JAMA Guide to Statistics and Methods

Estimating Risk Ratios and Risk Differences
Alternatives to Odds Ratios

Mathias J. Holmberg, MD, MPH, PhD; Lars W. Andersen, MD, MPH, PhD, DMSc

The goal of many medical research studies is to estimate the direction and magnitude of the effect of an intervention or treatment on a clinical outcome (in clinical trials) or the association between an exposure and an outcome (in observational studies). This effect or association can be presented in various forms, depending on the measured outcome. For example, if the outcome is a continuous measure (eg, blood pressure), the effect or association could be represented as a mean difference between the groups. If the outcome is a time-to-event outcome (eg, time to death), the effect or association is often expressed as a hazard ratio.

Related article page 1058

For binary outcomes (eg, 90-day survival), the measure of the effect or association is often presented as an odds ratio (ie, dividing the odds of the outcome in one group with the odds of the outcome in another), in which the odds are the probability divided by 1 minus the probability. Odds ratios are commonly reported in clinical research because of the frequent use of logistic regression when there is a need to adjust for various characteristics (eg, to adjust for potential confounders in an observational study). Logistic regression yields odds ratios, is relatively straightforward to perform, and is widely available in statistical software. However, as explained in an earlier JAMA Guide to Statistics and Methods article,[1] there are limitations to odds ratios. For instance, odds ratios do not approximate risk ratios when the outcome is frequent (**Table**) and odds ratios are easily misinterpreted by researchers, clinicians, and patients.

An observational study by Grunau et al[2] in this issue of *JAMA* evaluated survival to hospital discharge among patients who received ongoing resuscitation for out-of-hospital cardiac arrest during transport to the hospital compared with continuous resuscitation at the scene. Instead of reporting odds ratios, the authors estimated risk ratios and risk differences, measures of association that are more intuitive to interpret.

What Are Risk Ratios and Risk Differences?

A risk ratio is the probability (or risk) of an outcome in one group divided by the probability in another, whereas the risk difference is the probability of an outcome in one group minus the probability in another. For example, if survival is 50% in one group and 40% in another, the measures of effect or association are as follows: the risk ratio is 0.50/0.40 = 1.25 (ie, a relative increase in survival of 25%); the risk difference is 0.50 − 0.40 = 0.10 (ie, an absolute increase in survival of 10%), which translates into a number needed to treat of 10 (ie, 1/the risk difference, or 1/0.10); and the odds ratio is (0.50/0.50)/(0.40/0.60) = 1.50 (ie, a relative increase in odds of survival of 50%) (Table). An intervention that increases the relative odds of survival by 50% has the appearance of being more beneficial than a relative increase in risk of 25%, or an absolute increase in risk of 10%, although all measures are based on the same measures of effect or association. An effect or association that appears very beneficial according to a risk ratio or odds ratio might be negligible when applied to the absolute scale, which may present misleading information about the clinical benefit or harm of an intervention. These measures change with outcome prevalence. As shown in the Table, as the prevalence of the outcome increases, odds ratios become consistently farther from 1 compared with risk ratios.

How Are Risk Ratios and Risk Differences Estimated?

Although adjusted risk ratios and risk differences may be more clinically intuitive than adjusted odds ratios, they have traditionally not been used because of the complexity of the methods required to calculate them when adjustment for other variables is necessary. However, several methods are available for accomplishing this task. Simple calculations can be used to compute unadjusted estimates of risk ratios and risk differences. When adjusted estimates of risk ratios are needed, binomial models,[3] modified Poisson models,[4] and other techniques can be used to estimate them. Binomial and modified Poisson models are both regression-based approaches within the framework of generalized linear models. These are flexible models that assume a linear relationship between a set of variables and an outcome. The outcome can have different forms, depending on the link function of the model (ie, a function to transform the outcome; for example, a log link performs a logarithmic transformation).

To obtain risk ratios, both the binomial and modified Poisson methods assume a log link function to produce log risks, which, when exponentiated, can be directly interpreted as risk ratios. To obtain risk differences, the methods assume an identity link function (eg, no transformation) to obtain regression coefficients that are risk differences. The modified part of the Poisson method refers to the use of robust variance estimation (eg, a method to estimate valid standard errors for coefficients in a regression model) to account for model misspecification that occurs because the binary outcome does not follow a Poisson distribution. Although both approaches have limitations, they tend to produce correct estimates with valid CIs, and are easy to implement in standard statistical software, including in SAS,[5] Stata,[6] and R.[7]

