Health Technology Assessment in the Cost-Disutility Plane

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Abstract

The aim of this paper is to illustrate the potential advantages of presenting cost-effectiveness results on the cost-disutility plane rather than the cost-effectiveness plane.

We illustrate the standard geometric presentation of cost-effectiveness results in the incremental cost-effectiveness plane that has developed over the last ten to twenty years. We demonstrate that there is a correspondence between the cost-effectiveness plane presentation and the presentation of results in the cost-disutility plane, and go on to argue that the presentation of results on the cost-disutility plane offers both technical and conceptual advantages to the analyst and to the consumer of cost-effectiveness results.

Recently published examples of economic analyses of treatment strategies for gastro-oesophageal reflux disease and colorectal cancer screening are employed to illustrate these advantages. In particular, presenting result in cost-disutility space allows the exploitation of radial contraction properties commonly employed to measure efficiency with frontier methods such as Data Envelopment Analysis (DEA). We argue that such an approach allows simpler and more intuitive construction of efficiency frontiers, the ability to estimate the degree of dominance and bounded comparison of the net benefit of strategies.

In conclusion, we suggest that framing relative costs and effects in cost-disutility space has much to offer the analyst and provides a ‘missing link’ between the cost-effectiveness literature in health technology assessment and efficiency measurement with frontier methods.
Introduction

It is generally recognised that evidence of the effectiveness of health care interventions compared to an existing alternative is not sufficient grounds for recommending that those interventions should be provided within a health care system. Increasingly, evidence of cost-effectiveness is required to help convince payers that the interventions also provide value for money. Different countries have different levels of formality with which the ‘fourth-hurdle’ of cost-effectiveness needs to be demonstrated. Nevertheless, the emergence of bodies such as the Pharmaceutical Benefits Advisory Committee in Australia, the National Institute of Health and Clinical Excellence (NICE) in the UK and the Canadian Coordinating Office of Health Technology Assessment in Canada, reflect 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 just on effectiveness, but also on cost of interventions, it is natural to consider a two 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 with 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 two points on the cost-effectiveness plane as an incremental cost-effectiveness ratio.

In this paper, we argue for a further change to the two dimensional presentation of cost-effectiveness results. Framing relative measures of effects as entirely equivalent measures of relative ‘disutility’ and presenting results in the cost-disutility plane we argue that a number of technical and conceptual advantages are realised. These revolve around the ability to compare the relative efficiency of alternative interventions represented in cost-disutility space with radial contraction towards the origin of the cost-disutility plane. In doing so, we provide a formal link between the formerly disparate literatures of efficiency in cost-effectiveness analysis and the broader framework of assessing efficiency with frontier methods such as Data Envelopment Analysis (DEA) [6].

In this paper we begin in the next section by illustrating the ‘standard’ approach to cost-effectiveness analysis in the presence of multiple treatment options, using a recently published example of management strategies for Gastro Esophageal Reflux Disease (GERD) [7]. In particular, this example is used to illustrate the principles of dominance, extended dominance and the development of an ‘efficiency frontier’ in the incremental cost-effectiveness plane. The following section then provides a formal treatment of the ‘correspondence’ allowing an equivalent interpretation of maximising net benefit in the cost-effectiveness and cost-disutility planes. The GERD example and a more complex example for colorectal cancer screening strategies [8] are then presented on the cost-disutility plane, illustrating technical and conceptual advantages over comparison on the incremental cost-effectiveness plane.
Finally, a discussion and conclusion section summarise the relative merits of the advocated approach.

**Efficiency frontiers on the CE plane**

The presentation of multiple treatment options as an efficiency frontier on the cost-effectiveness plane has a long history. Particularly helpful illustrations are provided by Weinstein [9] and by Karlsson & Johanesson [10]. Here, however, we employ a more recent example of management strategies for GERD which provides a practical illustration of the principles of dominance and extended dominance and the construction of efficiency frontiers, and has the added advantage of including a probabilistic analysis so that uncertainty can be interpreted in a statistical way [7].

The GERD example involves six potential management strategies for patients presenting to their physicians with endoscopically proven erosive esophagitis. The analysis models twelve-month healing and recurrence rates based on a comprehensive review of the literature, with the six strategies evaluated being chosen for their clinical relevance by a panel of gastrointestinal clinicians [11]. The expected costs and benefits (in terms of weeks free of GERD symptoms) were calculated and plotted on the incremental CE plane, which is presented in Figure 1.
In the incremental cost-effectiveness plane the efficiency frontier is constructed by:

1. rank ordering all interventions in terms of their effect (i.e. along the horizontal axis of Figure 1);
2. excluding any strictly dominated options (in this case option D is strictly dominated being both more expensive and less effective than either options C, A or E);
3. excluding any extended dominated options (Option F in this case is ‘extended dominated’ [12] by a potential combination of options E and B) and then;
4. linking remaining adjacent options to form a convex hull.

