Health Technology Assessment in the Cost-Disutility Plane

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Previously, comparisons of multiple strategies in health technology assessment have been undertaken on the incremental cost-effectiveness plane using efficiency frontiers and cost-effectiveness acceptability curves. This article proposes shifting the comparison of multiple strategies to the cost-disutility plane. Evidence-based decision making requires comparison of all strategies against each other. Consequently, the origin in the incremental cost-effectiveness plane cannot be the appropriate reference point in comparing multiple nondominated strategies. A linear transformation onto the cost-disutility plane allows an equivalent comparison of net benefit and permits the use of standard efficiency measurement methods to estimate 1) the degree of dominance (technical inefficiency) of dominated strategies and 2) the net benefit inefficiency (i.e., losses in net benefit relative to an optimal strategy). In comparing strategies under uncertainty, a comparison of loss in net benefit leads to the expected net loss frontier, which, unlike cost effectiveness acceptability curves, directly identifies differences in expected net benefit (net loss) and the expected value of perfect information. Thus, decision makers can be better informed about the choice of optimal strategy and the potential value of future research to resolve uncertainty. Comparing strategies in the cost-disutility plane is suggested to better inform decision making and to provide a link between the cost-effectiveness literature and efficiency measurement methods. **Key words:** health technology assessment; efficiency frontiers; maximizing net benefit; cost-disutility plane; net loss acceptability frontier; health economics; methodology; cost-effectiveness analysis. *(Med Decis Making 2008;28:172–181)*

The emergence of bodies such as the Pharmaceutical Benefits Advisory Committee in Australia, the National Institute of Health and Clinical Excellence in the United Kingdom, and the Canadian Agency for Drugs and Technologies in Health reflects a growing awareness of the importance of cost-effectiveness evidence, particularly within publicly provided health systems.1–3

In moving to the provision of evidence not only on effectiveness but also on cost of interventions, it is natural to consider a 2-dimensional representation. To date, the incremental cost-effectiveness plane has become the most popular way of providing a geometric interpretation of cost-effectiveness results. The first presentations of this plane showed the difference in effectiveness on the vertical axis and cost difference on the horizontal axis.4 This presentation coincided closely with the standard economic presentation of a production function, in particular with regard to the economic law of diminishing marginal returns in outputs (effectiveness) to increasing inputs (cost). In practice, however, most analysts and commentators have preferred to plot the difference in effect on the horizontal axis with cost difference on the vertical axis,5 chiefly because this allows the geometric interpretation of the slope of the line joining any 2 points on the cost-effectiveness plane as an incremental cost-effectiveness ratio.

In this article, we argue for reframing measures of effects as measures of relative disutility and presenting results on the cost-disutility plane. This provides a link between the literatures of efficiency in cost-effectiveness analysis and the broader framework of assessing efficiency with frontier methods.

We use a previously published probabilistic sensitivity analysis of management strategies for gastroesophageal reflux disease (GERD)6,7 to illustrate the principles of dominance, extended dominance, the development of an efficiency frontier, and comparison...
of net benefit in the incremental cost-effectiveness plane. The following section then provides a formal treatment of the correspondence between net benefit on the incremental cost-effectiveness plane and net loss on the cost-disutility plane. The GERD example is then presented on the cost-disutility plane, demonstrating equivalent interpretation of frontiers, dominance, and net benefit but with the added ability to apply standard efficiency measurement methods. Consequently, the proposed method is shown to allow the estimation for each strategy of

1. degree of dominance (technical inefficiency) relative to the efficiency frontier and
2. economic (net benefit) inefficiency relative to the optimal (net benefit–maximizing) strategy at a given threshold value for health effects.

The natural consideration of loss in net benefit relative to an economically efficient (net benefit–maximizing) strategy on the cost-disutility plane leads to construction of an expected net loss acceptability frontier. This frontier has advantages over cost-effectiveness acceptability curves both in directly identifying differences in expected net benefit (expected net loss) and representing the expected value of perfect information across strategies.

