Number Needed to Treat (NNT)

William H Cordell, MD

From the Emergency Medicine and Trauma Center, Methodist Hospital, Clarian Health Partners, and Indiana University School of Medicine, Indianapolis, IN.

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Because decisions regarding therapy are so common in clinical practice, the application of number needed to treat (NNT) is one of the most important evidence-based medicine skills to be acquired. NNT provides a clinically useful "yardstick" of the effort required to have a beneficial outcome or prevent a bad outcome with a therapy. A brief overview of the concept, derivation, and application of NNT is presented.

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INTRODUCTION

"Should I recommend this therapy to my patient?" is one of the most common questions in emergency medicine decisionmaking. However, it is not surprising that clinicians have difficulty translating research regarding therapies into practice because results of clinical trials are reported in a variety of ways including odds ratio, risk difference, relative risk, absolute risk reduction, and *P* value (statistical significance). Moreover, the results of a study could be statistically significant yet lack the clinical significance or magnitude of effect that would convince a clinician to offer it to an individual patient or incorporate it into routine practice. Therefore clinicians need a "yardstick"[1] to measure and compare the benefits and risks of various therapies.

Among the many ways to represent results from clinical trials, the expression *number needed to treat* (NNT) is gaining widespread use and acceptance. The reasons for its use are based in part on the deficiencies and inadequacies of alternative expressions, as well as the clinical sensibility of NNT to both clinicians and patients. NNT is a meaningful way of expressing the benefit of an active treatment over a control[2] (either placebo or standard care) that can also be applied to adverse events (harm).[3] Because NNT defines the treatment specific effect of an intervention, it has been proposed as "a currency for

making decisions about individual patients" in regard to therapy.[3] A brief overview of the concept, derivation, and application of NNT is presented and is intended to serve as a brief teaching guide for this important evidence-based medicine skill.

WHAT IS NNT?

NNT is an expression of the number of patients a clinician would need to treat to prevent 1 additional adverse outcome or attain 1 additional benefit. NNT is presented as a rounded whole number, often accompanied by a 95% confidence interval.[4-6] The numerical value represented by NNT is a function of 4 elements: the condition or disorder, the intervention, the events being prevented or benefits being achieved, and the duration of follow-up (Table).

NNT can be used to gauge the magnitude of effect for therapies that prevent bad outcomes. For example, the NNT for patients with asthma exacerbations discharged from the emergency department treated with oral or intramuscular corticosteroids (intervention) to prevent 1

Table.
Examples of NNT.

		Therapies to Prevent One Additional Bad Outcome				
Condition or Disorder	**Intervention**	**Events Being Prevented**	**CER (%)**	**EER (%)**	**Duration of Follow-up**	**NNT**
Diastolic blood pressure 90 to 109 mm Hg*	Antihypertensive drugs	Death, stroke, or myocardial infarction	5.45	4.67	5.5 y	128
Acute myocardial infarction*	Streptokinase and aspirin	Death at 5 wk Death at 2 y	13.4 21.6	8.1 17.4	5 wk 2 y	19 24
Healthy women, ages 50 to 69 y*	Breast examination plus mammography	Death from breast cancer	.345	.252	9 y	1,075
Patients who have had a first episode of deep venous thrombosis or pulmonary embolism†	Oral anticoagulation therapy for 6 mo as opposed to 6 wk	Recurrent venous thromboembolism	18.1	9.5	2 y	12
Asthmatic patients discharged from an acute care setting (usually the ED)‡	Steroids (oral or intramuscular)	Relapse	6	17	7 to 10 d	9

		Therapies to Achieve One Additional Benefit				
Condition or Disorder	**Intervention**	**Benefits Being Achieved**	**CER (%)**	**EER (%)**	**Duration of Follow-up**	**NNT**
Acute ischemic stroke§	TPA compared with placebo	Minimal or no disability (Barthel index)	38	50	90 d	8
Migraine headache‖	Intranasal lidocaine compared with placebo	50% pain reduction	21	55	15 min	3

CER, Control event rate; **EER,** experimental event rate.

