Risk Assessment 1: Relative Risk and Absolute Risk Reduction

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A new over-the-counter medication boasts that 75% of people with colds get better within 3 days with treatment. In a related story, compared with driving a 2-seat convertible, driving a minivan has been associated with a 3-fold increase in the risk of catching a cold.

There would be little reason for statistical analysis if all untreated diseases resulted in death and all treatments in cures. Similarly, it would be easy to identify risk factors if disease always developed with exposure and never without. As this is not the case, we need to consider not just the chance of observing a particular outcome, but also the chance of observing a particular outcome when certain conditions are present and absent. The scenario at the opening of this article is similar to claims we hear in the media every day, but if we do not know how many colds get better in 3 days without treatment (The cure rate might even be higher without treatment!) or what confounders are present in the minivan study (and the baseline rate of colds), we cannot draw any meaningful conclusions.

Calculating the *relative risk* allows you to quantify the magnitude of the influence a factor's presence has on an outcome. Determining the *absolute risk reduction* (ARR) and *number needed to treat* (NNT) allows you gauge the impact of the difference in risks on populations, which will help you decide if you should incorporate a finding into your practice. This article is the first in a 2-part series that reviews risk assessment. It will review relative risk, ARR, and NNT; Part 2 of the series will review a related concept, *odds ratios*.

RISK

Stated most simply, risk is the probability of an outcome of interest. If 1 out of 10 patients with a disease die, the risk of death is 10% or 0.1. (Probabilities can be expressed as a percentage, as a fraction, or as a number between 0 and 1.) Say you are studying 2 groups of 200 people with a certain type of cancer, and you treat one group with a new drug and the second group with an older drug. Say that in the group treated with the new drug, 180 patients respond, while in the group treated with the old drug, 140 patients respond. The risk of response with the new drug is 180 out of 200 or 180/200 or 0.9 or 90%. (Although the term used is "risk," it does not have to mean the worse outcome.) The risk of response with the old drug is 140 out of 200 or 140/200 or 0.7 or 70%.

There are several ways to express the difference in response rates between the 2 treatments. The first we will illustrate is the relative risk.

RELATIVE RISK

We are presented with 2 cancer therapies, the new drug has a response rate of 90%, the old one 70%. The relative risk is the ratio between the 2:

$$\text{Relative risk} = \frac{\text{Risk of outcome with factor present}}{\text{Risk of outcome with factor absent}}$$

In this example, if we consider the new drug to be the factor of interest, and the baseline response rate is that of the old drug, then the relative risk of response is:

$$\text{Relative risk} = \frac{\text{Risk of response with new drug}}{\text{Risk of response with old drug}}$$

$$= 0.9/0.7 = 1.29$$

This means that the risk of response with the new drug is 1.29 times greater than the risk of response with the old drug.

Values for relative risk can be any number zero or greater (no negative relative risks). A number between 0 and 1 implies that the risk of the outcome is greater when the factor is absent, and a relative risk greater than 1 implies the risk of the outcome is greater when the factor is present. A relative risk of 1 suggests the factor's presence does not influence the outcome.

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(It is beyond the scope of this article, but note that when you are looking at studies that report relative risks, they will typically report the 95% confidence intervals around the relative risk. For the relative risk observed to be considered statistically significant, the 95% confidence interval around a relative risk cannot include 1. More information on confidence intervals will be provided in a future article in this series.)

Consider now another treatment designed to reduce the frequency of heart attacks. Let's say that during the study period, 15 of 750 (2%) of those given placebo have heart attacks, and 15 of 1000 (1.5%) of those treated have heart attacks. The relative risk of heart attacks with treatment will be 0.015/0.02 = 0.75.

DON'T LET THEM FOOL YOU

It would be great if we could superficially survey study results and glean practice-changing conclusions, but data, even data objectively obtained and appropriately analyzed, can legitimately be presented in forms that, if not carefully considered, may result in your being more impressed with the apparent magnitude of the findings than the data may warrant. One technique used to magnify the findings is the presentation of *relative risk reduction* (or *relative risk increase*) in place of relative risk. Relative risk reduction is the percent change in risk, and, as a percent reduction in risk rather than a ratio of risks, the numbers usually sound more impressive.