Efficiency Frontiers on the Cost-effectiveness Plane

The GERD example compared 6 management strategies for patients presenting to their physicians with endoscopically proven erosive esophagitis. The analysis modeled 12-mo healing and recurrence rates based on a comprehensive review of the literature. Expected costs and effects (weeks free of GERD symptoms) of the 6 strategies are plotted on the incremental cost-effectiveness plane in Figure 1.

Improved performance on the incremental cost-effectiveness plane is indicated by southeast movement (reduced costs, greater effect). Hence, an efficiency frontier can be constructed by

1. rank ordering all interventions in terms of their effect,
2. excluding strictly dominated options (in this case, option D is strictly dominated, being both more expensive and less effective than C, A, or E),
3. excluding any extended dominated options (option F in this case is extended dominated by combinations of E and B), and then
4. linking adjacent nondominated options to form a convex hull.

To ensure the efficiency frontier passes through the origin and that the relevant comparison is contained in the northeast quadrant, the origin can be set as the least-cost strategy rather than necessarily current practice. This is the approach presented in Figure 1, in which the least-cost intervention strategy, C (based on management of GERD with H2RAs), is set as the origin of the plane, rather than usual practice (option D based on a prokinetic agent).

Geometrically, applying this process results in the illustrated frontier CAEB, where the slope of the frontier corresponds to the estimated incremental cost-effectiveness ratio between adjacent nondominated treatment options.

The use of the least-cost strategy, rather than current practice, as the origin may seem arbitrary. However, more important, the origin cannot be used as a single reference point in the comparison of more than 2 nondominated strategies because the appropriate point of reference shifts along the efficiency frontier. For example, in the base case for GERD, strategy A should be compared with C (implicitly for a value of $0 up to $10 per week GERD avoided), strategy E with A (from $10 up to $36), and strategy B with E (from $36 up to $243).

More recently, the net-benefit approach to cost-effectiveness analysis, which explicitly considers decision makers’ values for health effects, has become more popular in comparing strategies. This approach offers particular advantages when comparing multiple strategies, as net benefit statistics allow a consistent ordering of strategies irrespective of comparator. Formally, at a given decision maker’s threshold value for a unit of effect (k), the net monetary benefit (NMB) of a strategy (i) is the monetary value of effects (k × Ei) less costs (Ci),

\[ NMB_i = k \times E_i - C_i, \]

and the incremental net monetary benefit (INMB) between 2 strategies i and j can be expressed as

\[ INMB_{ij} = NMB_i - NMB_j = (k \times E_i - C_i) - (k \times E_j - C_j) = k(E_i - E_j) - (C_i - C_j). \]

Alternatively, but equivalently, the incremental net health benefit (INHB) can be calculated as the incremental effect less the incremental cost converted to equivalent health effects at a value per unit (k):

\[ INHB_{ij} = (E_i - E_j) - (C_i - C_j)/k. \]

In general, net benefit statistics, although conditional on monetary values for health effects, have
the advantage over ratio measures in that differences are additively separable, a property of their linear form. Levels of net benefit at a given $k$ can be represented geometrically as iso–net benefit lines with slope $k$ on the incremental cost-effectiveness plane, where lines further southeast represent a higher net benefit at $k$. Figure 1 illustrates such iso–net benefit lines for $k =$ $100$ per week of GERD avoided.

When comparison is restricted to 2 strategies (a new strategy and current practice), a net benefit line passing through the origin with slope $k$ defines acceptance and rejection regions, with the new therapy maximizing net benefit where it is southeast of this line. However, with more than 2 strategies, a line through the origin does not allow identification of the optimal intervention. For example, in Figure 1, the iso–net benefit line passing through the origin (intervention C) can establish only that at $100$ per week of GERD avoided, each of strategies A, E, F, and B have a higher net benefit than strategy C.

The strategy maximizing net benefit can be simply identified as that with an iso–net benefit line lying farthest southeast. Hence, the net benefit–maximizing strategy will be at the point of tangency between this iso–net benefit line and the efficiency frontier. In Figure 1, at $k =$ $100$, strategy E maximizes the net benefit at the point of tangency between the iso–net benefit line with an INMB of 350 and the efficiency frontier CAEB.