*These 3 examples were obtained from Sackett DL, Richardson WS, Rosenberg W, et al: *Evidence-based Medicine: How to Practice and Teach EBM.* New York: Churchill Livingstone, 1997. See textbook for source articles. Used with permission.
†From The EBM Toolbox at the Centre for Evidence-Based Medicine (Oxford, England) Internet Web site (http://cebm.jr2.ox.ac.uk). See Web site for source article. Used with permission.
‡From Rowe BH, Spooner CH, Ducharme FM, et al: The effectiveness of corticosteroids in the treatment of acute exacerbations of asthma: a meta-analysis of their effect on relapse following acute assessment. *Cochrane Database of Systematic Reviews* 1998;3:3.
§From Anonymous: Tissue plasminogen activator for acute ischemic stroke. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. *N Engl J Med* 1995;333:1581-1587. (NNT calculated from data provided in the article.)
‖From Maizels M, Scott B, Cohen W, et al: Intranasal lidocaine for treatment of migraine: a randomized, double-blind, controlled trial. *JAMA* 1996;276:319-321. (NNT calculated from data provided in the article.)

additional relapse (events being prevented) within 7 to 10 days (duration of follow-up) is 9 (Table). The NNT of 9 was derived from a systematic review of effectiveness of corticosteroids in the treatment of acute exacerbations of asthma published in The Cochrane Database of Systematic Reviews.[7] In this example, an NNT of 9 could be translated, "A clinician would have to treat 9 asthmatic patients at discharge from the ED with oral or intramuscular steroids to prevent 1 additional patient from relapsing within 21 days of treatment."

NNT can also be used to assess the magnitude of effect for therapies that achieve benefits. As an example, the National Institute of Neurological Disorders and Stroke (NINDS) study published in 1995 compared intravenous recombinant tissue plasminogen activator (t-PA) with placebo administered to patients within 3 hours of onset of acute ischemic stroke.[8] Four main outcomes were studied, including the Barthel index, a 0 to 100 scale that measures the ability to perform activities of daily living such as eating, bathing, walking, and using the toilet. At 90 days after therapy, 50% of the treatment group (t-PA) versus 38% of the control group (placebo) had minimal or no disability as measured by the Barthel index, yielding an NNT of 8 (Table). Here, the NNT of 8 was calculated from data provided in the article (the calculation is discussed in the section titled "How Is NNT Calculated?). In this example, the NNT of 8 could be translated, "A clinician would have to treat 8 patients with acute ischemic stroke (condition or disorder) with t-PA compared with placebo (intervention) to have 1 additional patient achieve minimal or no disability (benefit being achieved) at 90 days after treatment (duration of follow-up)."

An article by Laupacis et al[1] published in 1988 provides an excellent explanation of the derivation of NNT. The authors used the results of a 3-year study comparing the efficacy of antihypertensive therapy with placebo in preventing adverse outcomes (including death, acute myocardial infarction, and congestive heart failure). The rate of adverse outcomes was 9.8% in the control group compared with 4.0% in the treatment group. They explained that if 100 control patients had been followed for 3 years, 10 adverse outcomes (risk of bad outcome, .098) would have been expected. If, however, 100 such patients had been treated with antihypertensive agents and followed for 3 years (risk of adverse event, .040), only 4 events would have been expected. Thus, on average, treating 100 such patients for 3 years would have prevented 6 (10–4) bad outcomes, meaning that 17 patients (100÷6) would have required treatment to prevent 1 adverse outcome. (NNT=17). NNT, as will be seen, is equivalent mathematically to the reciprocal of the absolute risk reduction (in this case 1/5.8%).

HOW LARGE IS LARGE?

