

Relative risks and odds ratios: Simple rules on when and how to use them

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Abstract

Aim: Relative risks and odds ratios are widely reported in the medical literature, but can be very difficult to understand. We sought to further clarify these important indices.

Methods: We illustrated both relative risks and odds ratios using bar charts, then looked at the types of study for which each statistic is suited. We demonstrated calculation of relative risks and odds ratios through analysis of tabled data from a recent published longitudinal study, using a 2×2 table and R, the open-source statistical programming language. Simple rules for when and how to use relative risks and odds ratios are presented.

Conclusion: Understanding the difference between relative risks and odds ratios and when and how to use them may aid clinical interpretation, dissemination and translation of research findings.

KEYWORDS

clinical research, communication, health promotion and prevention, research methods, statistics

1 | INTRODUCTION

In order to encourage healthy behaviours and facilitate informed medical decision-making, physicians often need to interpret and convey the results of relevant medical research.¹ For example, patients might wish to know the association between “risk factors” or exposures, such as levels of pre-operative red cell distribution width and outcomes such as the chance of developing postoperative sepsis and pneumonia following coronary bypass surgery.² Research results are often expressed in terms of relative risks (RRs) and odds ratios (ORs). Odds ratios may be particularly difficult to understand and may incorrectly be interpreted as relative risks. Such misinterpretation may lead to overestimation of the relative risks, especially if the disease or other event is relatively common.^{3–6} In this paper, we seek to clarify the meaning of RRs and ORs using a 2 by 2 table and bar charts and to examine which types of design can be employed for each statistic,

with reference to recently published studies. Finally, a list of simple rules on when and how to use relative risks and odds ratios is presented.

1.1 | Risks and odds

A risk is generally defined as the frequency of an event occurring in relation to all possible events. Odds, on the other hand, compare the frequency of an event occurring, with the frequency of the event not occurring.^{3–8} Odds were originally defined in sixteenth century Italy by the Renaissance physician, mathematician and gambler Girolamo Cardano.^{9,10} The odds in favour of a single number, a “3”, for example, coming up on a single throw of a fair dice are one to five. One represents the side of the dice coming up as a “3”, and the five represents the other five sides of the dice. In other words, there is one chance of “winning”, in which the dice comes

up as a “3”, and five chances of “losing”, in which the dice comes up as one of the five other numbers. Odds of one to five could also be expressed as one divided by five, or 0.20. Odds can take any value from zero to infinity.

The probability or “risk” of rolling a “3” on a dice is the number of outcomes of interest over the total number of outcomes, which equals one (rolling a “3”) over six (the number of sides of a single dice) or 0.17. Risks (and probabilities) can only take values between zero and one. In the above example, the odds (0.20) are slightly higher than the risk (0.17), the denominator (five for odds and six for risk) being slightly different in each case.⁵ The difference in definitions and hence in denominators must be constantly kept in mind. Calculation of risks requires dividing n , the number of events of interest, by N , the total number of events. Calculation of odds requires dividing n , the number of events of interest, by $N-n$ or the number of events of interest not occurring.⁵

Definitions of risks and odds are summarized in Table 1. In addition, the difference between risks and odds is highlighted in Figure 1, based on a graphic technique employed by Wilber and Fu.¹¹ Risks are represented by the bar chart on the left. The number of events of interest n , such as the number of persons with an exposure or risk factor having a particular outcome, is divided by the total number of events N . In the bar chart, $n/N = 1/6$ or 0.17. Odds are represented by the bar chart on the right. The number of events of interest n is divided by the number of events not of interest $N-n$. In the bar chart, $n/(N-n) = 1/5$ or 0.20.

