

## NNT for studies with long-term follow-up

The first article in the series for learners of evidence-based medicine discusses the concept of number needed to treat (NNT).<sup>1</sup> However, studies involving patients who need long-term follow-up, such as those with cancer or chronic cardiac conditions, commonly use time-to-event or survival analysis. It is important to realize that the NNT is not calculated in the same way for these studies.

NNT from survival analysis data should be estimated by the hazard ratio<sup>2</sup> and is not based on the difference in event rates between treatment groups at the end of follow-up.<sup>3</sup>

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### References

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2. Altman DG, Andersen PK. Calculating the number needed to treat for trials where the outcome is time to an event. *BMJ* 1999;319(7223):1492-5.
3. de Lemos ML. How to survive the survival plots [letter]. *Lancet* 2002;360(9337):954.

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### [Three of the authors and a colleague respond:]

Mario de Lemos advises that for trials in which survival analysis is used, clinicians should ideally calculate

the NNT from the hazard ratio.<sup>1</sup> We agree, but would emphasize that more important than the small differences created by the choice of method to calculate NNT are the very large differences consequent on different baseline risks. In this letter we review issues related to the calculation of NNT directly from trial data and illustrate what we believe is the appropriate approach, taking into account patients' baseline risk.

Consider 2 women. One is a tall, slightly overweight 50-year-old recently postmenopausal woman, who exercises regularly and who has normal bone mineral density. The second is a small 75-year-old woman who does not exercise and has a history of 4 vertebral fractures. The question we address here is how much hormone replacement therapy would reduce fracture risk in these women.

Before going any further in our consideration of these particular women, however, we will look at the "average" patient, using data from the Women's Health Initiative (WHI) trial, a large randomized trial of hormone replacement therapy,<sup>2</sup> which reported both event rates and a survival analysis.

**NNT from event rates at the end of follow-up:** Our first analysis is the "crude" or naïve approach that de Lemos criticizes. As described in our paper,<sup>3</sup> clinicians can calculate the NNT as the inverse of the difference in event rates (or absolute risk reduction) at the end of the study follow-up. According to the WHI data, among the

8506 women who were randomly assigned to receive active treatment, 44 had a hip fracture; in the placebo (control) group, 62 of 8102 had a hip fracture by the end of the study (after an average of 5.2 years of follow-up). These data are shown in Table 1, together with the NNT of 403, obtained by taking the reciprocal of the absolute risk reduction. In other words, this analysis suggests that we would need to treat 403 women with hormone replacement therapy over 5.2 years to prevent one hip fracture. Table 1 highlights the fact that the NNT is different over different time frames. For example, per year, we would have to treat approximately 2000 women to prevent one hip fracture. This can be calculated most easily by multiplying the NNT by 5 ( $403 \times 5$ ) and a little more tediously by calculating the event rates per year in treatment and control groups (Table 1). Clearly, the time frame is critical for NNT, and clinicians should insist on knowing the time frame associated with any NNT.

**NNT from trials reporting survival analysis:** In the paper cited by de Lemos, Altman and Andersen<sup>2</sup> outlined 2 methods (methods 1 and 2 below) for calculating NNT from trials that report the results of survival analyses; one method uses the difference in estimated survival probabilities between the treatment and control groups, and the other uses the hazard ratio and the survival probability in the control group. The rationale for using a survival analysis (i.e., time-to-event

**Table 1: Number needed to treat for hip fracture, calculated from event rates and absolute risk reduction over different times\***

Time	Group; event rate (ER)		ARR ( $ER_c - ER_t$ )	NNT (inverse of ARR)	Comments
	Treatment ( $ER_t$ )	Control ( $ER_c$ )			
Over 5.2 yr	44/8506 = 0.52% ( $0.00517 \times 100$ )	62/8102 = 0.77% ( $0.00765 \times 100$ )	0.248% ( $0.765\% - 0.517\%$ )	403 ( $100\%/0.248\%$ )	Based on number of events at end of follow-up, average 5.2 yr <sup>3</sup>
Over 1 yr	0.10% ( $0.52\%/5.2$ yr)	0.15% ( $0.77\%/5.2$ yr)	0.05% ( $0.15\% - 0.10\%$ )	2000 ( $100\%/0.05\%$ )	From annualized event rates <sup>3</sup>

Note: ARR = absolute risk reduction, NNT = number needed to treat.

\*Data from the Women's Health Initiative trial.<sup>2</sup>