More generally, vertical distances between iso–net benefit lines represent differences in the net monetary benefit ($INMB_{ij}$), and horizontal distances between lines represent differences in the net health benefit ($INHB_{ij}$). For example, comparing strategies E and C at $100$ per week of GERD prevented in

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Figure 1  Gastroesophageal reflux disease (GERD) base case in the incremental cost-effectiveness plane.
A Linear Transformation Allowing the Use of Efficiency Methods

Eckermann\textsuperscript{16} identified a linear transformation that allows the use of economic efficiency methods to compare performance consistent with maximizing the net benefit on the cost-disutility plane. To see how this transformation can be applied to compare multiple strategies, recall from equations 1 and 2 that an option is preferred over another if it has a greater net benefit (the incremental net benefit is positive). Option \( i \) is preferred to option \( j \) if

\[
k \times E_i - C_i > k \times E_j - C_j.
\]  

(4)

Now, define the disutility of an option as the difference between the maximum health effect of the available options, \( E_{\text{MAX}} \), and the health effect of the current option, that is,

\[
DU_i = E_{\text{MAX}} - E_i.
\]

Rearranging gives an expression for effectiveness of \( E_i = E_{\text{MAX}} - DU_i \).

Substituting this expression into equation 4, noting that the \( k \times E_{\text{MAX}} \) terms cancel, and multiplying through by \(-1\), we obtain...
For any given $k$, the standard decision rule of maximizing the net benefit in equation 4 corresponds to minimizing the net loss in equation 5:

$$C_i + k \times DU_i < C_j + k \times DU_j.$$  \hspace{1cm} (5)

Effects on the cost-effectiveness plane are presented as reductions in morbidity or disability-adjusted life years (DALYs)\(^{17}\) or additional incremental survival, life years, or quality-adjusted life years (QALYs) relative to a comparator. Equivalent effects on the cost-disutility plane translate to incremental morbidity, DALYs, mortality, and reduction in life years or QALYs, relative to the most effective strategy. To allow a standardized incremental framework for costs as well as effects framed from a disutility perspective (implicit in the definition of disutility as $DU_i = E^{MAX} - E_i$), the cost of each option can be similarly measured relative to that of the cheapest option, $C^{MIN}$, as illustrated in the following example for GERD.

Comparing Strategies on the Cost-Disutility Plane: The Case of GERD

Figure 2 shows the GERD example plotted on the cost-disutility plane. The cost-effectiveness frontier is convex to a vertex (the origin) representing the lowest per patient cost across strategies and the lowest disutility event rate per patient across strategies. Performance improves when moving directly toward this vertex (equipropotionally reducing cost and disutility), and hence, ratio measures of performance can be estimated.

For example, the degree of dominance of a strategy can be calculated as the proportion by which costs and disutility can be simultaneously reduced by moving to the efficiency frontier. Graphically, the degree of dominance of a strategy is the ratio of line segments from the strategy to the frontier (in moving toward the origin) and from the strategy to the origin,
Intuitive method for identification of on the cost-disutility plane provides a simple and intuitive method for identification of technical inefficiency. In summary, measuring technical efficiency has a positive degree of dominance (technical inefficiency). Whereas strategies D and F off the frontier have a 0 degree of dominance (technical inefficiency). Hence, from equation 8, the net loss is greater than 0 for dominated strategies regardless of k. This establishes a relationship between dominance and loss in net benefit, reminding us that only nondominated strategies on the frontier (TE of 1) can optimize the net benefit (have an EE of 1 at any k).

Reframing of the economic objective on the cost-disutility plane as minimizing the net loss relative to an optimal strategy can be expressed using equation 5 as

\[ \text{INMB}_{i} = (k \times DU_{i} + C_{i}) \times (1 - EE_{i}) \]

This loss in incremental net benefit can be represented as a function of economic inefficiency. Rearranging equation 6 to substitute for \((k \times DU_{i} + C_{i})\), into equation 7, we obtain

\[ \text{INMB}_{i} = NMB_{i} - NMB_{i} \]

Comparing ISO–net benefit lines representing equal levels of net benefit have a slope equal to \(- k\) on the cost-disutility plane. Lines closer to the vertex (origin) represent a higher net benefit per patient. Hence, the net benefit–maximizing strategy at a given k is the strategy on the net benefit line closest to the origin. For example, in the case of GERD, strategy E maximizes the net benefit for \(k = \$100\) with an INMB of $350, as illustrated in Figure 2.

