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Odds ratios deconstructed: A new way to understand and explain odds ratios as conditional risk ratios

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Abstract

Objectives: The aim of this analysis was to provide an alternative derivation of the odds ratio (OR) to provide an intuitive meaning, freeing it from any mention of odds, which may make it a more useful concept for clinicians to use when describing treatment effect.

Study Design and Setting: By examining the four possible combinations of treatment/control and corresponding outcomes, we considered the conditional risk ratio (RR, also known as relative risk) of an event with the treatment compared with an event with the control for pairs of patients for whom treatment and control would yield different results. Both matched and unmatched studies are considered.

Results: We found that the OR could be derived as the RR of an outcome with treatment compared with an outcome with control conditional on the treatment and control resulting in different outcomes, thus providing a measure of the net benefit of treatment.

Conclusion: It has been claimed that the OR comparing the effect of treatment vs. control does not have the same clinical interpretability as RR because it involves ratios of odds and so is difficult to explain in terms of patient numbers. This new derivation provides an interpretation of the OR as an RR but conditional on treatment and control resulting in different outcomes. This may help explain the reason ORs cause interpretation difficulties in practice. Moreover, the OR may be a more clinically useful parameter to patients because it deals with only those situations where the outcome differs between the two groups.

Keywords: Conditional probability; Matched pairs; Number needed to treat; Odds; Odds ratio; Relative risk; Risk; Risk difference; Risk ratio; Unmatched pairs

1. Introduction

There are a number of commonly used numerical measures of clinical effect that report the results of clinical trials, whether they be randomized controlled trials, cohort studies, or case–control studies. These measures are estimates of probabilities, namely parameters that represent the likelihood of an event or an outcome under different conditions in a hypothetical population of patients. Sometimes, the term risk is used interchangeably with probability although risk involves conditions such as time duration or a population denominator. A treatment effect is generally measured by the probabilities of the occurrence of events.

For comparing two populations with rates p_1 (treatment) and p_2 (control) for adverse events,[1] a number of commonly used measures (defined in the Appendix) in the literature are risk difference (RD), risk ratio (RR), odds ratio (OR), relative risk reduction, and number needed to treat (NNT). The emphasis in this article is on the OR and its comparison with RR.

These populations are conceptual only. The samples come from the same pool of patients, and it is the randomization to treatment or to control that generates samples. In addition, the manner in which data are collected to estimate parameters does not change their meaning. An OR should

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[1] Instead of adverse events, we may instead consider beneficial events in which risk is replaced by the probability of a beneficial event, but for the purpose of this article, events are taken as adverse. A parallel interpretation for beneficial events extends appropriately, mutatis mutandis, so will not be repeated here.

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What is new?

- It has been widely asserted that the odds ratio comparing the effect of treatment vs. control does not appear to have the intuitive interpretability that the risk ratio has because it involves ratios of odds and is therefore difficult to explain from a probabilistic perspective that can be understood in terms of patient numbers.
- In this article, we provide a novel derivation of the odds ratio as a ratio of probabilities rather than a ratio of odds, that is, a conditional risk ratio of an event with treatment compared with an event with control among pairs of patients, both matched and unmatched, for whom treatment and control would yield different results, thus providing a measure of the net benefit of treatment.
- This derivation obviates some of the concerns that have been expressed, all of which emanate from the fact that odds are not probabilities.

represent the same quantity regardless of whether it is estimated by independent cohort studies or by matched pairs. It is a quantity that depends only on p_1 and p_2.

To keep the discussion concrete, consider data extracted from a blinded randomized trial in which a tibial shaft fracture was treated with either reamed intramedullary nailing or unreamed intramedullary nailing [1]. Table 1 shows the data for patients having closed fractures. The adverse event involved a primary composite outcome, including nonunion requiring implant exchange or bone grafting and dynamization of the nail.

The estimated treatment risk is shown as $\widehat{p}_1 = \frac{a}{a+b} = \frac{45}{416} = 0.1082$, whereas the control risk is $\widehat{p}_2 = \frac{c}{c+d} = \frac{68}{410} = 0.1659$, giving an RR of treatment to control[2]

$$\widehat{\mathrm{RR}} = \frac{\widehat{p}_1}{\widehat{p}_2} = \frac{0.1082}{0.1659} = 0.65.$$

The statistic used to estimate the OR would be

$$\widehat{\mathrm{OR}} = \frac{\widehat{p}_1/(1-\widehat{p}_1)}{\widehat{p}_2/(1-\widehat{p}_2)} = \frac{\widehat{p}_1(1-\widehat{p}_2)}{\widehat{p}_2(1-\widehat{p}_1)} = \frac{ad}{bc} = 0.61 \qquad (1)$$

Thus, if 1,000 patients were treated with reamed intramedullary nailing, we would expect about $45/416 \times 1000 \approx 108$ to experience an adverse event, whereas of 1,000 treated with unreamed nailing, we would expect about $68/410 \times 1000 \approx 166$ to experience an adverse event. Thus, the proportion of treated patients relative to control who would be expected to experience an adverse event is $108/166 = 0.65$, which is the RR shown in Table 1.

The RR thus has a direct meaning to a physician in terms of patient numbers as a comparison of two risks. What about the OR?

ORs and RRs are different measures and because a larger odds reflect a larger risk, and vice versa, then the ratio of two odds, just like the ratio of two probabilities, clearly provides some measure of the relative effectiveness of treatment vs. control or two treatments. Is there a corresponding meaning in terms of patient numbers?

A number of articles in this journal have recently used the OR in epidemiologic studies but generally with respect to comparison of conclusions with those derived using RR instead [2–6]. In fact, as pointed out in the Cochrane Handbook [7] "The nonequivalence of the risk ratio and odds ratio does not indicate that either is wrong: both are entirely valid ways of describing an intervention effect. Problems may arise, however, if the odds ratio is misinterpreted as a risk ratio."

Yet, among all comparison measures, the OR seems to be the measure that is least understood intuitively [8].

It is our view, that if users are going to refer to the OR, then they should have a careful and rigorous appreciation of what the OR conveys as a parameter in simple language. Unfortunately, denoting an OR as a ratio of odds does not endow it with such an intuitive meaning. We therefore wondered whether ORs have a meaning that could be simply understood in a manner similar to how an RR may be understood.

In this note, we hope to provide a simple novel derivation of the OR that completely bypasses odds and uses only probabilities, from which the OR is then derived as a bona fide ratio of risks.

Precisely, we point out that the OR is the RR of an outcome with the treatment compared with an outcome with the control *conditional* on there being a difference in outcomes between the treatment and the control. This is obvious, once stated, but we have not found such a statement in the literature and believe that this observation is new, useful, and obviates some of the concerns that have been expressed, all of which emanate from the fact that odds are not probabilities.

2. Common OR as a conditional RR: parallel groups

Whichever of RR or OR is used for comparison of two treatments or comparison of treatment with control, the choice is to provide a comparison between two probabilities (risks) p_1 and p_2. Applying such comparison to an individual patient, a researcher may then envisage the possibility of giving the treatment and control simultaneously to the same sample from the target population of individuals and under the same conditions. Of course, this is not possible. Instead, one might have a parallel group

[2] For clarity of exposition, we distinguish between parameters such as RR and their estimates, correspondingly denoted as $\widehat{RR}$, for instance, even if the meaning is clear from the context.