Consider the heart attack data above with the treated group's heart attack rate of 1.5% and the placebo group's heart attack rate of 2%. We calculated the relative risk of heart attack with the new drug compared with the baseline risk placebo to be 0.75. The data could just as well have been summarized as the relative risk reduction by calculating the percentage improvement—in this case the baseline heart attack rate is 2%; with treatment, the rate is 1.5%, and the relative risk reduction is (0.02 – 0.015)/0.02 = 0.25, which is a 25% reduction in heart attacks with treatment. Certainly a 25% reduction in heart attacks sounds more impressive than a relative risk of heart attack of 0.75, but it's the same data!

Also appreciate that relative risks can become magnified when outcomes are rarer. Consider the risk of developing a disease with and without a risk factor's presence. If disease develops in 2% of those with the risk factor and in 0.25% of those without, the relative risk of disease in the presence of the risk factor is 0.02/0.0025 or 8. Or, even more extreme, with a change in risk from 1% to 0.05%, the relative risk is 200.

You can also be misled by headlines that *only* report relative risk. Learning that the relative risk of catching a cold is 3 for driving a minivan (minivan drivers can then be said to be 3 times more likely to catch a cold than are non-minivan drivers) does not allow you to determine if the risk of catching a cold as a minivan driver is 60% compared with 20% for non-minivan drivers (which would imply a huge difference), or 3 in 1000 compared with 1 in 1000. (This would imply that even though there may be a real difference, it might not be sufficient to influence car purchase decisions.) Keep in mind that well-calculated relative risks do not make up for poor study design. Perhaps people who have minivans may have more small children and are thus exposed to more colds. Confounders and biases must be identified before the validity of any results is considered.

Knowing that risk data can be manipulated to present different risks in a more or less favorable light, how can we reliably draw conclusions from risk data? One way is to consider *absolute risk reduction* and *number needed to treat.*

ABSOLUTE RISK REDUCTION AND NUMBER NEEDED TO TREAT

Consider 2 of the examples above: treatment with the new cancer drug demonstrating a relative risk for response of 1.29, and the relative risk of a heart attack of 0.75 in treated patients compared with untreated patients. It is proper to conclude from this information that the new cancer treatment improves the chance of response and that the treatment reduces the chance of a heart attack. But by how much and at what cost? More perspective on the magnitude of the impact can be gained by determining the ARR and the NNT.

The simpler of these concepts is ARR. The ARR is the difference (not the ratio) between the risk in the exposed group and the risk in the unexposed group. For the cancer treatment example, the exposed (new treatment) group had a response rate of 90%, and the unexposed (old treatment) group had a response rate of 70%. The ARR is then the difference between the two: 20% or 0.2. In the heart attack example, the unexposed group had a 2% rate of disease, and the exposed group had a 1.5% rate of disease; the ARR is the difference, 0.5% or 0.005. This means that the new treatments results in 20% more responders and 0.5% fewer heart attacks.

From the ARR value, we can calculate the NNT. NNT answers the question, how many patients do I need to treat to expect 1 additional patient to experience the outcome of interest? In the cancer treatment example, NNT will tell you how many patients must be treated with the new drug to see 1 additional patient response. For the heart attack example, NNT will tell

you how many patients must be treated to avoid 1 additional heart attack.

The NNT is calculated simply as the inverse of the ARR:

$$\text{NNT} = \frac{1}{\text{ARR}}$$

In the cancer therapy example, the ARR is 20% (or 0.2) and the NNT is 1/0.2 or 5, which means you would have to treat 5 patients in order to benefit 1 additional person. In the heart attack example, if the ARR is 0.5% or 0.005, the NNT is 1/0.005 or 200. This means you would have to treat 200 people with the drug to avoid 1 additional heart attack. Note how the 2 treatments have similar relative risk reductions or improvements (29% more cancer responders, 25% fewer heart attacks), but the NNT makes it apparent how many more people have to be exposed to the heart attack preventative treatment to prevent 1 heart attack than the number of people who have to be treated with the new cancer drug for 1 additional responder.