Figure 1
GERD expected case in the incremental CE plane
Geometrically, this process corresponds to the illustrated frontier CAEB in Figure 1 with the slope of the frontier corresponding to the estimated incremental cost-effectiveness ratio (ICER) between adjacent non-dominated treatment options.

In the incremental cost-effectiveness plane improved performance is indicated by south-east movement (reduced costs and greater effect), with dominance and extended dominance indicated by points north-west of this frontier. Note, however, that as improvement in performance does not expand from or contract to a vertex, concepts of dominance and the construction of the frontier itself in the incremental cost-effectiveness plane are not based on ‘radial’ properties. In the absence of such radial properties, standard frontier methods such as data envelopment analysis (DEA) [6] cannot be employed in constructing the efficiency frontier or identifying dominance in the incremental cost-effectiveness plane. More generally identification of the frontier and extended dominance has no natural unique direction for comparison.

In the incremental cost-effectiveness plane it is also the case that where the origin of the plane represents current practice:

(i) the efficiency frontier will only pass through the origin if there is not (extended) dominance over current practice and;

(ii) the efficiency frontier will only be constrained to the north-east quadrant if current practice is the lowest cost strategy.

To ensure the efficiency frontier passes through the origin and is contained in the north-east quadrant, the origin can be set as the least cost strategy, rather than necessarily current practice. This is the approach taken in the GERD example presented in figure 1, where the least cost intervention strategy C (based on
management of GERD with H2RAs) is set as the origin of the plane, rather than the usual practice (at time of writing) of option D (treatment based around a prokinetic agent).

Nevertheless, even where the least costly strategy is set as the origin, in comparing multiple non-dominated strategies the appropriate strategy for comparison changes when moving up the frontier, as the decision makers’ threshold value implicitly increases. Incremental cost effectiveness should be defined relative the next best treatment alternative [13]. In the case of the GERD frontier, this implies incremental cost effectiveness ratios for strategy A should be compared relative to C (implicitly for a WTP from 0 to $10 per week GERD avoided), strategy E relative to A (implicitly for WTP from $10 to $36) and strategy B relative to E (implicitly for WTP from $36 to $243).

More recently the net-benefit approach to cost-effectiveness analysis which explicitly considers decision makers values for effects of care has become more popular [14-16]. 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 makers’ willingness to pay for a unit of effect \(k\), the net monetary benefit \(NMB\) of a strategy \(i\) is the monetary value of incremental effects \(E\) less incremental costs \(C\) is:

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

(1)

and the incremental net monetary benefit \(INMB\) between two 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, incremental net effect benefit (INEB) can be calculated as incremental effect less incremental cost converted to equivalent effects at a WTP \( k \):  

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

In general net benefit statistics (whether incremental or measured in monetary or effect units) have the advantage over ratio measures of differences being additively separable [15] a property of their linear form.

Levels of net benefit can be represented geometrically on the incremental cost-effectiveness plane as straight parallel lines with slope \( k \) (as illustrated in figure 1 for \( k=$100/ week of GERD prevented), with net benefit lines further south east representing higher net benefit. A net benefit line passing through the origin is equivalent to that used to identify acceptance and rejection regions in comparison of two interventions, and hence the optimal (net benefit maximising) strategy at a given WTP threshold \( k \). However, in comparison of multiple non-dominated strategies a line through the origin does not allow identification of the optimal intervention at any WTP threshold \( k \). For example in figure 1, at $100 per week of GERD avoided, the net benefit line through the origin (intervention C) can only establish that each of strategies A, E, F and B are preferred to C (lie to the south-east of its net benefit line), at this WTP. However, the intervention maximising net benefit at a given \( k \) is simply identified from comparison of net benefit lines on which strategies lie, as that furthest south-east tangent to the convex efficiency frontier. In figure 1 this is strategy E with
net benefit line tangent to the efficiency frontier CAEB at $100 per week GERD avoided.

