This module will present a refresher on simple statistics needed to understand Absolute Risk and Number Needed to Treat.
Which of these drugs would you take. Patients taking drug A had 33% fewer MI’s than those on placebo. 19% of patients taking drug B had MI’s vs. 28% on placebo. And 11 people needed to take drug C in order to prevent one MI. [pause] They are actually all the same drug with outcomes expressed using three different types of statistics.
Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S)

The present trial was designed to evaluate the effect of cholesterol lowering with simvastatin on mortality and morbidity in patients with coronary heart disease (CHD). 4444 patients with angina pectoris or previous myocardial infarction and serum cholesterol 5.5-8.0 mmol/L on a lipid-lowering diet were randomized to double-blind treatment with simvastatin or placebo. Over the 5.4 years median follow-up period, simvastatin produced mean changes in total cholesterol, low-density-lipoprotein cholesterol, and high-density-lipoprotein cholesterol of -23%, -35%, and +8%, respectively, with few adverse effects. 256 patients (12%) in the placebo group died, compared with 182 (8%) in the simvastatin group. The relative risk of death in the simvastatin group was 0.70 (95% CI 0.58-0.85, p = 0.0003). The 6-year probabilities of survival in the placebo and simvastatin groups were 87.6% and 91.3%, respectively.

There were 189 coronary deaths in the placebo group and 111 in the simvastatin group (relative risk 0.59, 95% CI 0.46-0.73), while noncardiovascular causes accounted for 49 and 46 deaths, respectively. 622 patients (28%) in the placebo group and 431 (19%) in the simvastatin group had one or more major coronary events. The relative risk was 0.66 (95% CI 0.59-0.75, p < 0.00001), and the respective probabilities of escaping such events were 70.5% and 79.6%. This risk was also significantly reduced in subgroups consisting of women and patients of both sexes aged 60 or more. Other benefits of treatment included a 37% reduction (p < 0.00001) in the risk of undergoing myocardial revascularisation procedures. This study shows that long-term treatment with simvastatin is safe and improves survival in CHD patients.

The data is from the 4S study, the first major study to show the benefits of statins in patients with coronary heart disease. In this large study, 431 patients taking Simvistatin, which is equal to 19%, had one or more major coronary events and 622 patients in the placebo or control group, 28%, had major coronary events.
Let's look at the numbers

- Patients taking Drug A had 33% fewer Myocardial Infarctions than those taking placebo (Relative Risk Reduction)

- 19% of patients taking Drug B had MI’s vs. 28% on placebo (Absolute Risk)

- 11 people had to take Drug C before one MI was prevented (Number Needed to Treat)

Drug A is an example of a Relative Risk Reduction, Drug B and Absolute Risk Reduction, which is sometimes referred to as Attributable Risk, and Drug C is the Number Needed to Treat. The next slide shows how to calculate some of these numbers.
Let's look at the numbers

### Absolute Risk

**MI of Simvastatin 19%; Placebo 28%**

**Absolute Risk Reduction** (difference percent in intervention & placebo groups) =

19% - 28% = 9%

**Number Needed to Treat** =

\[
NNT = \frac{100}{19\% - 28\%} = 11
\]

To calculate the Absolute Risk Reduction, take the Absolute Risk of patients in the Simvastatin or Intervention group, 19%, and subtract by the Absolute Risk in the Placebo or Control Group, 28%. The Absolute Risk Reduction is 9%. And, as in this case, if the sum is a negative number, it is not an issue and it can be ignored, as the Absolute Risk Reduction is the difference between the two Absolute Risks. The Number Needed to Treat is the inverse of the Absolute Risk Reduction. To calculate the NNT, divide the Absolute Risk Reduction by 100, rounding the result down to the nearest whole number. The Number Needed to Harm can be calculated the same way, using the percentages of adverse effects in an intervention group versus a control group. NNH should always be rounded up to the nearest whole number. Absolute Risk Reductions, whether large or small, do not correlate with statistical significance in a study.
<table>
<thead>
<tr>
<th>Relative Risk Reduction</th>
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<td>28% - 19% / 28% = 33%</td>
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Not to be confused with **Relative Risk** = Number of times more or less than 1 an event will happen in one group compared to another. 4S Study → RR = 0.66

**CAUTION** – Relative Risk Reduction can often over-inflate significance of study findings. An example:

The Relative Risk Reduction is just that – the Relative Difference between the Absolute Risks. This figure is often used to over-inflate the significance of study findings. The next slide shows a good example.
This is the advertisement from when Fosamax, or Alendronate, was first approved for use in osteoporotic women. The claim is that Fosamax reduces hip fractures by 51% in women over a five-year period. This figure is a Relative Risk Reduction. The Absolute Risks tell a different story. The Absolute Risk of a hip fracture in women taking Fosamax was 2.2%. The Absolute Risk in the placebo group was 1.1%. Using the calculations from the previous slide, 2.2% minus 1.1% equals and Absolute Risk Reduction of 1.1%. 100 divided by 1.1% equals a Number Needed to Treat of 90 in this population group. The 51% highlighted in this ad is not false, as 1.1% is indeed 50% of 2.2%. It is just using data that make the outcomes look more spectacular than they might actually be.
Be careful when reading clinical study results, especially when reading the abstract, as researchers without strong data will often use a Relative Risk Reduction to describe their findings instead of Absolute Risks. And these are the figures that patients most often see in pharmaceutical advertising on TV, the radio and in newspapers and magazines. The role of a clinician that understands Evidence-Based Medicine is to be able to have a conversation with a patient to help explain the differences between what they hear and what they might actually expect to find with a new treatment.