How to Interpret Risk Ratios, Odds Ratios, and Hazard Ratios

Do's	Don'ts
• Compare the probability of experiencing an event in two groups with the *risk ratio*. • Compare the odds of experiencing vs. not experiencing an event in two groups with the *odds ratio*. • Compare the instantaneous rate of experiencing an event in two groups with the *hazard ratio*.	• Interpret odds ratios as risk ratios unless the risk of the event is low in both groups. • Interpret hazard ratios as risk ratios.

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1 Measuring the effectiveness of a new drug for lung cancer

The goal of many clinical studies is to understand the association between an exposure or risk factor and an outcome or disease. Suppose you are interested in investigating the effectiveness of a new drug for treating advanced lung cancer. To this end, you assign 1,000 patients to the exposure group who receive the new drug and 1,000 different patients to the control group who receive the standard chemotherapy treatment. After one year, 699 of the 1,000 patient who received the new drug died and 909 of the 1,000 patients who received standard treatment died. Risk ratios, odds ratios, and hazard ratios are three commonly reported measures that quantify how effective exactly the new drug is compared to the standard treatment.

2 Risk ratio

The risk ratio – also called *relative risk* – compares the *risk* of death in the exposure group who received the new drug and the control group who received standard treatment. Risk is simply a different term for probability and is consequently a number between 0 and 1. The upper part of Figure 1A displays how to calculate the risk ratio. In the exposure group, 699 of the 1,000 patients died, so the risk of death is 699 / 1,000 = 0.699 or 69.9%. In the control group, 909 out of 1,000 patients died, so the risk of death is 909 / 1,000 = 0.909 or 90.9%. The risk ratio is the

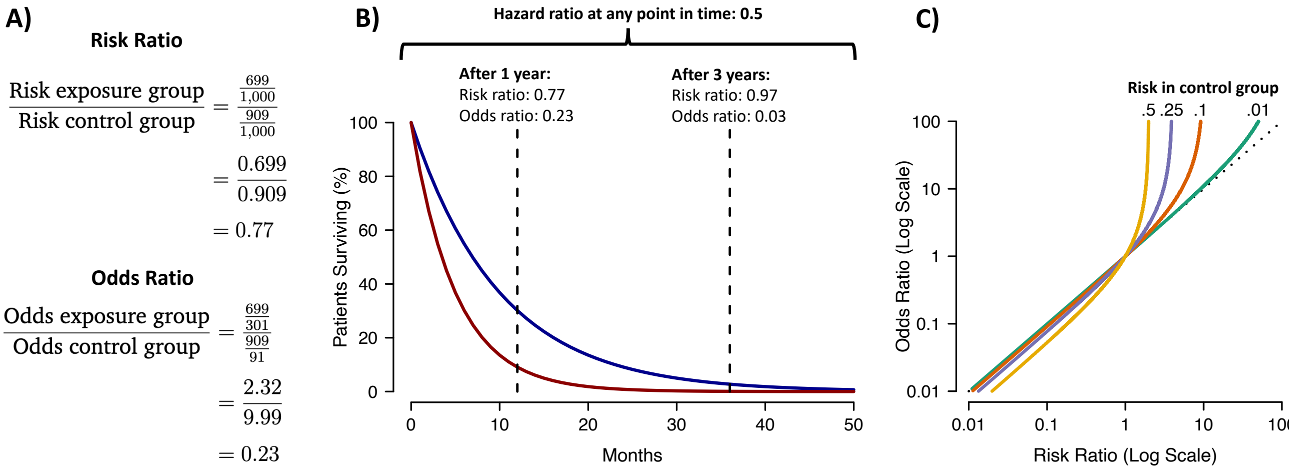

Figure 1: Panel A): Risk ratio and odds ratio formulas. Panel B) Percentage of patients surviving in the exposure (blue) and control group (red) over time. Panel C): Relation between risk ratio and odds ratio for four levels of risk in the control group.

ratio of these two risks: 0.699 / 0.909 = 0.77. This risk ratio indicates that the risk of death for patients who received the new drug is 0.77 of the risk of death for patients who received standard treatment. A risk ratio smaller than 1 indicates that the drug decreases the risk of death, a risk ratio larger than 1 would indicate it increases the risk of death. A risk ratio of 1 would indicate no difference.