The constant distance between parallel net benefit lines makes it clear that differences in net benefit between strategies are independent of choice of comparator. This also allows vertical distances between net benefit lines to be interpreted as differences in net monetary benefit and horizontal distances between lines represent differences in net effect benefit. Differences in net benefit at a given WTP between strategies \((i,j)\) are most easily represented by the distance between net benefit lines as \(INHB_{ij}\) on the cost axis and \(INMB_{ij}\) on the effect axis. For example, comparing net benefit of strategies E and C at $100 per week of GERD prevented in figure 1, \(INHB_{EC}\) is 3.50 weeks GERD prevented per patient measured on the horizontal axis and \(INMB_{EC}\) is $350 per patient measured on the vertical axis. Differences in net benefit equal INB in the incremental cost-effectiveness plane where comparison is with the strategy at the origin, since the INB of the strategy at the origin is 0. However, in general differences between the net benefit of strategies in the incremental cost-effectiveness plane require differences in incremental net benefit to be considered, with the origin acting as a point of reference, not necessary in direct comparison. It should also be noted that while defining the origin as the least costly strategy allows the frontier to lie in the north-east quadrant, the comparison of differences in net monetary and effect benefit of strategies at axes is not bound in this quadrant in the incremental cost-effectiveness plane.

In summary, the principles applied in comparing multiple strategies in the incremental cost-effectiveness plane are to exclude strategies where there is extended dominance,
with non-dominated strategies forming an efficiency frontier. The strategy with highest net benefit is identifiable by that with the south-east most net benefit line tangent to this frontier at a given WTP (k). However, while the incremental cost-effectiveness plane allows construction of an efficiency frontier and identification of dominance and relative net benefit with performance improving in a south-east direction, they are not based on radial properties, as there is no vertex to contract to. Hence, construction of efficiency frontiers and identification of extended dominance become technically difficult, and while the frontier can be restricted to the north east quadrant by setting the least cost strategy as the origin, comparison of net benefit is not bound to this quadrant.

**A correspondence permitting radial comparison of performance**

Eckermann [17] recently identified that comparison of relative performance in the cost-disutility plane allows radial measures of relative performance consistent with maximising net benefit under conditions of a correspondence theorem. The net benefit correspondence theorem states that:

*There is a one-to-one correspondence between maximising net benefit per patient and minimising costs plus disutility per patient valued as in net benefit, where:

1. relative disutility rates cover relative effects of care, and;
2. compared providers face a common comparator (differences in expected costs and disutility rates in patient populations treated are adjusted for).*

This theorem, while initially applied to compare efficiency of health care providers at a clinical activity level allowing for health effects of care consistent with maximising net benefit can also be applied to permit radial properties when comparing multiple
strategies in HTA. In fact, correspondence conditions of comparability and coverage are more naturally satisfied in comparing strategies for HTA with appropriate randomised control trial evidence and methods of comparison. In satisfying the comparability condition evidence based on appropriately randomised control trials (RCTs) minimises chance differences in patient populations, while use of regression methods such as Cox regression adjusts for differences where they occur by chance. In satisfying the coverage condition, the scope and follow up period for outcomes included in RCTs involving economic evaluation should cover incremental effects and resource use across interventions for a common follow-up period.

To see how the correspondence theorem can be applied in comparing strategies in HTA recall from Equations 1 and 2 that an option is preferred over another if it has a greater net-benefit or equivalently the incremental net-benefit is positive in equation 3. Without loss of generality, option \(i\) is preferred to option \(j\) if

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

Now define the disutility of an option as the maximum effectiveness of the available options, \(E^{\text{MAX}}\), less the effectiveness of the current option, that is

\[
 DU_i = E^{\text{MAX}} - E_i ,
\]

which rearranging gives an expression for the effectiveness of:

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

Substituting this expression into Equation 4, multiplying through by minus one and noting that the \(k \cdot E^{\text{MAX}}\) terms cancel gives:
\[ C_i + k \times DU_i < C_j + k \times DU_j \quad (5) \]

The decision rule of maximising net benefit in Equation 4 corresponds to minimizing net loss in Equation 5 using the same willingness to pay for a unit of effect, \( k \).

To allow a standardised incremental framework for costs as well as disutility (implicit in the definition of disutility as \( DU_i = E^{\text{MAX}} - E_i \)), the cost of each option can be measured relative to that of the cheapest option, \( C^{\text{MIN}} \). Subtracting, \( C^{\text{MIN}} \), from each side of Equation 5 does not change the correspondence with net benefit. To allow incremental comparison in HTA [18] the net benefit correspondence theorem [17] is therefore suggested as applied in the incremental cost, incremental disutility plane.