More generally, at a given k, the vertical distance between the ISO–net benefit lines represents differences in net monetary benefit, whereas the horizontal distance between the ISO–net benefit lines represents differences in net health benefit. In each case, the net benefit increases in moving toward the origin. For example, comparing ISO–net benefit lines at \$100 per week of GERD avoided, strategy E has a higher net benefit than strategy C by 3.5 weeks of GERD prevented (intercepts of 2.18 and 5.68 measured on the horizontal axis) and $350 (intercepts of $219 and $569 on the vertical axis). These represent the same differences in net health and monetary benefit shown in the incremental cost-effectiveness plane in Figure 1.

### Economic (Net Benefit) Efficiency on the Cost-Disutility Plane

The calculation of degree of dominance (technical inefficiency) of a strategy does not rely on a decision maker’s choice of k. However, if the k is known or conditioned on, then economic (net benefit) inefficiency can also be calculated in the cost-disutility plane.

The economic efficiency (EE) for each strategy (i) is calculated for a given k as the objective function (equation 5) for the optimal (net loss–minimizing) strategy, divided by that for strategy i:

\[ EE_{i} = (DU_{i} \times k + C_{i})/(DU_{i} \times k_{i} + C_{i}) \]

where * indicates the optimal strategy.

Now, the loss in the incremental net monetary benefit for strategy i relative to the optimal strategy can be expressed using equation 5 as

\[ \text{INMB}_{i} = NMB_{i} - NMB_{i} = (k \times DU_{i} + C_{i}) - (k \times DU_{i} + C_{i}) \]

### Table 1 Comparisons of Efficiency for the Gastroesophageal Reflux Disease (GERD) Management Options

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Incremental Cost per Patient ($)</th>
<th>Additional Weeks with GERD</th>
<th>Technical Inefficiency (Degree of Dominance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>28</td>
<td>3.04</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>438</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>5.69</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>147</td>
<td>7.81</td>
<td>0.682</td>
</tr>
<tr>
<td>E</td>
<td>87</td>
<td>1.32</td>
<td>0</td>
</tr>
<tr>
<td>F</td>
<td>297</td>
<td>0.72</td>
<td>0.103</td>
</tr>
</tbody>
</table>

Zk/Z0 for strategy D in Figure 3. Existing methods for efficiency measurement can be applied to calculate the degree of dominance as technical inefficiency (1 – technical efficiency) on the cost-disutility plane, as described and illustrated for the case of GERD in the appendix. Degrees of dominance for the 6 GERD strategies are presented in Table 1. Strategies B, E, A, and C on the frontier have a 0 degree of dominance, whereas strategies D and F off the frontier have a positive degree of dominance (technical inefficiency). In summary, measuring technical efficiency on the cost-disutility plane provides a simple and intuitive method for identification of
Comparing Multiple Strategies Under Uncertainty: The Net Loss Acceptability Frontier

To model uncertainty for GERD, Briggs and others \(^6\) used a Bayesian approach, in which, for each variable in the model, a value is drawn from a probability distribution specified for that variable to reflect its second-order uncertainty. \(^17\) Costs and effects are recalculated across strategies for each set of values to form a realization of the frontier and comparison of strategies. From these realizations, the cost-effectiveness acceptability curve (CEAC) can be constructed for each strategy to represent the proportion of realizations for which the strategy maximizes the net benefit at each possible \(k\). \(^6\) However, although allowing comparison of multiple strategies, CEACs do not tell the decision maker about the relative expected net benefit of strategies at any \(k\). \(^18\) Conversely, the net benefit curves cannot represent the uncertainty associated with the incremental net benefit in the case of multiple strategies.

