Number Needed to Treat Can Be Helpful: A Response to Andrade

To the Editor: We read with interest the March 2015 Clinical and Practical Psychopharmacology column by Dr Andrade regarding numbers needed to treat and harm (NNT, NNH).[1] We applaud Dr Andrade for writing an exceptionally clear explanation of what NNT and NNH are and how they may be calculated. In our own experience, NNT and NNH are the simplest ways of explaining effect sizes in a clinically relevant manner to medical practitioners who would otherwise mistakenly believe that all they need to be aware of are *P* values. Although *P* values can help convince us that we are most likely dealing with a truth, effect sizes are essential in helping determine if such a truth is clinically important. Therefore, in our view, the statement "The NNT is an academically useful statistic, but it has limited value for the practicing clinician"[1(p e332)] is unduly pessimistic, as NNT is easy to calculate and *can* help practicing clinicians appraise benefits and harms in a meaningful way. This is demonstrated in a number of published works examining different interventions, as, for example, in bipolar depression.[2] Thus, we contend that clinicians can rapidly calculate NNT from published randomized controlled studies, easily comprehend this effect size (which reflects magnitude of therapeutic benefit in "patient units"), and intuitively integrate it into practice.

We agree with Dr Andrade's statement that "a lot of information is lost when outcomes are dichotomized into response and nonresponse categories,"[1(p e332)] but emphasize that NNT and NNH are tools of particular value to clinicians and not intended to replace the usual statistical analytic techniques when designing and reporting on clinical trials. We advocate that NNT and NNH based on well-accepted and clinically relevant dichotomous benefits (such as response and remission) and harms (such as ≥ 7% weight gain) can provide a "birds-eye" view of real-world clinical outcomes that can be expected with a potential intervention. Although Dr Andrade suggests that "it is far better to directly examine by what margin drug outperforms placebo on a rating scale than to see by what margin drug outperforms placebo on an arbitrary cutoff value that defines response on that rating scale,"[1(p e332)] this more granular and esoteric approach implies a greater knowledge about statistics and rating scales than many clinicians possess and minimizes the importance of the "outliers" who respond by a clinically relevant amount. We contend that most clinicians will find it more difficult to understand the clinical relevance of a mean ± SD difference of 3.5 ± 1.6 points between groups on a rating scale, compared to understanding a 25% advantage in response (≥ 50% improvement) rate (ie, an NNT for response of 4).

By adhering to best practices when reporting NNT or NNH values, we can avoid the important potential problems that Dr Andrade wisely describes. These practices include (1) reporting 95% confidence intervals (CIs) for NNT and NNH and noting if the CI includes infinity (a CI that includes infinity means that the NNT and NNH estimates are not statistically significant at the *P* value threshold selected); (2) reporting the time frame from which data were obtained—the effect of time on benefits such as treatment response can be profound, and the longer the clinical trial, the greater the opportunity for harms such as adverse events to occur or resolve[3]; and (3) reporting the absolute rates from which NNT or NNH estimates were calculated—an NNT of 10 calculated from responder rates of 95% versus 85% is a very different clinical scenario compared to the same NNT calculated from responder rates of 15% versus 5%. Moreover, the individual baseline characteristics of the person being treated, and their values and preferences, will be important to know in order to optimize the use of NNT and NNH in clinical decision making.

Lastly, it needs to be emphasized that NNT values of 1 or −1 are mere theoretical constructs, as they imply absolutely perfect or absolutely imperfect therapeutic outcomes, respectively, which clearly do not have real-world clinical correlates. Because whole numbers are preferred when describing NNT or NNH, the lowest numeric absolute value (most robust effect size) encountered in clinical trials is 2, and such a value is indeed rare.

REFERENCES

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Dr Andrade Replies

To the Editor: Drs Citrome and Ketter provide a vigorous defense of the usefulness of the numbers needed to treat and harm (NNT, NNH) statistics. My article,[1] on which they comment, primarily sought to present a simple, easy-to-understand explanation for the calculation of these statistics, describe how to interpret them, and illustrate their applications. However, my article also sought to discuss the limitations of these statistics because just as the *P* value has its uses and limitations, so too do the NNT and NNH. Clinicians would be doing themselves a disservice if they adopted the NNT and NNH as evidence-based mental health evaluation tools without understanding their limitations. In this regard, Drs Citrome and Ketter offer excellent suggestions for the additional information that should accompany the presentation of the NNT and NNH so that these statistics can be properly interpreted. I support their suggestions with enthusiasm and hope that the suggestions will be adopted by the international community so that the limitations that I described[1] can be offset.

The above notwithstanding, I retain my personal concern that the NNT and NNH have limited value for the practicing clinician. This is because what the practicing clinician really needs to know are the actual response and adverse event rates with drug and placebo. These rates are clinically meaningful, informative, easier to understand, and (most important of all) less likely to be misunderstood than statistics that describe how many patients need to be treated for 1 "extra" patient to be benefited or harmed. Furthermore, if these rates are provided, as Drs Citrome and Ketter suggest, then the NNT and NNH statistics become superfluous because they are derived from the stated rates.

On a parting note, I accept the concern that Drs Citrome and Ketter express about clinician unfamiliarity with differences in means on clinical ratings scales and hence the practical need for dichotomized outcomes such as response and remission.

Reference

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