**Illustrating HTA in the incremental cost-incremental disutility plane**

Figure 2 shows the GERD example plotted on the incremental cost, incremental disutility plane where the cost-effectiveness frontier is convex to an origin representing the lowest cost and lowest disutility event rate per patient. Net-benefit lines (shown for strategy C and E in figure 2 as in figure 1) can be plotted on the plane with slope equal to \(-k\) and greater value as they move closer to the origin.
In the incremental cost-incremental disutility plane, performance improves where incremental cost and incremental disutility are reduced, providing an intuitive direction for relative performance comparison with radial contraction towards the origin. This radial property in the incremental cost-incremental disutility plane allows simple construction of efficiency frontiers and identification of dominance using existing frontier methods such as data envelopment analysis (DEA) [6].

The efficiency frontier in the cost-disutility plane is analogous to a unit isoquant with inputs of incremental cost and incremental disutility and output of 1. The assumption of constant returns to scale, implicitly assumed in constructing an efficiency frontier and identifying extended dominance in the incremental cost effectiveness plane is explicit in this isoquant. Therefore, efficiency frontiers can be simply constructed in
the cost disutility plane with DEA formulated under constant returns to scale (CRS), with inputs of incremental cost relative to the cheapest strategy and incremental disutility event rates (e.g. life years lost relative to the most effective strategy) and an output of 1, as described in appendix 1.

Technical inefficiency scores calculated with this CRS DEA formulation represent the degree by which incremental costs and disutility events can be projected onto the efficiency frontier in radially contracting towards the vertex. The frontier represents convex combinations of strategies where it is not possible to contract (such as B, E, A and C in Figure 2) and hence technical efficiency is 1 or equivalently technical inefficiency (1- technical efficiency) is 0. Dominated strategies in the cost-disutility plane such as D and F in Figure 2 are easily identifiable as where cost and disutility event rates can be equi-proportionally reduced (radially contracted) to that of a combination of other strategies, and hence technical inefficiency is greater than 0 (technical efficiency less than 1). In the case of GERD, technical efficiency scores estimated with DEA are presented for each of the six strategies in Table 1.

Table 1: Comparisons of efficiency for the GERD management options

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Incremental cost per patient ($) relative to least costly strategy</th>
<th>Additional weeks with GERD relative to the most effective strategy</th>
<th>Technical efficiency under CRS</th>
<th>Economic efficiency at WTP $100 per week GERD prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>28</td>
<td>3.04</td>
<td>1.00</td>
<td>&lt;1</td>
</tr>
<tr>
<td>B</td>
<td>498</td>
<td>0</td>
<td>1.00</td>
<td>&lt;1</td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>5.69</td>
<td>1.00</td>
<td>&lt;1</td>
</tr>
<tr>
<td>D</td>
<td>147</td>
<td>7.81</td>
<td>0.319</td>
<td>&lt;1</td>
</tr>
<tr>
<td>E</td>
<td>87</td>
<td>1.32</td>
<td>1.00</td>
<td>1.000</td>
</tr>
<tr>
<td>F</td>
<td>297</td>
<td>0.72</td>
<td>0.956</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
Strategies A, B, C and E lie on the efficiency frontier with technical efficiency of 1.

For dominated strategies the degree of dominance can be estimated as technical inefficiency (1- technical efficiency). For example the expected degree of dominance for strategy D is 0.681 (1-0.319), implying that expected cost in excess of the cheapest strategy and disutility event rates in excess of the most effective strategy could both be reduced by 68.1% if a convex combination of strategies A and E were adopted.

In the incremental cost-incremental disutility plane, defining disutility event rates relative to the most effective strategy and costs as incremental to the cheapest strategy ensures that dominated strategies can be equi-proportionally reduced (radially contracted) to a target on the efficiency frontier, preventing slacks in estimated technical efficiency scores. The only exception to this would be where one strategy dominates all others, in which case there is no efficiency frontier, simply the dominant (cheapest and most effective) strategy at the origin.

The preferred (net benefit maximising) strategy at a given WTP is easily identified at the point of tangency between the net benefit line closest to the origin and the convex efficiency frontier. This corresponds to the strategy with economic efficiency of 1 under a DEA formulation with the relative price of disutility events are set at the decision making threshold WTP ($k$). For example in the case of GERD, at WTP of $100 per week of GERD avoided strategy E is identified as the optimal strategy, with economic efficiency of 1 in table 2 and net benefit line tangent to the frontier CAEB.
In the cost-disutility plane as in the incremental cost-effectiveness plane, the vertical distance between any two net benefit lines (i.e. the difference in intercepts on the cost axis) represents differences in net monetary benefit, while the horizontal distance (i.e. the difference on the incremental disutility axis) represents differences in net health benefit. For example in figure 2, at $100 per week of GERD avoided the difference between strategies E and C in net health benefit is 3.5 (4.68-1.18) weeks GERD prevented and net monetary benefit $350 ($569-$219), as in the incremental cost-effectiveness plane. However, unlike the incremental cost effectiveness plane (figure 1) this comparison is now strictly bound by axes in the cost-disutility pane.