The net loss statistic (equation 7) provides an appropriate point of reference for comparison of the net benefit of multiple strategies. Applying equation 7 to strategies across each realization, the distribution and expected net loss relative to the optimal strategy is calculated for each strategy at any \(k\). For example, Table 2 reports 95% confidence intervals and expected values across 1000 replicates of net loss relative to the optimal strategy for \(k = \$100\). Strategy E minimizes the expected net loss for \(k = \$100\), with an average loss in net monetary benefit of \$4.90 per patient across 1000 replicates. This expected net loss for strategy E arises as there are a proportion of replicates (111/1000) in which E is not expected to be the optimal strategy.

Table 2 compares the expected net loss across strategies at \(k = \$100\). Conditioning on \(k\), an expected net loss curve for each strategy can be constructed as the expected loss in net benefit calculated using equation 6 plotted against \(k\). Figure 4 presents expected net loss curves for GERD strategies A to F. The lower bound of expected net loss curves across strategies, conditional on \(k\), represents an expected net loss frontier. This frontier identifies the optimal

![Figure 4 Expected net loss curves and acceptability frontier for gastroesophageal reflux disease (GERD) strategies.](image-url)
strategy for a risk-neutral decision maker across realizations at any $k$. For example, for the 1000 GERD realizations, the expected net loss is minimized with strategy C from $k$ of $0$ to $10.26$, strategy A for more than $10.26$ to $35.02$, strategy E for more than $35.02$ to $265.79$, and strategy B for more than $265.79$.

The expected net loss frontier also represents the expected value of perfect information (EVPI) across strategies at any $k$, given current uncertainty. For example, at $k = $100, strategy E minimizes the expected net loss at $4.90$ per patient (and hence maximizes the expected net benefit) across 1000 realizations. However, choosing strategy E with current uncertainty, we expect that in 111 of 1000 realizations, another strategy would be optimal. If we had perfect information, this loss of $4.90$ could be avoided by picking the optimal strategy in each realization. More generally, the expected net loss frontier tells us the EVPI at any $k$. In the case of GERD, the expected value of perfect information is maximized at $44.20$ per patient at $k = $265.79, the point of indifference between strategy E and B. However, the EVPI is less than $5$ per patient for $k$ between $100$ and $150$, where there is little uncertainty that strategy E is optimal. EVPI is minimized at $3.26$ per patient at $k = $137.

In summary, the expected net loss acceptability frontier enables identification of the optimal strategy for a risk-neutral decision maker and the EVPI per patient at any $k$. Expected net loss frontier curves therefore simultaneously address optimal strategies for risk-neutral decision makers and the potential value of further research given current decision uncertainty.

**CONCLUSION**

A simple linear transformation from the cost-effectiveness plane to compare strategies on the cost-disutility plane allows equivalent identification of the efficiency frontier, dominance, and net benefit maximization at a decision maker's willingness to pay for health, $k$, but unlike the incremental cost-effectiveness plane, this transformation permits

1. use of efficiency methods, with movement toward the origin representing better strategies, and
2. ratio measures of inefficiency (degree of dominance and net benefit inefficiency at a given $k$).

Furthermore, in comparing strategies under uncertainty, the common reference point of losses in net benefit relative to the optimal strategy in each replicate allows construction of expected net loss curves conditional on $k$ and the expected net loss frontier. This frontier directly identifies strategies that maximize expected net benefit (minimize expected net loss) and the EVPI across strategies.

**APPENDIX**

**Efficiency Measurement Methods on the Cost-Disutility Plane**

Standard efficiency measurement methods such as the linear programming method of data envelopment analysis (DEA) have been widely used in comparison of health care providers and other public service providers. However, the application of such methods to aid with comparing multiple strategies for health technology assessment has been prevented by the inability to formulate meaningful ratio measures of performance with the presentation of outcomes on the cost-effectiveness plane. This article provides a missing link between efficiency methods and health technology assessment by a proposed reformulation of analysis onto the cost-disutility plane. In the cost-disutility plane, a simple form of the linear programming method of data envelopment analysis DEA\textsuperscript{8–10} can be used to identify

1. strategies on the efficiency frontier in which no proportional reduction in cost and disutility is possible and
2. the degree of dominance of strategies off the frontier as the proportional reduction possible in cost and disutility.

