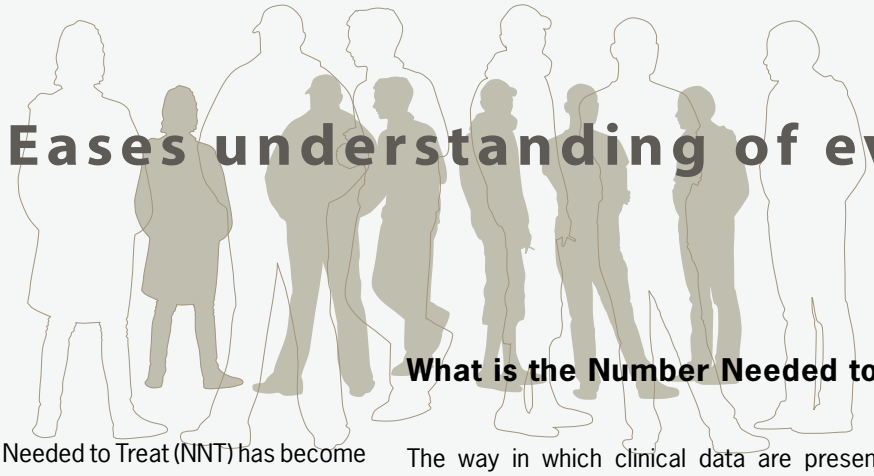
NNT – Eases understanding of evidence



Summary

- The use of Number Needed to Treat (NNT) has become popular in evidence based medicine to express the clinical effectiveness of interventions.
- NNT is computed from changes in absolute risk and gives a better indication of effectiveness than relative risk.
- NNTs can be compared for different agents treating the same condition or disease.
- As with other statistical parameters a quoted NNT is a point estimate and 95 % confidence intervals should also be available.
- NNTs calculated from meta-analysis of randomised controlled trials generally provide the highest level of evidence for the effectiveness of an intervention but there are some important limitations.
- When applying population derived NNTs to individual patient care it may be important to consider the patients background level of risk to determine the value of the intervention.
- With every NNT there is a number needed to harm (NNH). Knowledge of the NNH is sometimes important in weighing up the benefits versus risks of treatment.

What is the Number Needed to Treat (NNT)?

The way in which clinical data are presented can have a strong impact on clinical decision making. Relative risk (RR) is often used to summarise treatment comparisons, especially in drug advertising and journal abstracts, but it does not take in to account variation in baseline risk or the absolute size of the treatment effect. Absolute risk reduction (the difference in risk between treatments) gives this information but it can be difficult to interpret in the clinical context.

The NNT is the number of patients who need to be treated in order to prevent one additional bad outcome or to attain one additional benefit. NNT is the reciprocal of the absolute risk reduction associated with an intervention. It may also be calculated as 100 divided by the absolute risk reduction expressed as a percentage (Table 2).

NNTs in context

NNTs can be calculated from any trial data which give dichotomous outcomes, e.g. event or non-event, death or survival or cure from infection/lack or response. The outcomes may be more complex, such as an analgesic effect measured by pre-determined reduction in pain score at a specified time (response) vs failure to reach the target reduction in pain score (non-response). The NNT also needs additional information to indicate how long the treatment needs to be given for likely benefits to be observed. This is particularly the case in prophylaxis or when treatment effects are delayed. Some examples of NNTs are shown in Table 1.

Table 1: Examples of NNTs

Condition	Treatment	Comparator	Duration of Intervention	Outcome	NNT (CI)
Peptic Ulcer	Triple Therapy	H2-antagonist	6 – 10 weeks	*H. pylori* eradication	1.1 (1.08 – 1.15)
Migraine	Oral sumatriptan	Placebo	One Dose	Headache relieved at 2 hr	2.6 (2.3 – 3.2)
Painful Diabetic neuropathy	TCA	Placebo	4 – 12 weeks	At least 50% pain relief	2.9 (2.4 – 4.0)
High 5 year risk of CV mortality	Simvastatin	Placebo	5 years	Prevention of major coronary event	33 (26 – 46)

The acceptability of the NNT depends on whether the intervention is for treatment or prevention. An NNT of over 100 may be acceptable for prevention of death in a common condition such as cardiovascular disease but for the treatment of migraine headache a much smaller value of 4 or 5 would be expected.

