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What is an NNT?

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- NNT (number-needed-to-treat) has become a popular measure of effectiveness of interventions. NNTs are much easier to comprehend than some statistical descriptions, and NNTs for different agents can be easily compared.

- An NNT is treatment-specific and describes the difference between treatment and control in achieving a particular clinical outcome. It can be used to describe any outcome where event rates are available for both treatment and control.

- Clearly defining a useful clinical outcome is the best way of calculating and using NNTs.

- NNTs calculated from systematic reviews of randomised controlled trials provide the highest level of evidence because systematic reviews contain all of the relevant information and the largest numbers of patients available for analysis.

- An NNT is just one part of the information required in making a purchasing decision. There are many other factors, including adverse effects, costs, and individual, social and medical priorities.

Abbreviated prescribing information is on page 5

NNTs as a measure of effectiveness

The* number-needed-to-treat (NNT) *is the reciprocal of the change in absolute risk brought about by an intervention.

What does that mean? A few examples will serve to show how it works.

Example 1

We give an analgesic agent to 100 people and find that 70 have their pain relieved within two hours. But if we give those same 100 people a placebo tablet containing no active drug, we observe pain relief in only 20. So the analgesic is responsible for 50 of these 100 people obtaining pain relief. That is, 50% or an absolute risk reduction of 50/100, or 0.5. The reciprocal is 1/0.5, and the NNT is therefore 2.

That means that two people have to be given the analgesic for one of them to obtain effective pain relief.

Example 2

Consider the use of a thrombolytic agent after myocardial infarction. If 10,000 men have no thrombolytic treatment after a heart attack, perhaps 1,000 of them would die within six weeks. If they were given a thrombolytic agent, then the number dying within six weeks would be reduced to 800. So the treatment saves 200/10,000 lives, giving an absolute risk reduction of 0.02 and an NNT of 50.

Thus 50 people have to be given the thrombolytic therapy after a heart attack for one of them to avoid dying within six weeks who would have died had they not been given thrombolysis.

Examples of NNTs calculated from systematic reviews

Condition	Treatment	Comparator	Duration of intervention	Outcome
Peptic ulcer	Triple therapy	Histamine antagonist	6–10 weeks	*H pylori* eradication
Peptic ulcer	Triple therapy	Histamine antagonist	6–10 weeks	Ulcers remaining cured at 1 year
Migraine	Oral sumatriptan	Placebo	One dose	Headache relieved at 2 h
Fungal nail infection	Terbinafine	Griseofulvin	6 months	Cured at 1 year compared with griseofulvin – fingernails
Painful diabetic neuropathy	Antidepressant	Placebo	4–12 weeks	At least 50% pain relief
Postoperative vomiting	Droperidol	Placebo	Single dose	Prevention over 24 h in children undergoing squint correction
Peptic ulcer	Triple therapy	Histamine antagonist	6–10 weeks	Ulcers healed at 6–10 weeks
Venous thromboembolism	Graduated compression stockings	No stockings	Not stated	Episodes of venous thromboembolism
Amyotrophic lateral sclerosis (motor neurone disease)	Riluzole (Rilutek®)	Placebo	12 months	Survival without a tracheostomy
Labour	Epidural analgesia	Other treatment	During labour	Caesarean section
Anticipated preterm delivery	Corticosteroids	No treatment	Before delivery	Risk of fetal RDS
Dog bites	Antibiotics	Placebo	Single course	Infection
Hypertension in the elderly	Drug treatments	No treatment	At least 1 year	Overall prevention of cardiovascular event over 5 years
Myocardial infarction	Aspirin alone	No treatment	1 month	Prevention of one 5-week vascular death
Myocardial infarction	Thrombolytic therapy 5 h earlier	Later treatment	Appropriate period	Prevention of one 5-week vascular death

NNT (CI)
1.1 (1.08–1.15)
1.8 (1.6–2.1)
2.6 (2.3–3.2)
2.7 (1.9–4.5)
2.9 (2.4–4.0)
4.4 (3.1–7.1)
4.9 (4.0–6.4)
9 (7–13)
9.2 (5.2–38)
10 (8.4–13.2)
11 (8–16)
16 (9–92)
18 (14–25)
40
100

Treatment specificity

NNT is treatment-specific. It describes the difference between active treatment and control in achieving a particular clinical outcome.

