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Statistics Review Part 2: Relative Risk, Relative Risk Reduction, Absolute Risk Reduction, and Number Needed to Treat

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This is the second article in a series of articles designed to review the basic, fundamental concepts of biostatistics. This article describes different measures of effect size and discusses their applicability to clinical practice.

Objectives

1. Define Relative Risk (RR), Relative Risk Reduction (RRR), Absolute Risk Reduction (ARR), and Number Needed to Treat (NNT).
2. Describe the differences between the measures of effect size (RRR vs. ARR).
3. Determine how to evaluate the statistical significance of the RR, RRR, ARR and NNT measures.

Determining whether results are clinically important is useful for the transition of clinical research to patient care. When evaluating literature for application to clinical practice, it is useful to consider various measures for reporting effect size. Depending upon which measure is chosen, the effect size of the reported results may appear to be larger or smaller; thus, understanding the meaning of each of these measures is very important. Two commonly used measures of treatment effect are the RRR and the ARR. Often, clinical trials report the RRR instead of the ARR as the results are often more compelling; however, such results should be carefully interpreted as the RRR can be misleading.

Relative Risk and Relative Risk Reduction

The relative risk (RR) is the risk of an event or outcome occurring in a group of interest in relation to a control group. The group of interest can be an intervention (e.g., a medication) or a pre-specified characteristic (e.g., those with type 2 diabetes). An example would be the risk of heart attack in patients taking a study drug versus a control group of patients taking a placebo. The RR can be calculated by dividing the event rate (i.e., heart attacks) in the intervention group by the event rate in the control group (Table 1). If the RR is 1, there is no difference between the two groups; or, in other words, there is no association between exposure to a factor and the outcome of interest (e.g., there was no association between the study drug and heart attacks). An RR less than 1 indicates a negative association (e.g., an RR of 0.5 means the risk of heart attack in patients taking the study drug was less than in the control group), while an RR greater than 1 indicates a positive association (e.g., an RR of 2 means the risk of heart attack in patients taking the study drug was greater than in the control group).

The relative risk reduction (RRR) is another measure of effect size, which reports how much the treatment reduced the risk of an outcome relative to the control group. The RRR can be calculated by subtracting the relative risk from 1 (Table 1). It should be carefully interpreted as the results can be misleading, especially if baseline risk is not considered. The RR of an intervention is consistent across any baseline risk; however the absolute benefit can change depending on the baseline risk for the specified outcome. For example, the clinical implications of a large RRR for a relatively rare event (low baseline risk) may be different than the same RRR for a relatively common event (high baseline risk), and may make a treatment seem more effective than it actually is.

Absolute Risk Reduction

Perhaps the most useful measure for comparing effect size is the absolute risk reduction (ARR). This represents the absolute difference of the event rate between the treatment and control groups. The ARR is often not presented in the literature, but can be easily calculated by subtracting the event rate in the intervention group from the event rate in the control group. Similar to the RRR, baseline risk should be considered when interpreting the ARR. For example, a small ARR for a relatively

rare but severe event (e.g., heart attacks) may be more clinically relevant than a larger ARR for a relatively common event (e.g., duration of a cold).

Often times, the RRR is more commonly reported, but in terms of applicability and clinical usefulness, the ARR is a clearer representation of the difference between the two groups. As mentioned previously, the RRR is often more compelling than the ARR; however, it can easily be misinterpreted. For example, if a drug was shown to reduce the risk of stroke from 10% to 5%, the RRR would be 50%, which seems like a much larger impact than the ARR of only 5%. Even though the RRR and ARR are very different, both risk reductions are calculated using the same study information. Ideally, both measures should be presented for clarity. An additional example is provided in Table 1.

TABLE 1. Formulas for Measures of Effect

Measure of Effect	*Formula*	*Example*
Relative Risk (RR)	(event rate in intervention group) ÷ (event rate in control group)	Risk of heart attack with drug is 3% and 7% with placebo. Example RR: 3% ÷ 7% = 0.42
Relative Risk Reduction (RRR)	(1 - Relative Risk)	Example RRR: 1 – 0.42 = 0.58 (or 58% risk reduction)
Absolute Risk Reduction (ARR)	(event rate in control group) - (event rate in intervention group)	Example ARR: 7% - 3% = 4%
Number Needed to Treat (NNT)	1 ÷ ARR	Example NNT: 1 ÷ 0.04 (or 4%) = 25 patients treated to avoid one heart attack

Number Needed to Treat

The number needed to treat (NNT) is a representation of the number of patients who need to be treated to prevent one additional event compared to treating the same number of patients with the control therapy. The NNT is based on the ARR and therefore has less potential to be misleading. It can be easily calculated as it is the inverse of the ARR (Table 1).

A similar concept can be described as the number needed to harm (NNH), except this would represent the number of patients who need to be treated in order to induce one additional negative outcome compared to treating the same number of patients with the control regimen. The NNH is often used to assess side effects. The NNT and NNH calculations are useful as they help to put results into a clinical perspective, although the clinical utility varies greatly based on what outcome is being assessed. The NNT and NNH are not always clearly indicated in the literature; however, they can be easily calculated by the reader. The NNT and NNH should always be rounded up to the nearest integer, as you cannot have a fraction of a patient (e.g., an NNT of 1.6 would be rounded up to an NNT of 2).

It is important to be able to calculate and interpret the RR, RRR, ARR and NNT when evaluating a study's findings. Table 1 summarizes these effect measures and provides equations andexamples of each measurement. The calculated relative risk in this example is less than 1, which can be interpreted as a negative association, or that the intervention therapy is associated with fewer heart attacks. Also note how the RRR seems much larger than the ARR, even though the same outcome is being assessed. The NNT in this example demonstrates that for every 25 patients treated, 1 additional heart attack can be avoided compared to treating those patients with the control therapy. This represents meaningful data; however, the clinical significance can vary based on the evaluator, medical condition, and outcome being assessed.

Summary

This article reviewed relative risk, relative risk reduction, absolute risk reduction, and number needed to treat. The next article in this series will cover how to evaluate the variability of a study finding, including standard deviations and confidence intervals. ●

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Practice questions

1. If the risk of stroke was 5% in the intervention group and 8% in the control group, what would be the calculated relative risk reduction?
   a. 0.625
   b. 3%
   c. 37.5%
   d. 33
2. What would be the absolute risk reduction if the incidence of heart attack was 3% in the intervention group was and 9% in the control group?
   a. 12%
   b. 6%
   c. 33%
   d. 3%
3. If the calculated absolute risk reduction was 6.3%, what would be the number needed to treat?
   a. 16
   b. 1.58
   c. 6.3
   d. 21

Answers:

1. **c** First you must calculate the RR (5% ÷ 8%), and then you can calculate the RRR (1-RR).
2. **b** (9% - 3%) = 6%
3. **a** (1 ÷ 0.063) = 15.8; rounded up to nearest integer is 16.

References and suggestions for further review:

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