Number Needed to Treat (NNT) and Number Needed to Harm (NNH) in Psychiatry

Introduction

When healthcare providers (HCPs) evaluate therapeutic interventions, they often review clinical trials. HCPs typically rely on P values to represent statistical significance for the differences observed between interventions. However, P values are limited to understanding statistical significance, quantifying our degree of confidence that the results observed are real and not due to chance. P values do not convey information about the size of the treatment effect or describe the clinical relevance of the results observed.[1,2]

Having a method to quantify the clinical significance of trial results may help HCPs to better interpret and indirectly compare efficacy and safety data from clinical trials when head-to-head trial data is not available.

Effect size can represent the magnitude of a clinical response observed and is a way to measure the clinical relevance of trial results. Expressing effect size in terms of patient units using the number needed to treat (NNT) or number needed to harm (NNH) may be helpful for HCPs to interpret and communicate efficacy and safety data more easily.[2,3]

What are NNT and NNH?

NNT

How many patients need to be treated with 1 treatment instead of an alternative before you can expect to see 1 additional patient with that **positive outcome?**

NNT can be used to describe the **efficacy** of a therapeutic intervention.[2]

NNH

How many patients would you need to treat with a treatment instead of an alternative before you can expect to see 1 additional patient who experiences the **adverse event** in question?

NNH can be used to describe the **adverse events** associated with a therapeutic intervention.[2]

How are NNT and NNH calculated?

NNT and NNH are calculated by subtracting the rates of the outcome of interest for 2 different therapeutic interventions (eg, medication versus placebo from a randomized clinical trial).[1,4]

First, attributable risk (AR) is calculated by subtracting the rate of outcome for the placebo (R_P) from the rate of outcome for the treatment, Drug A (R_A). Then, you obtain the NNT or NNH by dividing 1 by the AR calculated in the first step (ie, the inverse of AR).[4,5]

R_A = rate of outcome for the treatment arm (Drug A)

R_P = rate of outcome for the placebo arm

Attributable Risk (AR) = $R_A - R_P$

NNT = 1/AR

NNH is calculated the same way as NNT. If the NNT or NNH calculated is not a whole number, it should be rounded up to the next higher whole number. Each whole number represents an individual patient.[1,6]

Example NNT and NNH calculations for a hypothetical treatment, Drug A

Outcome	Rate on Drug A (R_A)	Rate on Placebo (R_P)	NNT/ NNH
Response	40%	15%	4
Adverse Effect 1	18%	7%	10
Adverse Effect 2	7%	2%	20

Table 1. Adapted from Citrome L. *Innov Clin Neurosci.* 2014;11(5-6):26-30.

NNT

The rate of **response** in the treatment group was 40%, while the rate of response in the placebo group was 15%.

$R_A = 0.40$

$R_P = 0.15$

AR = 0.40 - 0.15 = 0.25

NNT = 1/0.25 = 4

NNT = 4

Drug A's NNT of 4 means that for every 4 patients treated with Drug A instead of placebo, you would expect to see 1 more patient who would benefit from that medication.[4]

NNH

The rate of **adverse effect 1** in the treatment group was 18%, while the rate of adverse effect 1 in the placebo group was 7%.

$R_A = 0.18$

$R_P = 0.07$

AR = 0.18 - 0.07 = 0.11

NNH = 1/0.11 = 9.09 ≈ round up to 10

NNH = 10

The NNH of 10 means that for every 10 patients treated with Drug A instead of placebo, you would expect to see 1 more patient who would experience adverse effect 1 from that medication.[4]

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Likelihood of Being Helped vs Harmed (LHH)

NNT and NNH can be combined to express the likelihood of being helped or harmed (LHH). LHH is a metric used to express the potential "trade-offs between a specific benefit and a specific harm" of a treatment. It may represent how much more likely it is for a treatment to be associated with a benefit than a harm and is obtained by calculating the ratio of NNH to NNT.[4]

LHH = NNH/NNT

Example LHH calculation for Drug A (Table 1)

Please refer back to Table 1 on the previous page. The NNT for response is 4, and the NNH for adverse effect 1 is 10.

LHH = 10/4 = **2.5**

The LHH of 2.5 can be interpreted to mean that Drug A was 2.5 times more likely to be beneficial (leading to a response) than harmful (leading to an adverse effect) for the patients.[5]

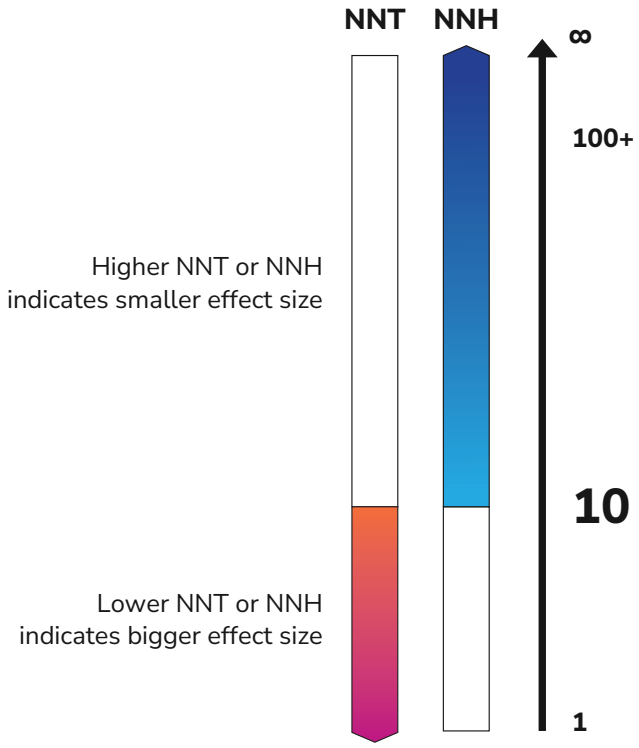

Figure 1. Interpretating NNT and NNH values. Adapted from Citrome L. *Acta Psychiatr Scand.* 2008;117(6):412-419.

What could be considered 'good' NNTs and NNHs?

The lower the NNT values, the bigger the effect size difference is between the 2 interventions and, presumably, the better the efficacy of the treatment when compared to the alternative.[4] NNT values under 10 may indicate a meaningful difference between the 2 interventions.[2]

Conversely, the higher the NNH values, the less often you would expect to encounter 1 additional patient experiencing the adverse event you would like to avoid.[4] NNHs greater than 10 are generally considered acceptable for psychotropic medications when compared against the placebo on their rate of most commonly occurring adverse events.[2]

It is important to remember that there may be a wide range of adverse events associated with a treatment. The NNH values for specific adverse events will vary. NNH values for adverse events that are more concerning to a patient or could have more severe consequences should be considered when evaluating the tolerability of a treatment.[4]

Limitations of NNT and NNH

- They can be calculated only for binary or dichotomous comparisons.[1]
- They report absolute measures of the effect size and do not provide information on the relative size of the treatment effect. Therefore, in published papers, the underlying rates used to calculate NNT and NNH should also be reported.[2]
- NNT and NNH estimates should be presented with 95% confidence intervals in published papers to indicate their precision.[1,7]
- They are most informative when the subjects and the conditions (ie, patient demographics and medication dose and duration) tested in the clinical trials are similar to the patient profile and the treatment parameters commonly encountered in clinical practice.[1,2]

References

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