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.
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, 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 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

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple to interpret</td>
<td>No standardised unit in terms of time or outcomes</td>
</tr>
<tr>
<td>More indicative of resources</td>
<td>Needs similar risk population</td>
</tr>
<tr>
<td>Clarity of data purpose</td>
<td>Requires similar time horizon</td>
</tr>
<tr>
<td>Clear communication of data</td>
<td>May be overestimated if a positive effect is due to the placebo effect</td>
</tr>
<tr>
<td></td>
<td>No cut-off level for effectiveness</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Able to evaluate systemic vs lifestyle strategies (eg, statins)</td>
<td>Can we afford to implement the results?</td>
</tr>
<tr>
<td>Can calculate events prevented from NNT figure (see Table 1)</td>
<td>Opportunity for personal bias in interpretation and presentation</td>
</tr>
<tr>
<td>Understanding of risk:benefit ratio through NNH:NNT</td>
<td>Non-agreed strategy/No consensus</td>
</tr>
<tr>
<td>Establish more meaningful dialogue with all involved in healthcare (eg, purchasers, providers, pharmaceutical industry)</td>
<td>Still not widely quoted</td>
</tr>
</tbody>
</table>

Implementing NNTs

2
elsewhere as 9 at one year (for preventing tracheostomy or death), 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. 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. 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.

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.

### Table 1. NNTs for cardiac interventions*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG in left main stenosis</td>
<td>Prevent 1 death in 2 years</td>
<td>6</td>
</tr>
<tr>
<td>Carotid endarterectomy in high-grade symptomatic stenosis</td>
<td>Prevent 1 stroke or death in 2 years</td>
<td>9</td>
</tr>
</tbody>
</table>

### NNTs for hypertension treatment

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple antihypertensives for severe hypertension</td>
<td>Prevent 1 stroke, MI or death in 1 year</td>
<td>15</td>
</tr>
<tr>
<td>Simple antihypertensives for mild hypertension</td>
<td>Prevent 1 stroke, MI or death in 1 year</td>
<td>700</td>
</tr>
<tr>
<td>Treating hypertension in the over-60s</td>
<td>Prevent 1 coronary event</td>
<td>18</td>
</tr>
</tbody>
</table>

### NNTs for angina treatment

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin in severely unstable angina</td>
<td>Prevent MI or death in 1 year</td>
<td>25</td>
</tr>
<tr>
<td>Aspirin in healthy US physician</td>
<td>Prevent MI or death in 1 year</td>
<td>500</td>
</tr>
</tbody>
</table>

*Adapted from Bandolier 1995; 17: 7.

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

\[
\text{NNH} = \frac{1}{\text{risk in treated population} - \text{risk in untreated population}}
\]
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); and yet the most effective NNT calculated for simple hypertensives in severe hypertension has been established as 18 (see Table 1).

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.

References
2. Bandolier June 1997; (6).

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
7. Rajkumar SV, Sampothkumar P, Gustafson AB. Number needed to treat is a simple measure of treatment efficacy for clinicians. JGIM 1996; 11: 357–358.

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.
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 4AR. **Date of preparation:** November 2000.