TABLE 1 Simple rules for using relative risks and odds ratios

	Relative Risk	Odds Ratio
Definition	Risk of outcome in those individuals with exposure (equals number of individuals with outcome and exposure, divided by the <i>total</i> number of individuals with the exposure), divided by risk of outcome in those individuals without exposure (equals number of individuals with outcome but not exposure, divided by the <i>total</i> number of individuals without the exposure)	Odds of outcome in those individuals with exposure (equals number of individuals with outcome and exposure, divided by the number of individuals with the exposure but <i>without</i> the outcome) divided by odds of outcome in those individuals without exposure (equals number of individuals with outcome but not exposure, divided by the number of individuals <i>without</i> the outcome or the exposure) Can also be used to compare the odds of having exposure in those individuals with and without a particular outcome
Type of regression required	Binomial regression or Poisson regression, with robust standard errors	Logistic regression
Cautions	Should not be used in case-control studies	Approximates relative risk for rare outcomes but otherwise overestimates the risk Odds ratios should be interpreted in terms of odds not as risks or probabilities
Study design applicable?		
Prospective cohort	Yes	Yes
Randomized Clinical Trial	Yes	Yes
Case-control	No	Yes
Retrospective cohort	Yes	Yes
Cross-sectional	Yes, as prevalence ratio	Yes, as prevalence odds ratio

1.2 | Risks and odds in medical research

The choice of which statistic(s) to generate and report is determined by the type of study, as outlined in Table 1.

1.3 | Longitudinal studies

For a prospective cohort study, or a randomized controlled trial (RCT), both RRs and ORs can be calculated. A prospective cohort study is a type of observational study, in which each participant is followed up over a period of time, their exposure/s measured and their eventual outcome/s recorded.¹² A recent example of a prospective cohort study examined the association between risk factors such as loss of consciousness and the later development of post-concussion symptoms in individuals with mild traumatic brain injury.¹³ For a conventional two-arm RCT, the eventual outcome/s of those individuals receiving an intervention is compared with the eventual outcome/s of those individuals randomized to the control group. A major international community-based RCT, for example, compared mortality and other outcomes in an intervention group receiving 100 mg of enteric-coated aspirin and a control group receiving a placebo.¹⁴

Both relative risks and odds ratios may be used with prospective cohort studies and RCTs. Both measures allow comparison of outcomes in those individuals with a particular risk factor or intervention (ie those in the treatment arm

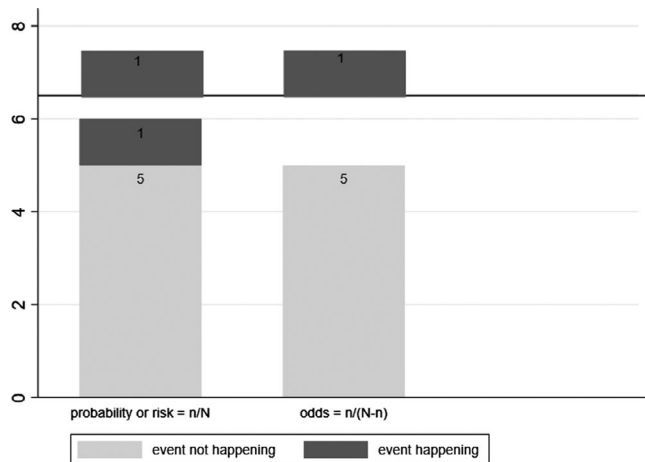


FIGURE 1 Bar charts representing calculation of risks and odds. n, number of events of interest, N, total number of events

of the RCT) versus those individuals without the risk factor or intervention (those in the control arm). One measure is directly concerned with risk, and the other is concerned with odds. Unless the outcome is comparatively rare, (often defined as an incidence of less than 10%⁵) the odds ratio will overestimate the relative risk if the former is employed as a measure of risk.^{5,6}

