The recent discussions on the limitation of the cost-effectiveness acceptability curves (CEACs) was helpful in reevaluating the value of CEACs in cost-effectiveness studies. One of the limitations of the CEACs, as pointed out by Groot Koerkamp and colleagues as well as other authors, is that they may mislead policy makers regarding the preferred alternative. This refers to the fact that the ranking of strategies based on CEAC might be different from their ranking based on expected net benefit. This known phenomenon has so far been attributed to the higher positive skew of the distribution of the incremental net benefit (INB) of the optimal strategy. We would like to point out that CEACs can also be misleading when correlated strategies are compared.

To be explicit, let us imagine that the decision maker is interested in a model-based cost utility analysis of 2 new strategies as compared with a current strategy for treating a malignancy. Strategy 0 is the current (baseline) practice, strategy 1 is based on the new drug A, and strategy 2 is based on drug A plus the palliative drug B, with slightly additional costs and small increase in quality of life. Assume that the output of the model can be approximated using the following distributions:

\[
\Delta c_{1,0} \sim \text{Normal}(-1000,200), \Delta e_{1,0} \sim \text{Normal}(0.1,0.4), \\
\Delta c_{2,1} \sim \text{Normal}(50,50), \Delta e_{2,1} \sim \text{Normal}(0.001,0.001),
\]

where \(\Delta c_{i,j}\) and \(\Delta e_{i,j}\) are the incremental cost and quality-adjusted life years (QALYs), respectively, of strategy \(i\) vs. \(j\). Because the outcome of strategy 2 is defined relative to strategy 1, there would be a high degree of correlation between the INBs of strategies 1 and 2 as compared with the baseline strategy. Such correlation could be the result of the fact that strategies 1 and 2 share several parameters such as the probability of remission, cure, mortality, and several costs and effectiveness components.

Obviously, both treatments result in lower costs and higher effectiveness compared with the baseline strategy. Therefore, it is obvious that given the observed data, the best strategy is either strategy 1 or 2 at any level of willingness to pay (\(\lambda\)). In addition, the incremental cost-effectiveness ratio (ICER) of strategy 2 v. 1 is \(\$50,000/QALY\). So a decision maker with \(\lambda\) of \(\$50,000/QALY\) will be indifferent between strategies 1 and 2.

However, the CEAC is nonintuitive and is in conflict with the results based on the expected net benefit. As shown in Figure 1, the CEAC of the baseline strategy is above that of the 2 alternative strategies at a wide range of \(\lambda\), despite the fact that this strategy is dominated and should not be selected at any positive value of \(\lambda\). In other words, strategies 1 and 2, which have a large overlap in their region of optimality, carve up their share of the joint distribution, rendering their probability of cost-effectiveness below that of the baseline strategy.
From a theoretical viewpoint, there is nothing wrong with such CEAC as it serves its purpose of illustrating the probability of each option being the optimal choice at different values of $\lambda$. Such CEAC is, however, counterintuitive for the decision maker given the dominancy of strategies 1 and 2 over 0. Being indifferent in choosing strategy 1 or 2, the decision maker might proceed to select the strategy that has the highest value on CEAC at $\lambda = $ 50,000 and will find the results totally conflicting with the ranking of the strategies based on their expected INBs.

The high degree of correlation between the alternative strategies was the essential part of this phenomenon in our example. In the absence of correlation, the proportion of the joint distribution falling in quadrant III while its center is in quadrant I is no more than 25%, so it cannot make the baseline strategy ranking first in CEAC. Such correlations are fairly common in economic comparisons, especially when alternative strategies are based on similar interventions (the example presented here) or the same intervention applied to different populations.

As this example demonstrated, other conditions besides the skewness of the distribution of INB could alter the rank of strategies in CEAC. As such, and given other points brought about by Groot Koerkamp and others\textsuperscript{1} and Schwartz,\textsuperscript{3} we agree with them that unless the consumer of a cost-effectiveness analysis is sophisticated enough not to overinterpret acceptability curves, CEACs might defeat the purpose of facilitating decision making under uncertainty.

REFERENCES


