0.46	- 116.67
0.40	0.80	0.5	0.17	0.33	- 200.00
0.45	0.90	0.5	0.09	0.18	- 450.00
0.495	0.99	0.5	0.01	0.02	- 4950.00

Now, if P1 as well as P0 are small, then we can ignore them in denominators while calculating Odds. In that case,

Odds Ratio ~ P1/P0
i.e. OR ~ RR

Hence, use of Odds Ratio as a measure of association in case control studies is appropriate (Knol, 2012). If outcome under study is rare in the population (incidence below 10 %), then Odds Ratio will closely approximate Risk Ratio and Rate Ratio (Schoenbach and Rosamond, 2000).

However, if probability of outcome being studied is very high, Odds Ratio should not be considered as a good estimate of Risk Ratio or Rate Ratio, except in case-cohort studies and density case control studies, where assumption of rarity is not necessary (Rothman, 2002).

On the other hand, in cohort studies and RCTs, we can directly measure Risk Ratio or Rate Ratio. Hence, Odds Ratio should not be used as an estimate of relative risk in prospective studies, though it is a valid measure of association in its own right (Moyses Szkolo and Nieto, 2000). Moreover, in majority of prospective studies, outcome is not rare; therefore, there will be significant differences between Odds Ratio and Risk Ratio in this type of analysis. It may also be possible that a weak association between exposure and outcome can get overstated by the use of Odds Ratio in results (Balasubramanian *et al.*, 2015). Non collapsibility and incomprehensibility are other disadvantages associated with use of Odds Ratio in prospective studies as in case control studies (Schoenbach *et al.*, 2000).

Measure of association from multi variable analysis in prospective studies

Another reason why Odds Ratio is reported in results as measure of association in multi variable analysis of prospective studies is that widely used logistic regression analysis provides us results in form of log Odds Ratio (Knol *et al.*, 2011). So many authors find it convenient to report results in form of Odds Ratio only and sometimes, adjusted Odds Ratio is misinterpreted as relative risk and incorrect phrases like 'more likely' and 'risk' are used to describe association between exposure and outcome based on Odds Ratio calculated (Kim *et al.*, 2012; Ospina *et al.*, 2012; Kaufman and Harper, 2012; Altman *et al.*, 1998).

Even if authors don't present their results based on Odds Ratio as relative risk in prospective studies, readers and policy makers can still easily misinterpret Odds Ratio as Relative Risk (Knol *et al.*, 2011; Kim *et al.*, 2012). Hence, it is better if results from multi variable analysis of prospective studies are reported in terms of Risk Ratio or Rate Ratio, especially when outcome probability is not low (Andrade, 2015). There are different methods available for calculating adjusted Risk Ratio or Rate Ratio from multi variable analysis such as conversion of odds ratio from logistic regression into risk ratio, using Cox regression, log-binomial regression and Poisson regression. Many statistical software packages are available to fit such models (Knol *et al.*, 2012; Camey *et al.*, 2014; Grant *et al.*, 2014; Greenland, 2004).

Conclusions

Using Odds Ratio to present results of cohort studies and RCTs can lead to reporting of exaggerated magnitude of association between the risk factor and outcome, especially when outcome is not rare. Odds Ratio reported in cohort studies and RCTs should not be interpreted as relative risk. It is better to report results of prospective studies as Risk Ratio or Rate Ratio rather than Odds Ratio.

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