3 Odds ratio

Another common measure are odds ratios. Risks ratios are easier to interpret than odds ratios, however, correctly interpreting odds ratios is important as well since they are commonly reported, for instance, in the context of logistic regression. Instead of comparing the risk in the exposure and control group, an odds ratios compares the *odds* of death vs. survival in each of these groups, that is, the number of patients dying vs. the number of patients surviving. The lower part of Figure 1A displays how to calculate the odds ratio. In the exposure group, the odds are 699 / (1000 - 699) = 699 / 301 = 2.32, in the control group, the odds are 909 / (1000 - 909) = 909 / 91 = 9.99. The odds ratio is the ratio of these two odds: 2.32 / 9.99 = 0.23. This odds ratio indicates that the odds of death for patients who received the new drug is 0.23 of the odds of death for patients who received standard treatment. An odds ratio smaller than 1 indicates that the drug decreases the odds of death, an odds ratio larger than 1 would indicate it increases the odds of death. An odds ratio of 1 would indicate no difference.

4 Hazard ratio

Risk ratios and odds ratios assess the effect of an exposure or risk factor on an outcome or disease at a fixed point in time (e.g., after one year). However, what if one had decided to assess the effectiveness of the new drug after three years instead? In this case, one might obtain a different risk ratio and odds ratio, thus different conclusions. *Hazard ratios* address this issue. Instead of comparing the risk or odds in the exposure and control group at a particular point in time, hazard ratios compare the *hazard*, the instantaneous event rate which can be thought of as the probability of dying in the next one time unit given one has survived so far. Consider the hypothetical example in Figure 1B which plots the percentage of patients surviving in the exposure (blue) and control group (red) over time. For this hypothetical example the hazard in both groups is constant over time and can be thought of as the answer to the question: "Given I have survived until now, what is the probability that I will die within the next month?". Suppose the hazard of dying in the treatment group is 0.1 and the hazard of dying in the control group is 0.2. The hazard ratio is the ratio of these two hazards: 0.1 / 0.2 = 0.5. This hazard ratio indicates that the hazard of death for patients who received the new drug is 0.5 of the hazard of death for patients who received standard treatment. A hazard ratio smaller than 1 indicates that the drug decreases the hazard of death, a hazard ratio larger than 1 would indicate it increases the hazard of death. A hazard ratio of 1 would indicate no difference.

5 Common misconceptions

There are two common misconceptions one should be aware of:

Misconception 1: Interpreting odds ratios as risk ratios

Odds ratios are often interpreted in the same way as risk ratios. In general, *this is incorrect and should be avoided*. However, in specific scenarios the odds ratio approximates the risk ratio and can thus be interpreted as such. Specifically, it can be mathematically shown that odds approximate risk when the risk is close to 0. Thus if the risk both in the exposure and control group is close to 0, the odds ratio approximates the relative risk. This is known as the *rare disease assumption*. Figure 1C plots the relation between relative risk and odds ratio by varying the risk in the exposure group from close to 0 to close to 1 for four different risks in the control group. The figure corroborates that the odds ratio approximates the relative risk for risk values close to 0. The figure also highlights that odds ratios are in general further away from 1 than risk ratios. Therefore, if one incorrectly interprets the odds ratio as a risk ratio, one will overstate the effect.

Misconception 2: Interpreting hazard ratios as risk ratios

The hazard ratio is not the same as a risk ratio. The easiest way to remember that a hazard ratio cannot be the same as a risk ratio is to recall that no one is immortal, so eventually, 100% of the patients in the exposure and control group will die. Therefore, after enough time has passed, the risk of death in each group, and therefore also the relative risk, will be close to 1. However, the hazard ratio does not necessarily need to converge to 1 over time since the hazard in each group is the probability of dying in the next one time unit *given one has not died so far*.

6 Further reading

- George, A., Stead, T. S., & Ganti, L. (2020). What's the risk: Differentiating risk ratios, odds ratios, and hazard ratios. *Cureus, 12*. doi:10.7759/cureus.10047
- Sashegyi, A., & Ferry, D. (2017). On the interpretation of the hazard ratio and communication of survival benefit. *The Oncologist*, *22*, 484–486.
- Cummings, P. (2009). The relative merits of risk ratios and odds ratios. *Archives of Pediatrics & Adolescent Medicine*, *163*, 438–445.