An NNT of 1 means that a favourable outcome occurs in ***every*** patient given the treatment and in ***no*** patient in a comparison group – the 'perfect' result in, say, a therapeutic trial of an antibiotic compared with a placebo, such as eradication of *Helicobacter pylori* infection (see Table, left).

Studies of treatments usually involve big effects in (relatively) small numbers of patients, and therefore may have 'better' NNTs than those for prophylactic interventions. There are no set limits for NNTs to be considered clinically effective, but it is generally considered that the lower the NNT the better.

A correctly specified NNT must always give the comparator, the therapeutic outcome, the duration of treatment necessary to achieve that outcome and the 95% confidence interval (CI).

Calculating NNTs

The NNT can be calculated from the simple formula: 1/(proportion benefiting from experimental intervention minus the proportion benefiting from control intervention).

A fuller mathematical description is given in the box to the right.

For prophylaxis, where fewer events occur in the treated group, the calculation shown will produce negative NNTs. You can use those by simply ignoring the sign (the numbers will still be correct), or you can switch the active and control groups around to provide NNTs with a positive sign.

NNTs can also be calculated from statistical outputs of clinical trials of systematic reviews, from odds ratios (ORs) and from relative risk reduction (RRR) – see the 'Further reading' section below for more information on these statistical measures.

There is no absolute value for an NNT that says whether something is effective or not. NNTs for treatments are usually low because we expect large effects in small numbers of people. Since few treatments are 100% effective and few controls – even placebo or no treatment – are without some effect, NNTs for very effective treatments are usually in the range of 2–4.

Exceptions might be antibiotics. The NNT for *Helicobacter pylori* eradication with triple or dual therapy, for instance, is 1.1.

NNTs may also be calculated from different outcomes. So,to use the same example, the NNT for preventing one ulcer recurrence at one year is 1.8 (see Table).

Larger NNTs can be found with useful interventions – for instance in prophylaxis, where few patients are affected in large populations. Aspirin used to prevent one death at five weeks after myocardial infarction has an NNT of 40 but is regarded as beneficial. The same is true for instituting thrombolytic therapy as early as possible (NNT=100 for beginning thrombolytic therapy five hours earlier).

The 'NNT method' is now being used in other ways. For instance, it can be used to examine adverse effects of treatments or interventions, when it becomes the **number-needed-to-harm (NNH)**. There are few examples, but, for one instance, the effect of using epidural analgesia during childbirth is reported to produce higher rates of caesarean section. If that were regarded as harm, then the NNH would be 10.

THE KEY FORMULA

Calculating an NNT

$$NNT = \frac{1}{(IMPact/TOTact) - (IMPcon/TOTcon)}$$

where:

IMPact = number of patients given active treatment achieving the target

TOTact = total number of patients given the active treatment

IMPcon = number of patients given a control treatment achieving the target

TOTcon = total number of patients given the control treatment

Implications of NNTs

NNTs are useful in making policy decisions and decisions regarding individual patients. There are some important points to remember, though:

- NNTs can be calculated where any dichotomous information is present. Information is needed on how many patients achieve a particular treatment benefit, such as pain relief to a certain level, or not dying, as in our examples above. So, some thought has to be given to defining a worthwhile outcome.

- When NNTs are calculated, the circumstances are all important. These include the comparison being made (with placebo, or another active treatment), the dose of drug and/or duration of treatment and the outcome.

- Any NNT is just a point estimate. All point estimates have some uncertainty around them, usually reflected in the 95% confidence interval. For example, an NNT of 5.0 (3.6–7.2) means that 19 times out of 20 the result would fall in the range of 3.6 to 7.2 if the studies were repeated. The confidence interval becomes narrower as the amount of data increases. So large trials give a smaller interval than small trials. NNTs calculated from systematic reviews of randomised controlled trials provide the highest level of evidence.

