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Implementing NNTs

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- **Number Needed to Treat (NNT) is becoming a popular tool for expressing the effectiveness of interventions.** The clarity gained from expressing data in this manner is remarkable since it portrays absolute effect in an intuitive way.

- **It is important to note that NNT results should not be used in isolation.** We also need to consider age, epidemiology, population needs, social factors and other local priorities.

- **The strengths of NNTs** lie in providing a communication tool for the different parties involved in healthcare provision. **The weaknesses** relate to the relative newness of the methodology: there is no standard unit for NNTs in terms of time and outcome and, where a positive effect is partly due to the placebo effect, the NNT is an overestimate.

- **Opportunities in presenting data through NNTs** include the possibility of calculating the Number Needed to Harm (NNH). An appreciation of the clinical risk:benefit ratio can therefore be portrayed through the NNH:NNT ratio.

- **NNTS should always be quoted alongside the time period of the trial in which the intervention was considered.** There may be problems if benefits are not derived linearly over this time.

Abbreviated prescribing information is on page 5

NNTs and managing the NHS

Number Needed to Treat (NNT) is becoming a popular tool for expressing the effectiveness of interventions.

An NNT of 1 means that every patient given treatment will achieve a particular outcome – however, this is an 'ideal'. Most preventive strategies will have NNTs that are higher than this, since they are effective in some but not all of the patient population. NNTs of 40 or above (such as aspirin) can be considered beneficial.

As outlined in a previous bulletin in this series,[1] the NNT of an intervention can be calculated from the reciprocal of the absolute risk reduction (ARR).

Calculating NNTs

A simple example of the calculation is as follows:

Assume that the rate of strokes in a normal population at high risk is equal to 60% (ie, 60 out of 100 patients would experience a stroke in one year). A prophylactic agent given to prevent ischaemic stroke may reduce the number of strokes in this patient group to 50% (ie, 50 out of 100 patients would experience a stroke in one year).

The difference in the event rates (60% – 50%) is the ARR, which in this case would be 10%.

In order to calculate the NNT for this intervention, we would take the reciprocal of the ARR (or $\frac{1}{ARR}$). The NNT for preventing strokes would, therefore, be 10 (or $\frac{1}{0.1}$).

Understanding NNTs

In order to help understand NNTs in the context of NHS management, a simple SWOT analysis has been undertaken (see Figure 1).

It is important to note that NNT results should not be used in isolation. We also need to consider age, epidemiology, population needs, social factors and other local priorities.

One of the **strengths of NNTs**, however, is that they can be used as a currency for determining effectiveness within and between therapeutic areas in order to inform clinical and purchasing decisions.

For example, the NNT table (Table 1, right) can form the basis for discussion around the most effective intervention for reducing heart disease. If the aim is to prioritise funding, severe hypertension should be funded over mild, although the final decision will also need to take into account other factors such as local population needs and available budget.

The weaknesses of NNTs relate to the relative newness of the methodology since it is unclear at present how to formulate a table such as Table 1 as effectively as possible.

There is no standard unit for NNTs in terms of time (eg, one year or six months?) and outcome (eg, death only or all coronary events?). This means that trial results are given with different time horizons and different combinations of outcomes.

Let us consider an example in central nervous system (CNS) drugs. This category of pharmaceuticals contains many products that do not have a direct competitor such as riluzole in amyotrophic lateral sclerosis (ALS). The NNT for riluzole has been calculated

Figure 1. SWOT analysis of NNTs

Strengths
- Simple to interpret
- More indicative of resources
- Clarity of data purpose
- Clear communication of data

Weaknesses
- No standardised unit in terms of time or outcomes
- Needs similar risk population
- Requires similar time horizon
- May be overestimated if a positive effect is due to the placebo effect
- No cut-off level for effectiveness

Opportunities
- Able to evaluate systemic vs lifestyle strategies (eg, statins)
- Can calculate events prevented from NNT figure (see Table 1)
- Understanding of risk:benefit ratio through NNH:NNT
- Establish more meaningful dialogue with all involved in healthcare (eg, purchasers, providers, pharmaceutical industry)

Threats
- Can we afford to implement the results?
- Opportunity for personal bias in interpretation and presentation
- Non-agreed strategy/No consensus
- Still not widely quoted

Table 1. NNTs for cardiac interventions*

Intervention	Outcome	NNT
CABG in left main stenosis	Prevent 1 death in 2 years	6
Carotid endarterectomy in high-grade symptomatic stenosis	Prevent 1 stroke or death in 2 years	9
NNTs for hypertension treatment		
Simple antihypertensives for severe hypertension	Prevent 1 stroke, MI or death in 1 year	15
Simple antihypertensives for mild hypertension	Prevent 1 stroke, MI or death in 1 year	700
Treating hypertension in the over-60s	Prevent 1 coronary event	18
NNTs for angina treatment		
Aspirin in severely unstable angina	Prevent MI or death in 1 year	25
Aspirin in healthy US physician	Prevent MI or death in 1 year	500

*Adapted from *Bandolier* 1995; **17:** 7.

$$\text{NNH} = \frac{1}{(\text{risk in treated population} - \text{risk in untreated population})}$$

Box 1. Calculation of Number Needed to Harm (NNH)

elsewhere as 9 at one year (for preventing tracheostomy or death),[1] but it is not possible to compare this figure within the same therapeutic area.

