Adding cost to NNT: the COPE statistic

During several years of teaching critical appraisal at both the undergraduate and postgraduate levels, I have used a modification of number needed to treat (NNT). The COPE—the Cost of Preventing an Event—is a "back-of-the-envelope," user-friendly, cost-effectiveness analysis for clinicians and policymakers. Economic evaluations can be defined as the "comparative analysis of alternative courses of action in terms of both their costs and their consequences" (1). These analyses can be complex and sensitive to particular population groups and health systems and are often unavailable for clinicians (especially in developing nations). Traditionally, economists have used 1 of 5 methods for economic analysis: cost-analysis, cost-minimization, cost-effectiveness, cost–utility, and cost–benefit analyses (1). The COPE is an approximate cost-effectiveness statistic that can be calculated by clinicians for a new drug for which a full economic evaluation is not available but a randomized controlled trial (RCT) exists.

How is the COPE calculated? From an RCT, the NNT can easily be determined (2): The number of patients required to be treated to produce a beneficial result or prevent a harmful event in 1 additional patient—that is, NNT = 1/(CER - EER) (see Glossary for explanation of terms). The NNT is usually quoted along with the length of time the trial was conducted, the inference being that you must treat the number of patients needed to treat for the same time to prevent or produce 1 additional event. COPE is calculated as follows: NNT times the number of years needed to treat times 365 days times the daily cost of therapy. Some examples of the COPE statistic are presented in the Table.

Examples of the COPE from a developing nation viewpoint*

Event	NNT	Years of treatment to prevent 1 event	Drug, dose/d (US $)	COPE (US $)
Secondary prevention of any fracture in a postmenopausal woman 55 to 81 y of age (3)	22	3	Alendronate, 10 mg (1.99)	47 939
Prevention of a major vascular event: nonfatal MI, coronary death, nonfatal or fatal stroke, or coronary or noncoronary revascularization in a high-risk adult 40 to 80 y of age using a statin (1)	19	5	Generic simvastatin, 40 mg (0.68)	23 579
Prevention of a coronary death in a man with angina pectoris or previous MI using a statin (5)	25	5.4	Generic simvastatin, 40 mg (0.68)	33 507
Prevention of the onset of heart failure in patients of high risk but no diminished ejection fraction or heart failure (6)	40	4.5	Ramipril, 10 mg (1.56)	102 492

*COPE = cost of preventing an event; MI = myocardial infarction; NNT = number needed to ttreat.

THE LIMITATIONS

This cost analysis is clearly an incomplete form of economic appraisal. A full evaluation would consider several other elements (1). Put simply, it would calculate the cost-effectiveness as (cost of treatment – *cost offsets*) / (gain of treatment – *adverse effects of treatment*) (1).

COPE ignores the 2 elements in italics. No assessment is made of potential cost offsets—for example, the cost of hospitalization or surgical or other procedures either avoided or induced by the treatment. Nor are the harmful effects of the drug and the cost associated with managing this effect considered. Finally, there is no attempt to put "value" on a particular outcome, such as the number of "years of life gained," or to determine through a cost–utility analysis the cost of "quality-adjusted life-years" gained (1, 7). Despite these limitations, for the student or clinician appraising and considering the implementation of a new therapy, COPE provides rapid insight into the drug cost at a population level for the given effectiveness as determined by the RCT.

One assumption of this model is that the results of the trials from which the above NNTs are derived are transferable to your particular patient population. This assumption often does not hold, but in the absence of similar trials reproduced in local settings we are often left to ask, "Is there any compelling reason why the results of the study should not be applied?" (2)

By using the number needed to harm (NNH) (2), we can also calculate a rough assessment of the cost of the clinical consequences of initiating a particular drug intervention—for example, in dealing with the side effects of a drug. By doing this type of analysis for a single drug, we are carrying out a cost–outcome description. If we compare 2 drugs, looking at their costs and consequences, we can carry out a more complete economic evaluation.

Individual practitioners then need to justify the cost of a particular therapy based on the prevalence of a disease in their setting, the severity of the outcome, the availability of generic forms of medications or the cost of the medicine and its efficacy, and the NNT. Similarly, despite the costs, individual patients may still opt for an expensive therapy in the context of a fearsome or feared disease.

CONCLUSIONS

I have found the consideration of the COPE statistic to be a valuable tool in teaching students who, in critically appraising an RCT, come to the question: "What are the potential benefits and harms from the therapy?" and begin asking about costs. In my developing world setting, the figures as shown above can be startling.

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