The DEA linear programming formulation required for this is simple, as constant returns to scale (CRS) are...
implicitly assumed in constructing the efficiency frontier as convex combinations of strategies. Under CRS, the linear programming problem simplifies to finding the proportion by which inputs of cost per patient and disutility (e.g., weeks with gastroesophageal reflux disease [GERD]) per patient can be reduced while remaining within the feasible set, defined by convex combinations of all strategies costs and disutility per patient.

Formally, for \( n \) strategies, the preferred linear programming formulation of DEA to estimate technical efficiency, \( \theta \), under CRS is

\[
\begin{align*}
\min_{\theta, \lambda} \\
\text{st} \\
\lambda \geq 1 \\
0x_i - n_i \lambda \geq 0,
\end{align*}
\]

where \( x_i \) is a vector of inputs for strategy \( i \) (\( i = 1 \) to \( n \)) of cost per patient in excess of the cheapest strategy and effects framed from a disutility perspective per patient (e.g., weeks with GERD); \( X = (x_1, \ldots, x_n) \), and \( \lambda \) represents a vector of weights for the \( n \) strategies, with \( X \lambda \) representing a convex combination of strategies for \( \lambda = 1 \).

The linear programming problem needs to be solved \( n \) times, once for each strategy (\( i = 1 \) to \( n \)). The value of \( \theta \) obtained in each of these \( n \) programming problems is the technical efficiency score for the \( i \)th strategy. In the case of GERD, for each of the 6 strategies (A to F), there were inputs of cost per patient and weeks with GERD per patient, as shown in Table 1. The technical efficiency for strategies A, B, C, and E of 1 indicates that these strategies were on the frontier, as shown in Figure 2. The technical efficiency scores (\( \theta \)) of 0.897 for strategy D and 0.319 for strategy F reflect the proportion of their original value to which both costs and effects for these strategies can be reduced in radially moving onto the frontier (target point) in Figure 2. Hence, inefficiency (1 – \( \theta \)), or degree of dominance, is 0.103 and 0.681 for strategies F and D, respectively. In the case of strategy D, the target on the frontier was a linear combination of strategies A (\( \lambda_1 = 0.680 \)) and E (\( \lambda_5 = 0.320 \)), whereas for strategy F, it was a linear combination of strategies B (\( \lambda_2 = 0.561 \)) and E (\( \lambda_5 = 0.439 \)). Explicitly, applying the formulation in equation A1, the technical efficiency of strategy D of 0.319 is the solution to the following linear program:

\[
\begin{align*}
\min_{\theta, \lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5, \lambda_6} \\
\text{st} \\
\lambda_1 + \lambda_2 + \lambda_3 + \lambda_4 + \lambda_5 + \lambda_6 \geq 1 \\
\begin{bmatrix} 2970 & -28\lambda_1 + 438\lambda_2 + 147\lambda_4 + 87\lambda_5 + 297\lambda_6 \\ 0.720 & -3.04\lambda_1 + 5.69\lambda_3 + 7.81\lambda_4 + 1.32\lambda_5 + 0.72\lambda_6 \end{bmatrix} \geq \begin{bmatrix} 0 \\ 0 \end{bmatrix}
\end{align*}
\]

With the target for strategy F a linear combination of strategies A and E, this can be further simplified to

\[
\begin{align*}
\min_{\theta, \lambda} \\
\text{st} \\
\lambda_1 + \lambda_5 \geq 1 \\
\begin{bmatrix} 2970 & -28\lambda_1 + 87\lambda_5 \\ 0.720 & -3.04\lambda_1 + 1.32\lambda_5 \end{bmatrix} \geq \begin{bmatrix} 0 \\ 0 \end{bmatrix}
\end{align*}
\]

While in the case of GERD effects were measured with a single effect framed from a disutility perspective, more generally multiple effects framed from a disutility perspective can be included as additional input vectors. Defining disutility event rates relative to the most effective strategy and costs as incremental to the cheapest strategy ensures that dominated strategies can be equiproportionally reduced (radially contracted) to a target on the efficiency frontier in the incremental cost-incremental disutility plane. This simplifies data envelopment analysis results by preventing slacks in estimating technical efficiency scores.9

REFERENCES


180 • MEDICAL DECISION MAKING/MAR–APR 2008