

Number Unnecessarily Treated in Relation to Harm

A Concept Physicians and Patients Need to Understand

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Physicians are legally and ethically compelled to present their patients with available evidence on the potentially beneficial and harmful effects of a proposed medical or surgical treatment. This, however, is only half the story. It does not offer the patient a clear view of the pros and cons of one treatment option versus another, or even versus no treatment at all. Explicitly stating the number of patients who will not benefit from the proposed treatment, in combination with the risk of a complication, may better inform patients and help them determine and express their treatment preference. This may also help standardize the informed consent procedure.

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NUMBER NEEDED TO TREAT AND NUMBER UNNECESSARILY TREATED

The number needed to treat (NNT) has been introduced to express the benefit of a certain intervention. It is defined as the number of patients who need to be treated with this intervention to achieve 1 extra beneficial result as compared to an alternative treatment option.¹ The number unnecessarily treated (NUT) represents the number of patients who will not benefit from treatment.

As an example, let us take patients with cancer who are treated with additional adjuvant chemoradiotherapy (CRT) after surgery to prevent local recurrence. Assuming that 100 of 1000 of these patients will benefit from CRT (as compared to no CRT) implies an NNT of 10. This means that if 10 patients need to be treated to prevent an extra recurrence in 1 of them, the remaining 9 will undergo CRT without extra benefit; this is the NUT.

HARM

Virtually no medical or surgical treatment is free of unwanted side effects. The possible harm of any treatment can simply be divided into mortality and morbidity. Patients who die due to a treatment have no benefit at all and therefore belong to the unnecessarily treated group. Those who survive may suffer from morbidity (ie, adverse effects, complications) because of the treatment. Although some patients are “more equal than others” and morbidity risks may differ, let us assume that these morbidity risks are similar for all survivors.

COMMUNICATION WITH THE PATIENT

Integrating the NUT in the communication with the patient can be done in 2 steps with the help of a natural frequency tree.² First, the numbers of patients that will and will not benefit from a treatment are presented. In the second step, the distribution of harm due to treatment is explained. This results in 5 possible outcomes: (1) full benefit without any morbidity, (2) benefit but also morbidity, (3) no benefit and no morbidity, (4) no benefit but morbidity, and (5) full harm, that is, death due to the treatment.

Figure 1 depicts the 5 possible outcomes in a natural frequency tree for the cancer patient example, assuming a 10% reduction of the recurrence risk after 5 years compared with no CRT and an also fictitious but realistic 10% morbidity as a result of CRT in the patients who survived the combined therapy, and 1% mortality risk due to additional CRT. Step 1 shows that if 1000 patients are treated with CRT, only 100 will benefit (NNT = 10), whereas 900 will not. Step 2 clarifies that 10 patients will suffer full harm (death) and that most of the 99 patients with complications from CRT belong to the group without benefit. The large number of patients who will not have any effect of treatment is remarkable.

In many articles, detailed information concerning all complications is lacking, and it is difficult (or even impossible) to provide full details for the 5 different groups. Moreover, some complications a surgeon aims to prevent through the procedure may also occur as a result of surgery. For example, in a Cochrane systematic review concerning the value of carotid endarterectomy compared to non-surgical treatment for $\geq 70\%$ symptomatic carotid artery stenoses the focus of the efficacy endpoint is on the prevention of stroke and death, whereas stroke and death are also defined as operative complications.³ Information about other operative complications is lacking. Under such circumstances, groups 1 and 2, and 4 and 5 can be pooled, while preserving a clear view on the NUT and the effect of the most serious operative complications: any stroke or operative death (Fig. 2). These numerical outcomes may also be presented as figurine plots (Fig. 3), which have been shown to improve patients’ understanding of potential outcomes.⁴

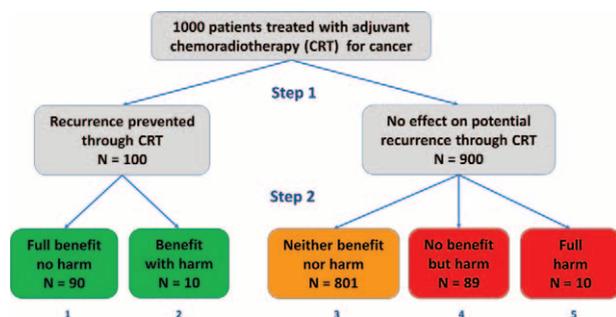


FIGURE 1. Natural frequency tree showing the 5 possible outcomes of adjuvant CRT compared with surgery without CRT in patients with cancer. Step 1 shows the benefit, step 2 the harm distribution.

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TOWARD GREATER AWARENESS

Few health care professionals and patients realize the high NUT or, conversely, the low efficacy of many medical and surgical interventions, and secondly, that most of the harm will occur in the unnecessarily treated patients. The notion that, in general, a considerable number of patients receive treatment without benefit should be an essential part of the information caregivers communicate with their patients, in particular because patients tend to overestimate intervention benefit and underestimate harm.² If physicians and patients become aware of this, they may better appreciate the true effectiveness of available treatment options. This can also help choosing wisely when treatments with significant side effects are considered in elderly or frail patients.