- NNTs can be used to calculate different end-points from the same studies. Thus the *H pylori* example in the Table has three separate end-points – *Helicobacter* eradication, ulcer healing at six weeks after treatment, and ulcers still cured one year later.

- Comparison across treatments may be sensible, but only when comparisons are on a like-for-like basis. So comparing NNTs from, say, lipid-lowering in one study with a six-month outcome against another study with a three-year outcome would present some difficulty.

- NNTs can be used to express other features, such as harm. Adverse effects of treatment will increasingly be examined in this way, and we will begin to see the number-needed-to-harm (NNH) as well as the NNT.

- NNT is only one part of any assessment about purchase of treatment. There are many other factors, including adverse effects, costs, social and medical priorities.

- When clinicians and policy makers were presented with research results in different formats (NNT and absolute and relative risk reduction) they made more conservative decisions when they received treatment effects expressed as NNTs than when they received them as relative or absolute risk reductions.

Further reading

1. McQuay HJ, Moore RA. Using numerical results from systematic reviews in clinical practice. *Ann Intern Med* 1997; **126:** 712–720.
2. Gray JAM. *Evidence-based Healthcare: How to make health policy and management decisions*. London: Churchill Livingstone, 1997 (ISBN: 0-443-05721-4).
3. Sackett DL, Richardson WS, Rosenberg W, Haynes RB. *Evidence-based Medicine: How to practise & teach EBM*. London: Churchill Livingstone, 1997 (ISBN: 0-443-05686-2).
4. *Bandolier*, the evidence-based journal, publishes information on NNTs on a monthly basis (for information on *Bandolier*, fax: 01865 226978).

Abbreviated prescribing information: Rilutek®

Presentation: Rilutek Tablets contain riluzole 50mg. **Indications:** Riluzole is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS). Clinical trials have demonstrated that Rilutek extends survival for patients with ALS. There is no evidence that riluzole exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength or motor symptoms. Riluzole has not been shown to be effective in the late stages of ALS. The safety and efficacy of riluzole has only been studied in ALS. **Dosage and administration:** Adults and Elderly: One 50mg tablet bd; Children: Not recommended; Renal impairment: Not recommended; Hepatic impairment: See warnings and precautions. **Contra-indications:** Severe hypersensitivity to riluzole. Patients with hepatic disease where baseline transaminases are greater than 3 times ULN. Pregnancy, breast feeding. **Warnings and Precautions:** Prescribe with care in patients with history of abnormal liver function or patients with increased transaminase, bilirubin and/or GGT levels. Measure serum transaminases regularly during initiation of treatment with riluzole and frequently in patients who develop elevated ALT levels during treatment. Treatment should be discontinued if ALT level increases to 5 times ULN. Discontinue riluzole in the presence of neutropenia. Any febrile illness must be reported to the physician. Do not drive or use machines if vertigo or dizziness are experienced. **Interactions:** *In vitro* data suggests CYP 1A2 as the primary isozyme in the oxidative metabolism of riluzole; inhibitors or inducers of CYP 1A2 may affect the elimination of riluzole. **Pregnancy and lactation:** Contra-indicated. **Side effects:** Asthenia, nausea and elevations in LFT's are the most frequent events seen. Less frequent events include pain, vomiting, dizziness, tachycardia, somnolence and circumoral paraesthesia. **Legal Category:** POM. **Package Quantities and Basic NHS Price:** Each box of Rilutek Tablets contains 4 blisters of 14 tablets; £286.00.
Marketing Authorisation Number: Rilutek tablets 50mg EU/1/96/010/001.
Full Prescribing Information and further information is available on request from Aventis Pharma Limited, 50 Kings Hill Avenue, Kings Hill, West Malling, Kent. ME19 4AH. **Date of preparation:** November 2000.

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This publication, along with the others in the series, is available on the internet at www.evidence-based-medicine.co.uk

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