It should be becoming obvious how useful the NNT is. From the NNT, you can calculate the cost of therapy for each additional outcome and compare this value for different therapies. The cost per treatment multiplied by the NNT will be the cost per additional desired outcome. If the new heart attack drug costs $10 and the NNT is 200, then the cost per heart attack avoided is $2000. From the side effect rate you can similarly calculate the "number needed to harm" (NNH) as the inverse of the absolute *increase* in risk of the side effect with treatment and determine after what number of people are treated you can expect an additional patient to experience a side effect. By computing the NNT and NNH, you can start to quantify the risk-benefit ratio for a given treatment.

SUMMARY

The chance, or risk, of particular outcomes under different conditions can be compared in several ways. The relative risk is the ratio of the risk of an outcome with and without a particular factor's presence. The relative risk reduction (or increase) is the percent change in risk under different conditions and can often seem a more impressive number than the relative risk. The ARR is the difference between the risk of an outcome with and without a factor's presence. The inverse of the absolute risk reduction is the NNT, which is the number of patients who must be treated in order to benefit 1 additional patient.

The following section presents some questions to reinforce the concepts reviewed in this article.

PRACTICE QUESTIONS

1. In a study of otitis media treatment, standard antibiotics result in a 95% 1-week cure rate, while a new antibiotic boasts a 97% cure rate ($P < 0.05$).
   (**A**) What is the relative risk of cure with the new drug?
   (**B**) What is the ARR?
   (**C**) What is the NNT?

2. A new treatment for stroke provides a good outcome in 20% of those treated compared with a good outcome in 10% of those treated with placebo. A major bleeding complication occurs in 10% of those treated with the new drug and 5% of those treated with placebo.
   (**A**) What is the NNT?
   (**B**) What is the NNH for the new drug when compared with placebo?

3. The new drug from question 2 costs $1000. An alternative to the new drug results in a 15% good outcome rate and costs $200. Calculate the cost per additional good outcome for the following:
   (**A**) New drug
   (**B**) Alternative drug

ANSWERS

1. (**A**) Relative risk = risk of cure with new drug/risk of cure with old drug = 0.97/0.95 = 1.02.
   (**B**) ARR = 0.97 – 0.95 = 0.02.
   (**C**) NNT = 1/ARR = 1/0.02 = 50. For every 50 patients treated with the new drug, 1 additional patient will get better compared with 50 patients treated with the old drug.

2. (**A**) NNT = 1/ARR. ARR = 0.20 – 0.10 = 0.10. NNT = 1/0.10 = 10.
   (**B**) NNH = 1/ARR. (In this case, the ARR is really the absolute risk increase in side effects.) ARR = 0.1 – 0.05 = 0.05. NNH = 1/0.05 = 20. For every 10 patients treated with the drug rather than placebo, an additional patient will have a good outcome; but for every 20 patients treated, an additional patient will experience harm from treatment.

3. (**A**) For the drug from question 2, the NNT = 10, cost = $1000. Cost per additional good outcome = cost for treatment × NNT = $1000 × 10 = $10,000. It will cost $10,000 overall to see

1 additional good outcome with the new drug, compared with no treatment.

(**B**) For the alternative drug, ARR = 0.15 – 0.10 = 0.05. NNT = 1/0.05 = 20. Cost per good outcome = $200 × 20 = $4000. The cost per additional good outcome is $4000. (Note that overall, there are fewer good outcomes with the alternative drug, but the cost is less. These simplified examples demonstrate how complicated these decisions can be in real life with many choices of treatments, varied efficacy, multiple side effects, and wider cost disparities.) **HP**

SUGGESTED READING

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Sackett DL, Haynes RB, Guyatt GH, Tugwell P. Clinical epidemiology. Boston: Little Brown and Company; 1991.

EDITOR'S NOTE

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