Table 2: Relative Risk Reduction, Absolute Risk Reduction and NNT

A new anti-inflammatory drug A reduces the risk of serious GI bleed (event rate) by 50 % compared with a traditional NSAID. This is calculated from:

$$\frac{\textbf{GI bleed rate with drug A}}{\textbf{GI bleed rate with traditional NSAID}}$$

In the trial referred to, the rate was 1% with drug A and 2% with the traditional NSAID.

Relative Risk (RR) = 1/100 divided by 2/100 = 0.5 or 50%. This appears very significant; however the corresponding Absolute Risk Reduction (ARR) is the risk difference which takes in to account the background risk rate and is 0.02 – 0.01 = 0.01 or 1%.

The NNT is 1/0.01 (or 100/1) or 100. Intuitively we can also see that we need to treat 100 patients with drug A to prevent one adverse event (GI Bleed).

The RR can be very misleading. In the above trial if the event rates were 1 in 10,000 and 2 in 10,000 respectively the RR would still be 50% but the ARR is 0.0001 and the NNT is 10,000.

The NNT therefore indicates how many patients we can expect to benefit from treatment. We also need to consider how many patients are likely to be harmed (e.g. from an ADR) from taking the drug or number needed to harm (NNH).

What about Numbers Needed to Harm (NNH)?

Trials may show negative or harmful effects instead of anticipated benefits and drugs may also cause minor or major adverse reactions. In systematic reviews it is becoming the usual practice to present NNH for major and minor events along with the NNT for benefits to assist in clinical decision making. The balance of the NNT versus NNH indicates the risks versus benefits of treatment. For example, consider if the NNT for a statin to prevent a major coronary event is 50 given for five years and the NNH for rhamdomyolysis (a major harm) is 10,000. In this case we can expect one case of rhabdomyolysis for every 200 patients who will benefit from treatment.

Confidence is required in our NNTs!

Any NNT is just a point estimate and as such has some uncertainty around it. By convention, a 95% Confidence Interval (95% CI) is used to indicate the upper and lower limits of the actual NNT so we can say that there is a 95% probability that the true value lies within this range. To look at this another way, if we have an NNT of 4 (95% CI 3.2 – 6.1) this means that if the studies were repeated, 95 times out of 100 the result would fall in the range 3.2 – 6.1. It also means that we may need to treat as few as three patients or as many as six to get an extra response. Narrow confidence intervals are obviously preferable as they indicate a consistent treatment effect and give assurance that the NNT is close to the point estimate. The upper limit of the 95% CI may cast considerable doubt on the benefits of an intervention, and wide confidence intervals are usually due to variable treatment effects or small numbers of subjects, in the trials analysed.

Caution is required when interpreting NNTs derived from meta-analysis.

Since the introduction of NNTs some 15 years ago a debate has raged about whether NNTs derived from meta-analysis are misleading. It is relatively simple to calculate NNTs from a single randomised controlled trial but pooling of data from multiple RCTs is often employed to give the highest level of evidence. Applying NNTs derived from meta-analysis presents two main problems. Firstly, NNTs from a meta-analysis are subject to variation in risk differences among the studies included in the meta-analysis, as well as in baseline risks. Secondly, applying NNTs to an individual requires adjustment for their baseline risk. In practical terms, meta-analysis should always state variation in baseline risk, and if this is significant the NNT calculation should be based on pooled estimates of relative rather than absolute risk. When appropriate, in future articles in BPJ we will give guidance on the application of NNTs in practice.

Further Reading

Marx A, Bucher HC. Numbers needed to treat derived from meta-analysis: a word of caution. ACP Journal Club 2003;138(2):11.

Schechtman E. Odds ratio, Relative Risk, Absolute Risk Reduction, and Number Needed to Treat - Which of these should we use ? Value in Health 2002;5(5):431-36.