1.4 | Retrospective studies

A retrospective study makes use of historical information. A well-known type of retrospective study is the case-control study. Those individuals who have experienced a particular outcome are the “cases” and those individuals who have not experienced that outcome are the controls.^{12,15} For example, a recent case-control study¹⁶ “looked backward” at cases who had presented with thunderstorm asthma at an Australian hospital emergency department during the Melbourne pollen season of 2016. Cases were then compared with controls who had presented to the emergency department with asthma during the same period of time in earlier years. The presence and absence of risk factors such as taking beta-blockers, obtained from case notes, were then compared in cases and controls. In a case-control study, the outcomes are already known, and the individuals are defined as cases or controls depending on whether they did, or did not, experience a particular outcome. Exposures or risk factors are then observed “backward in time.” Neither incidence nor prevalence of a particular outcome can be obtained from a case-control study, as it is not known how many individuals were originally exposed to the risk factor. Only ORs, based upon the comparison of how many cases were exposed to the risk factor, compared with how many controls were exposed, can be calculated in case-control studies.^{4,6}

Another type of retrospective study is the historical cohort study.¹⁵ Although information on risk factors, as well as

outcomes, is already known in this type of study, individuals are selected based upon whether they were, or were not, originally exposed to the risk factor. Such information is generally based on historical material such as medical, employment or education records, often stored in registries. Unlike case-control studies, which begin with the outcome and work backwards in time examining the exposures, historical or retrospective cohort studies begin from a point backwards in time, looking at the presence or absence of risk factors in a particular cohort of individuals. The cohort is then followed “forward in historical time,” up to the more recent past, to examine who did and who did not, eventually develop a particular outcome.¹⁵

For example, the association between self-reported cannabis use; the risk factor or exposure and a later diagnosis of schizophrenia; the outcome, was examined using a retrospective cohort design.¹⁷ Information on cannabis use was obtained via a battery of tests administered to a large cohort of Swedish males assessed for compulsory military training in 1969–1970. This information was then linked to hospital records of admissions for schizophrenia, for the period 1970–1996. The conscripts were therefore followed up from 1969 to 1996, employing historical data, to ascertain who did and did not eventually develop schizophrenia. As retrospective or historical cohort studies examine the incidence of a particular outcome in individuals with and without the presence of a particular risk factor, both RRs and ORs can be calculated.

1.5 | Cross-sectional studies

ORs, often referred to as prevalence ORs when comparing prevalence¹⁸ can be calculated in cross-sectional studies, in which exposures, as well as outcomes (eg the prevalence of a particular disease), are studied at a similar point in time.¹² Similarly, prevalence ratios can be calculated in place of relative risks. Prevalence ratios are calculated in the same manner as relative risks, but have a different interpretation.¹⁸ For example, a recent cross-sectional study compared the prevalence of high blood pressure; the outcome, between groups that differed based on their daily intake of potassium compared with magnesium; the exposure.¹⁹

1.6 | Illustrative example: relative risks and odds ratios for high cholesterol and myocardial infarction

To illustrate how RRs and ORs are employed, we calculated both statistics for prospective cohort data originally collected by the Wisconsin Longitudinal Study, USA. Data were collected prospectively from 1957 to 2011 and tabulated in a published study (Table 1 and Figure 1 of the

original publication).²⁰ Outcome variables included whether a myocardial infarction (MI) had occurred by the age of 72 years. In this example, the risk factor is the presence of high cholesterol by age 65 in 2450 males for whom cholesterol information was available. Further information on the Wisconsin Longitudinal Study is available at <http://www.ssc.wisc.edu/wlsresearch/>

2 | MATERIALS AND METHODS

2.1 | Statistical analysis

As this study is prospective, either relative risks and odds ratios can be calculated, although the original study calculated ORs. In the present illustrative example, we expanded the results to show the frequencies for cholesterol level and myocardial infarction in the form of a 2×2 table.

We then calculated both a RR and an OR and their 95% confidence intervals and p values for RRs and ORs from the observed frequencies in the published tabled data.²⁰ We utilized the *epitools* package (Tomas J. Aragon (2020). *epitools: Epidemiology Tools*. R package version 0.5-10.1. <https://CRAN.R-project.org/package=epitools>) implemented in the open-source R statistical programming language, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria, 2020).

