Cost-Effectiveness Acceptability Curves in the Dock: Case Not Proven?

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The article in this issue by Groot Koerkamp and others[1] discusses the limitations of cost-effectiveness acceptability curves (CEACs) for presenting uncertainty in cost-effectiveness analysis to policy makers and urges us to "rethink their use in communicating uncertainty."[1] We agree with the authors that uncertainty is important for policy makers and that the appropriate method to evaluate uncertainty is through an assessment of both the probability of making an error ("not selecting the 'true' preferred alternative") and the consequences associated with making an error. A Bayesian value of information (VOI) analysis provides this assessment of uncertainty. The question remains about what is/are the appropriate means to present information about uncertainty to policy makers. We take this opportunity to review the case against CEACs presented within the article and to defend the use and usefulness of CEACs for policy making in health care.

BRING FORTH THE CHARGES

The authors state that CEACs are "unable to distinguish dramatically different joint distributions of incremental cost and effect" and that this limits their usefulness for policy making.[1] They argue that the use of CEACs to represent uncertainty restricts the ability to synthesize evidence on cost-effectiveness from other sources. In addition, they suggest that the CEAC does not allow for integration of risk attitude, provides no insight into the assessment of the need for further research, and may mislead policy makers regarding the appropriate treatment choice.

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THE CASE FOR THE DEFENSE

We accept that CEACs are insensitive to any change in the joint distribution of incremental cost and effect in the northwest (NW) or southeast (SE) quadrants of the cost-effectiveness plane. This is not, however, a product of the cost-effectiveness acceptability curve but rather of cost-effectiveness analysis itself, which considers all points in each of these quadrants to be equivalent in cost-effectiveness terms—that is, dominant (SE) or dominated (NW). If information about dominance is considered important to policy makers, then the CEAC could be adapted very easily to provide it (see Severens and others[2]). We also accept that CEACs are insensitive to radial shifts in the joint distribution of incremental cost and effect in the northeast or southwest quadrant of the cost-effectiveness plane. This again is a consequence of cost-effectiveness analysis. Points lying on the same ray through the origin have the same incremental cost-effectiveness ratio (ICER) and thus, for any value of the maximum acceptable incremental cost-effectiveness ratio, will have the same outcome regarding cost-effectiveness (i.e., either cost-effective or not). As such, any radial shift of the incremental joint distribution, either toward or away from the origin, represents identical uncertainty regarding cost-effectiveness and will result in identical CEACs.

With regard to the integration of other evidence and opinions, we agree with the authors that "a quantitative analysis is rarely the only or final word on a decision."[1] Within a Bayesian framework, all available evidence should be included and considered within the decision context. However, we dispute the use of a summarized measure ("quantitative statement") of uncertainty as a means of weighting results for a synthesis of the evidence from other

sources. In our view, this type of integration of evidence should be done formally and should involve the individual components of the decision (e.g., parameters, costs, and effects) rather than the measure of cost-effectiveness (see Cooper and others[3] and Fenwick and others[4] for examples).

The misinterpretation of a high probability that a treatment alternative is cost-effective with medical urgency or importance is equivalent to confusing statistical significance and clinical importance. This is purely an education issue and is not specific to the use of CEACs, hypothesis testing, or confidence intervals.

In addition, we dispute the authors' suggestions that the CEAC does not allow for integration of risk attitude, provides no insight into the assessment of the need for further research, and may mislead policy makers regarding the appropriate treatment choice. Much of the article centers on the argument between the use of ICERs and net benefit (NB) for economic evaluation and confuses this with issues of presenting uncertainty. It was the difficulties inherent with constructing confidence intervals (CIs) for ICERs that led ultimately to the production of the CEAC and to its proliferation within the medical literature. The absence of these difficulties for NB promotes the presentation of CI, but there is no reason that CEACs cannot be presented for an analysis involving NB. Contrary to the authors' statement that "CEACs fail to capture the importance of uncertainty,"[1] we believe that CEACs encourage policy makers to think about decision uncertainty and the consequences of such uncertainty for policy making, allowing them to cast off the shackles of confidence intervals and hypothesis testing. The production and presentation of intervals for NB, however, are likely to encourage classical thinking regarding cost-effectiveness (i.e., if the interval excludes zero, then the intervention is cost-effective).

We accept that the CEAC does not present the policy maker with information concerning the appropriate treatment choice (this is given by the expected utilities), nor does it present information regarding the consequences of an incorrect decision, but it does present policy makers with graphical information regarding the probability that a treatment alternative is cost-effective over a range of values for the maximum acceptable ICER. In turn, the cost-effectiveness acceptability frontier (CEAF) presents the probability that the treatment choice made on the basis of expected values is correct. As such, the complement of the CEAF provides a graphical representation of the probability of making an error, which is a major component of the expected value of perfect information (EVPI).[5] Thus, there is a link between the CEAF and the EVPI: over the range where the CEAF is falling, the EVPI must be increasing as both the error probability and the maximum acceptable ratio (used in the calculation of the consequences of error) are increasing. Over the range where the CEAF is increasing, the direction of the EVPI will depend on the interaction between the rate of change in the uncertainty and the rate of change in the consequences. We have found that for ranges where the CEAF is flattening off toward a maximum (uncertainty is falling slightly), the change in the consequences will dominate, and EVPI will tend to increase.

THE WAY FORWARD

Having started boldly by proclaiming the issues and limitations associated with the CEAC, the authors are less clear when it comes to suggestions for alternative presentations of uncertainty. Indeed, the abstract favors NB and interval estimation, whereas the article itself suggests a more varied approach. For decisions involving 2 treatment alternatives, they appear to suggest the use of the (incremental) cost-effectiveness plane with the addition of "summary measures," although the exact nature of the summary measures are less clear—intervals for the ICER are dismissed, due to the issues surrounding ratios, but intervals for the incremental net benefit (INB) and EVPI are both suggested. We would suggest the use of CEACs and the CEAF. For decisions involving more than 2 treatment alternatives, the authors dismiss the use of the cost-effectiveness plane as "ambiguous"; intervals for INB should also be dismissed as an alternative in this situation as they are unable to provide a simultaneous assessment of the uncertainty in the decision when there are more than 2 treatment alternatives. This leaves the expected value of perfect information as the sole summary measure of decision uncertainty. We do not dispute that this is the appropriate measure of decision uncertainty. However, we argue for the presentation of CEACs and the CEAF for pragmatic reasons. They provide a useful bridge to the EVPI for policy makers unused to seeing this information presented. We acknowledge that there is still a place for education regarding their interpretation but feel that if they are ill understood, then the presentation of EVPI alone is unlikely to be well received by policy makers and journals. In addition, the EVPI simply identifies the maximum worth of further research to reduce

uncertainty. VOI analysis cannot and does not resolve the decision regarding the collection of further research without information regarding the costs of research or the "informativeness" of specific research. This information is presented via an analysis of the expected value of sample information (EVSI) and the expected net benefits of sampling (ENBS). At the present time, neither of these concepts is likely to be presented in a clinical paper. The best we can do is encourage policy makers to think about uncertainty and its consequences, and we believe that the CEAC and CEAF do this.

CONCLUDING STATEMENT

In Scottish courts, the jury in a criminal case has another option besides the usual "guilty" or "not guilty" verdicts. Case "not proven" reflects those situations where the jury feels unable to convict a defendant but nevertheless considers the verdict of not guilty too lenient. The authors' charges against the usefulness of CEACs curves have some merit; therefore, a "not guilty" verdict is inappropriate. However, we hope we have convinced you, the jury, that there remains a use for CEACs and that the case against them is, therefore, "not proven."

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