Limitations of Risk Ratios and Risk Differences

In addition to the usual limitations of estimating and interpreting measures of effect or association (ie, confounding, selection bias, and information bias), several caveats should be considered when adjusted risk ratios and risk differences are estimated. The statistical computations are more complex than conventional methods and it may be challenging to effectively communicate the methodology to a nonstatistical audience. For example, log binomial regression may result in computational errors such that the risk

Table. Hypothetical Scenarios Showing Differences in Measures of Effect or Association as Prevalence of Outcomes Increases

Group 1 prevalence, %	Group 2 prevalence, %	Risk difference, %	Risk ratio	Odds ratio
2	1	1	2.00	2.02
5	4	1	1.25	1.26
50	40	10	1.25	1.50
60	50	10	1.20	1.50

ratio and risk difference cannot be estimated.[8] Modified Poisson regression is more likely to produce results, but may lead to CIs that are too wide because of misspecification of the outcome distribution.[9] For both models, these situations may be more likely to occur with small sample sizes, when many variables are included in the model, or both.

How Did the Authors Use Risk Ratios and Risk Difference and How Should They Be Interpreted?

The observational study by Grunau et al[2] used modified Poisson regression to estimate survival among patients with out-of-hospital cardiac arrest who were transported to the hospital during ongoing resuscitation compared with those who received continuous resuscitation at the scene. The risk ratio for survival was estimated at 0.48 (95% CI, 0.43 to 0.54) and the risk difference was estimated at −4.8% (95% CI, −4.4% to −5.3%). In other words, transport to the hospital was associated with a relative reduction in survival of 52% and an absolute reduction in survival of 4.8%.

However, each measure of this association alone does not provide a complete representation of the intervention. Although the risk ratio is generally constant across different baseline risks, the risk difference is not.[10] To fully describe the exposure-outcome relationship, both absolute and relative measures should be reported, a practice recommended by both the Consolidated Standards of Reporting Trials (CONSORT) and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

ARTICLE INFORMATION

Author Affiliations: Research Center for Emergency Medicine, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Denmark (Holmberg, Andersen); Department of Cardiology, Viborg Regional Hospital, Viborg, Denmark (Holmberg); Prehospital Emergency Medical Services, Central Denmark Region, Denmark (Andersen); Department of Anesthesiology and Intensive Care, Aarhus University Hospital, Aarhus, Denmark (Andersen).

Corresponding Author: Lars W. Andersen MD, MPH, PhD, DMSc, Research Center for Emergency Medicine, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital, Palle Juul-Jensens Blvd 161, 8200 Aarhus N, Denmark (lwandersen@clin.au.dk).

Section Editors: Roger J. Lewis, MD, PhD, Department of Emergency Medicine, Harbor-UCLA Medical Center and David Geffen School of Medicine at UCLA; and Edward H. Livingston, MD, Deputy Editor, *JAMA*.

Conflict of Interest Disclosures: Dr Andersen serves as a statistical reviewer for *JAMA*. No other disclosures were reported.

REFERENCES

1. Norton EC, Dowd BE, Maciejewski ML. Odds ratios—current best practice and use. *JAMA*. 2018; 320(1):84-85. doi:10.1001/jama.2018.6971

2. Grunau B, Kime N, Leroux B, et al. Association of intra-arrest transport vs continued on-scene resuscitation with survival to hospital discharge among patients with out-of-hospital cardiac arrest. *JAMA*. Published September 15, 2020. doi:10.1001/jama.2020.14185

3. Wacholder S. Binomial regression in GLIM: estimating risk ratios and risk differences. *Am J Epidemiol*. 1986;123(1):174-184. doi:10.1093/oxfordjournals.aje.a114212

4. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702-706. doi:10.1093/aje/kwh090

5. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol*. 2005;162(3):199-200. doi:10.1093/aje/kwi188

6. Cummings P. Methods for estimating adjusted risk ratios. *Stata J*. 2009;9(2):175-196. doi:10.1177/1536867X0900900201

7. Donoghoe M, Marschner I. Logbin: an R package for relative risk regression using the log-binomial model. *J Stat Software*. 2018;86(9). doi:10.18637/jss.v086.i09

8. Williamson T, Eliasziw M, Fick GH. Log-binomial models: exploring failed convergence. *Emerg Themes Epidemiol*. 2013;10(1):14. doi:10.1186/1742-7622-10-14

9. Fitzmaurice GM, Lipsitz SR, Arriaga A, et al. Almost efficient estimation of relative risk regression. *Biostatistics*. 2014;15(4):745-756. doi:10.1093/biostatistics/kxu012

10. Sun X, Ioannidis JP, Agoritsas T, Alba AC, Guyatt G. How to use a subgroup analysis: Users' Guide to the Medical Literature. *JAMA*. 2014;311(4):405-411. doi:10.1001/jama.2013.285063