In the previous example of treating patients with acute ischemic stroke with t-PA, how do we know if an NNT of 8 is a large enough treatment effect to warrant offering it to our patients as a potentially beneficial therapy? Laupacis et al[1] noted NNT "tells clinicians and patients in more concrete terms how much effort they must expend to prevent one event, thus allowing comparisons with the amounts of effort that must be expended to prevent the same or other events in patients with disorders." In general, the lower the NNT is, the larger the magnitude of treatment effect. Clinicians are cautioned, however, that it is inappropriate to compare NNTs across disease conditions, particularly when the interventions, measurements of benefit and harm, and duration of follow-up differ.[3]

WHERE CAN NNTs BE OBTAINED?

There are 4 major sources for obtaining NNTs. First, when not presented by the authors of an article or systematic review, the NNT can usually be calculated by the clinician, using the simple equation presented in the Figure. Second, authors of systematic reviews or studies regarding therapies often provide NNTs in their results. Third, tables of NNTs are available in journals[3] and textbooks.[9] Finally, an increasingly more useful means of finding NNTs is the Internet. For example, the Centre for Evidence-Based Medicine based in Oxford, England, maintains a Web site (http://cebm.jr2.ox.ac.uk) that provides tables of NNTs. Because they are maintained in electronic form, the tables can be constantly updated.

HOW IS NNT CALCULATED?

NNT is simply the inverse of the absolute benefit of intervention—that is, the difference between the proportion (percentage) of events in the control group and the proportion of events in the intervention group.[2] Restated, NNT is the inverse of the absolute risk reduction (ARR) or absolute benefit increase (ABI) (Figure). ARR and ABI, which are expressed as percentages, are the absolute arithmetic differences in outcome rates between the experimental and control subjects in a trial. The magnitude of treatment effects can be thought of in 2 ways—how much they reduce the risk of a bad outcome, or con-

versely, how much the treatment increases the risk of having a good outcome (such as pain relief). For experimental treatments that reduce the probability of bad outcome, it is best to think in terms of ARR. For those treatments that increase the probability of a good outcome, it is best to think in terms of ABI.[10]

In the example of t-PA for acute ischemic stroke therapy[8] referred to previously, the event rate for the control group (CER) was .38 (38%) and the event rate for the treatment group (EER) was .50 (50%), yielding an absolute benefit increase (ABI) of .12 (12%). Because NNT is the inverse of ABI, the NNT is 1 divided by .12, which equals 8.3. Rounded to the nearest whole number, this yields an NNT of 8.

NUMBER NEEDED TO HARM

A decision to use a therapy always involves a variety of tradeoffs including risk versus benefit, cost, acceptance, and availability. In addition to conferring benefit (reducing adverse outcomes or increasing good outcomes), most therapies also have clinically important side effects.[1] The same concepts regarding NNT reviewed above can be used to assess harm and calculate *number needed to harm* (NNH). NNH is the number of patients who, if they received the experimental treatment, would lead to 1 additional patient being harmed, compared with patients who received the comparison treatment.[10] In addition to adverse events, other negative aspects of therapy including monetary cost and inconvenience can be considered if pertinent data are available,[1] but typically require more advanced statistical methods.

In summary, NNT provides a clinically useful "yardstick" to guide both clinicians and patients in decisions regarding therapy. It provides a clinically useful measure of the effort required to achieve a beneficial outcome or prevent a bad outcome with a therapy. Because questions and decisions regarding therapy are so common in clinical practice, the ability to calculate and interpret NNT from primary reports of clinical research is one of the most important evidence-based medicine skills to be acquired and incorporated into emergency medical clinical decisionmaking.

Figure.
Calculation of NNT.

Abbreviations

ARR Absolute risk reduction
ABI Absolute benefit increase
EER Experimental group event rate
CER Control group event rate
NNT Number needed to treat

Calculations

ARR =CER –EER

ABI =EER –CER

$$\textbf{NNT} = \frac{1}{\textbf{ARR}} \text{ or } \textbf{NNT} = \frac{1}{\textbf{ABI}}$$

Tips

- Round NNT to the nearest whole number.
- Don't forget to convert CER and EER to a demical fraction when expressed as a percentage.
- Pain scores and other continuous data must be presented as or converted to dichotomous data before calculating NNT.

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