3 | RESULTS

The association between cholesterol level and myocardial infarction is shown in Table 2.

3.1 | Calculation of relative risk

Relative risk represents the absolute risk of the incidence of disease (ie developing MI) amongst individuals who were positive on the risk factor (high cholesterol), divided by the absolute risk of the incidence of disease amongst those who were negative on the risk factor. Calculations for the relative risk, based upon the frequencies presented in Table 2, are shown in Box 1.

The absolute risk of MI for those males with high cholesterol by age 65 is given by the number of males with high cholesterol developing MI by age 72 (269) (n), divided by the total number of males with high cholesterol (1162) (N), = 269 divided by 1162 or 0.2315. The absolute risk of MI for those males without high cholesterol by age 65 is given by the number of males without high cholesterol developing MI by age 72 (108), divided by the total number of males without high cholesterol (1288). The absolute risk is therefore 108 divided by 1288, or 0.0839. The relative risk of MI for those males with

TABLE 2 Association between exposure/risk factor (high cholesterol) and disease (myocardial infarction) in males, Wisconsin Longitudinal Study²⁰

High cholesterol by age 65	Myocardial Infarction (MI) by age 72		
	Yes	No	Total
Yes	269 a	893 b	1162
No	108 c	1180 d	1288
Total	377	2073	2450

Box 1 Calculation of relative risk for risk of disease amongst exposed and nonexposed

Risk of disease amongst exposed = $a/(a + b)$
 $269/1162 = 0.2315$

Risk of disease amongst non-exposed = $c/(c + d)$
 $108/1288 = 0.0839$

Relative risk = $0.2315/0.0839 = 2.76$

high cholesterol, compared to those without high cholesterol, is therefore $0.2315/0.0839$ or 2.76. The risk of MI by age 72 in those men with high cholesterol by age 65 is almost three times as high as the risk of MI by age 72 in those men who did not develop high cholesterol by age 65. The 95% confidence interval (CI) for the above relative risk, generated using the default Wald method, was obtained using the *epitools* package in R 3.6.3. Entering the command *riskratio(c(1180,108,893,269))* into R obtained a 95% CI of 2.24-3.40, $P < .001$.

3.2 | Calculation of odds ratio

For a prospective study such as the Wisconsin Longitudinal Study,²⁰ the odds ratio represents the *odds* of the incidence of a particular outcome or disease (ie developing MI) amongst individuals with the exposure or risk factor (ie high cholesterol), divided by the *odds* of the incidence of a particular outcome or disease amongst individuals without the exposure. In more general terms, for a prospective study, the odds ratio represents the odds of disease amongst those individuals with the exposure, divided by the odds of disease amongst those individuals without the exposure. The first set of odds is equal to the number of individuals with both the exposure and the disease (n), divided by the number of patients with the exposure but without the disease (N-n). The second set of odds is equal to the number of individuals without the exposure but with the disease, divided by the number of individuals without the exposure or the disease.^{5,11}

For the present prospective study, calculations for the odds ratio, based upon the frequencies presented in Table 2, are shown in Box 2.

Box 2 Calculation of odds ratio for odds of disease amongst exposed and nonexposed