Although infographics have been proposed earlier,^{5,6} the natural frequency tree seems particularly powerful to communicate benefits and risks simultaneously.² Furthermore, it helps patients appreciate their chances and balance the pros and cons of a recommended treatment option. Particularly in an era where shared decision making is winning ground,⁷ in union with evidence-based medicine,⁸ the information provided should be more objective, realistic, and standardized. This notion may be advanced when discussing the benefits and harms of a treatment by introducing the NUT in the proposed stepwise fashion.

LIMITATIONS

The NUT and natural frequency models as presented here are limited in that they work with dichotomous outcomes only. Continuous outcomes require a different approach. Second, detailed evidence has to be available to calculate benefit and harm. If sufficient evidence is available, the magnitude of this benefit can be estimated based on the NNT and NUT and discussed with the patient. The magnitude of the possible harmful effects is usually known from previous RCTs or cohort studies. Third, it is important which outcome and adverse events are chosen from which to calculate the NNT and NUT. Some interventions tolerate higher NNTs and NUTs than others; medication may be stopped as soon as adverse effects occur, whereas surgical complications may lead to permanent damage. Fourth, patients may sustain more than 1 harmful effect. These complications may differ in severity

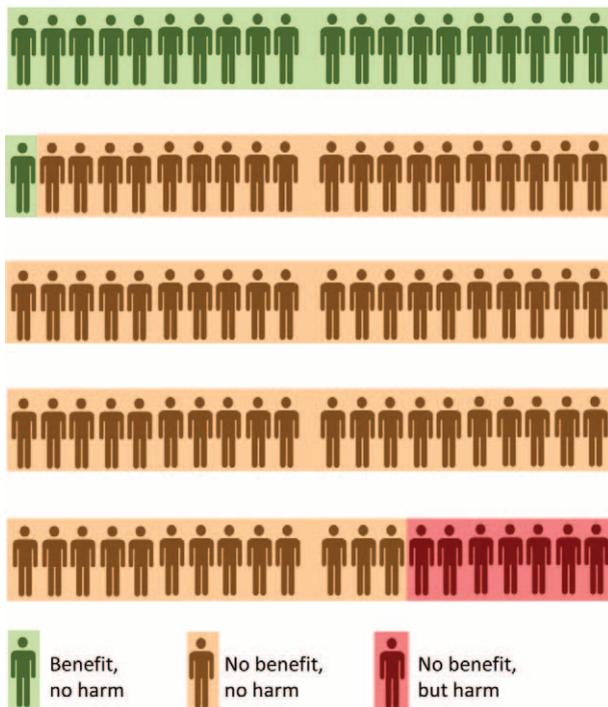


FIGURE 3. The 3 possible outcomes (approximately) of carotid endarterectomy compared to nonsurgical treatment for $\geq 70\%$ carotid artery stenoses.

and may occur in the short- or long term. Patients are often informed about the short-term effects, whereas the long-term effects of, for example, radiotherapy or chronic medication tend to be neglected. Fifth, harmful effects may be more acceptable if the burden of the condition or treatment is high. For example, scar formation after aesthetic surgery may be hard to accept, whereas the discomforts of chemotherapy may be tolerated if it lead to curation of cancer. Finally, one might argue that the NUT may carry negative connotations and that it would be better not to use this term in the communication with patients and that using “number not benefiting” is preferable.

CONCLUSIONS

In short, the communication between physicians and patients can and should be improved to ensure adequate information is provided. After all, the patient deserves information that objectively reflects medical prowess. The tools described here are an attempt to contribute to this clarity.

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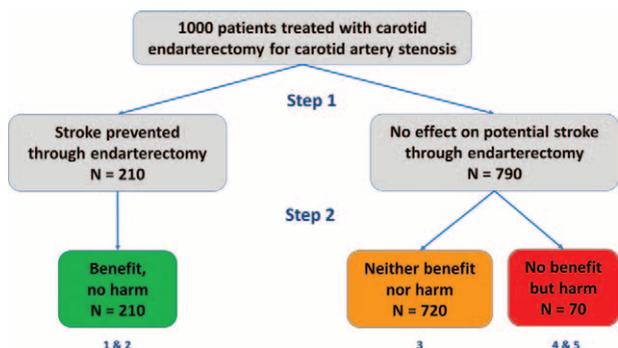


FIGURE 2. Natural frequency tree (approximate numbers) showing the 3 possible outcomes of carotid endarterectomy compared to nonsurgical treatment for a $\geq 70\%$ carotid artery stenosis. Step 1 shows the benefit, step 2 the harm distribution with regard to any operative stroke or death. The review shows 15% (90/589) stroke or death in the surgical arm and 29% (148/506) in the nonsurgical arm, resulting in a reduction of 14%.³ The operative stroke and death rate is 7% (groups 4 and 5). To calculate the overall number of patients who benefit, this 7% has to be added to the 14% resulting in 210 patients benefiting from surgery.