Comparisons with other CNS products such as donepezil are frustrated by the issue of outcome since riluzole has been shown to extend life without tracheostomy, whereas donepezil focuses only on improvements in symptoms.

Indeed, *Bandolier* was unable to calculate an NNT for the trials presented for donepezil.[2] This is due to the fact that the only comparative figure available was the report that 1 in 4 patients benefited on donepezil, while 1 in 10 patients benefited on placebo.[3] The definition of benefits was not clearly expressed, so the calculation of an NNT would have been fairly arbitrary.

This raises questions about the cut-off for consideration of effectiveness and the value placed on different outcomes. Should life-extending therapies have higher acceptable NNTs? If there is no life extension, should therapies such as donepezil be ranked against other quality-enhancing therapies – for example, second-line cancer treatment? There is no consensus to this dilemma at present – interpretation is therefore still open to individual bias.

It should also be noted that NNTs calculated from placebo-controlled trials may be overestimated, since the placebo may include some of the positive features of treatment. Consider the case of acupressure where the NNT from trials would lead to a figure of 6. However, the difference between inappropriate acupressure (placebo) and non-treatment is positive. Adjusting the figures to consider treatment or non-treatment would give an NNT of 3.[4]

Opportunities in presenting data through NNTs include the possibility of calculating the Number Needed to Harm (NNH).

NNHs are a reflection of the safety issues in new interventions; they reflect the number of people who would have to be treated in order for one person to be harmed (usually through adverse events).

The formula for calculating the NNH is given in Box 1.[5]

An appreciation of the clinical risk:benefit ratio can therefore be portrayed through the NNH:NNT ratio.

A ratio of less than 1 would indicate that the clinical risk outweighs the clinical benefit. An example of this is the use of high-dose thiazide diuretics in hypertension, where the NNH for impotency in men has been established as 8 (over and above the general population risk);[5] and yet the most effective NNT calculated for simple hypertensives in severe hypertension has been established as 18 (see Table 1).[6]

The main threat to the use of NNTs is that they may be used in isolation from other information and needs. Knowledge should be used in conjunction with experience and observation in order to become practice.

NNTs are only one consideration in providing effective healthcare; they need to be used alongside other information sources.

Conclusion

- Implementing NNTs requires an understanding of the strengths, weaknesses, opportunities and threats involved.
- The NNH should also be calculated since this reflects the risk involved in treatment.
- The NNH:NNT ratio is an important indicator of risk:benefit from interventions and should be greater than 1.
- Attention needs to be paid to other information sources that impact on local decision-making.

References

1. Moore A, McQuay HJ. *What is an NNT?* London: Hayward Medical Communications, June 1997.
2. *Bandolier* June 1997; **4**(6).
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4. de Craen AJM, Vickers AJ, Tijssen JGP *et al*. Number Needed to Treat and placebo controlled trials. *Lancet* 1998; **351:** 310.
5. Gray JAM. *Evidence Based Healthcare: How to make health policy and management decisions.* London: Churchill Livingstone, 1997 (ISBN: 0-443-05721-4).
6. *Bandolier* 1995; **2**(7).

Suggested further reading

1. *Bandolier,* the evidence-based journal, publishes information on NNTs on a monthly basis (for information on *Bandolier,* fax: (01865) 226978. email: http://www.jr2.ox.ac.uk/Bandolier
2. Cook RJ, Sackett DL. The number needed to treat: a clinically useful measure of treatment effect. *BMJ* 1995; **310:** 452–454.
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5. McQuay HJ, Moore RA. Using numerical results from systematic review in clinical practice. *Ann Intern Med* 1997; **126:** 712–720.
6. Moore RA, Tramèr MR, Carroll D, Wiffen PJ, McQuay HJ. Quantitive systematic review of topically applied non-steroidal anti-inflammatory drugs. *BMJ* 1998; **316**: 333–338.
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8. Sackett DL, Richardson WS, Rosenberg W, Haynes RB. *Evidence-based Medicine: How to practise & teach EBM.* London: Churchill Livingston, 1997 (ISBN: 0-443-05686-2).
9. Walshe K, Ham C. Who's Acting on the Evidence? *Health Service J* 3 April 1997: 22–25.

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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