Odds of disease amongst those with exposure = $a/b = 269/893 = 0.3012$

Odds of disease amongst those without exposure = $c/d = 108/1180 = 0.0915$

Odds ratio = $0.3012/0.0915 = 3.29$

Box 3 Calculation of odds ratio for odds of exposure with and without disease

Odds of exposure amongst those with disease = $a/c = 269/108 = 2.4907$

Odds of exposure amongst those without disease = $b/d = 893/1180 = 0.7568$

Odds ratio = $2.4907/0.7568 = 3.29$

The odds of MI; the outcome, by age 72 for those males with high cholesterol; the risk factor or exposure, by age 65, is equal to the number of persons with high cholesterol developing MI (269) compared with the number of persons with high cholesterol not developing MI (893). The odds in favour of MI in those males with high cholesterol are therefore 269 to 893, or 269 divided by 893, or 0.3012. The odds of having MI by age 72 in those males without high cholesterol by age 65 is equal to 108 to 1180, or 108 divided by 1180, or 0.0915. The odds ratio is equal to 0.3012 divided by 0.0915 = 3.29. Therefore, the *odds* of those males with high cholesterol by age 65 having an MI by age 72 are over three times as high as the *odds* of those males without high cholesterol by age 65 having an MI by age 72.

The 95% confidence interval (CI) for the above odds ratio, generated using the exact mid-*P* method, was obtained using the *epitools* package in R 3.6.3, employing the command `oddsratio.midp(c(1180,108,893,269))`. The 95% CI equals 2.59–4.19. $P < .001$.

Although the above example involves a prospective study, case-control studies compare the odds of having had an exposure in cases, with the odds of having had an exposure in controls. Calculation of the odds ratio, “working backwards” from the outcome to the exposure, is shown in Box 3. As can be seen, although the calculations are slightly different, the end result is identical. Working backwards from outcome to exposure would be meaningless employing relative risks.

4 | CONCLUSION

The RR and OR in the above example take different values. The two statistics are only comparable in size when the disease is rare. When the disease is more common, as is the case with MI in older populations (employing the values shown in Table 2, the overall incidence of MI is $377/2450 = 15.39\%$), the OR can magnify risk, if it is employed as a measure of risk.

Although in the present example the difference between the RR and the OR is only slight, the RR should be calculated whenever possible, that is in retrospective cohort and prospective or longitudinal studies, and in the form of a prevalence ratio, in cross-sectional studies.¹⁸ ORs can be used

in case-control studies whereas RRs cannot. Regardless of whether RRs or ORs are employed, an observed association between risk factors and outcomes does not necessarily imply the presence of a causal relationship. In other words, correlation does not necessarily imply causation.

For example, an apparent association between taking acetaminophen or paracetamol pain medication during pregnancy and the subsequent development of attention deficit hyperactivity disorder (ADHD) in offspring may be at least partly due to an association with another risk factor such as the presence of parental ADHD.²¹ The mixing or confusing of the effects of exposures or risk factors with the effects of other, possibly extraneous, variables is known as confounding.^{22–24}

Even for prospective cohort, RCT and retrospective cohort studies, where RRs are able to be calculated and are more readily interpreted than ORs, the latter may still be reported in practice. This may be due to researchers being more familiar with logistic regression,^{25,26} which only generates ORs. RRs can, however, be obtained using binomial regression or Poisson regression, with robust variance estimation.^{5,27,28} These types of regression are generally available in most statistical packages.

Odds ratios can be used in more types of research design than can relative risks but should always be interpreted as odds rather than as relative risks or probabilities.⁶ Medical journals could usefully develop guidelines on how to report odds ratios, perhaps by including odds, so that the reader can clearly see what the odds ratio is actually referring to. Similarly, a relative risk does not in itself provide information on the absolute risk of a disease and so both absolute and relative risks should be reported. Finally, graphs or diagrams should be presented wherever possible.^{6,11,22–24,29–34}

Further opportunities for biostatistical and epidemiological mentoring in medical school, as well as applied introductory courses that take students’ (and clinicians’) anxiety about statistics or “numerophobia”³⁵ into account, should be encouraged. Greater understanding of indices such as RRs and ORs may aid clinical interpretation and presentation of relevant information to patients.

CONFLICT OF INTEREST

None.

ETHICAL APPROVAL

This paper involved analysis of published, tabulated summary data from the Wisconsin Longitudinal Study.²⁰ Further information on the Wisconsin Longitudinal Study is available at <http://www.ssc.wisc.edu/wlsresearch/>

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