Ranges of WTP threshold over which non dominated strategies (technical efficiency of 1) on the frontier maximise net benefit can be simply identified back-solving for $k$ between adjacent strategies on the frontier (i and j) using:

\[ C_i + k \times DU_i = C_j + k \times DU_j \]
\[ \Leftrightarrow k = \frac{(C_j - C_i)}{(DU_i - DU_j)}. \]  

These ranges represent the slope of segments of the frontier, which under the net benefit correspondence theorem are the same as incremental cost effectiveness ratios in the incremental cost effectiveness plane. In the case of GERD strategies, ranges of WTP over which adjacent technically efficiency strategies on the efficiency frontier (A,B,C,E) are preferred are calculated with the above approach in Table 2.
Table 2: Willingness to pay ranges over which GORD strategies maximise net benefit ($ per week of GORD avoided)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost /patient in excess of cheap strategy($)</th>
<th>Weeks with GORD in excess of most effective</th>
<th>Threshold values over which strategy preferred ($ per GORD free week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>0</td>
<td>5.69</td>
<td>$0 up to $10</td>
</tr>
<tr>
<td>A</td>
<td>28</td>
<td>3.04</td>
<td>$10 up to $36</td>
</tr>
<tr>
<td>E</td>
<td>87</td>
<td>1.28</td>
<td>$36 up to $264</td>
</tr>
<tr>
<td>B</td>
<td>498</td>
<td>0</td>
<td>$264 or more</td>
</tr>
</tbody>
</table>

Modelling uncertainty in GERD

In modelling uncertainty across comparison of multiple strategies for GERD, Briggs et al. [7] suggested a Bayesian approach, where, for each variable specified in a decision analytic model, random samples are taken from specified distributions of parameters in the model to reflect their 2nd-order uncertainty [19]. These random samples enable replicates of performance comparison across strategies in modelling uncertainty of the relative performance of strategies. For each realisation across strategies an efficiency frontier can then be constructed to identify whether strategies are dominated or lie on the frontier.

Radial properties in the incremental cost-disutility plane simplify the identification of the efficiency frontier and dominance in each of these realisations, as in the expected case. For any given realisation of compared strategies, input orientated DEA under CRS in the cost-disutility plane easily identifies those on the frontier with degree of dominance 0 (technical efficiency of 1) and those dominated where degree of dominance is greater than 0 (technical efficiency is less than one). The proportion of simulated frontiers in which a strategy is dominated allows estimation of the probability of dominance, as in the incremental cost-effectiveness plane. However, in
the cost-disutility plane, confidence intervals for degree of dominance for each strategy can also be estimated from their distribution across realisations. For example in the case of GERD, ninety five percent confidence intervals for degree of dominance for each of the treatment strategies for GERD are estimated in table 3 as the 25th and 976th observation from their ordered distribution in 1000 realisations.

Table 3: Ninety five percent confidence intervals for degree of dominance

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Degree of dominance (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0 (0.0, 0.41)</td>
</tr>
<tr>
<td>B</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>C</td>
<td>0 (0.0, 0.64)</td>
</tr>
<tr>
<td>D</td>
<td>0.68 (0.57, 0.77)</td>
</tr>
<tr>
<td>E</td>
<td>0 (0.0, 0.01)</td>
</tr>
<tr>
<td>F</td>
<td>0.04 (0.0, 0.36)</td>
</tr>
</tbody>
</table>

Table 3 illustrates that under uncertainty degree of dominance may be particularly important to consider for extremal strategies which lie on the frontier in the expected case. For example, while strategy C lies on the frontier in the expected case (degree of dominance 0) and strategy F does not (degree of dominance 0.04), when allowing for uncertainty, strategy C has a significantly greater degree of dominance than strategy F at the upper 95% CI (0.64 vs. 0.36). The higher bound for degree of dominance for strategy C can be explained by the fact that when strategy C is dominated, it will usually be by strategy A having lower costs. When this is the case, C is likely to be dominated to a large degree by A given the significantly lower disutility event rate. In general strategies which lie on the extremes of the frontier (cheapest or most effective) may have high degrees of dominance when dominated, given the potential discontinuities in degree of dominance.

In summary, in allowing for uncertainty, radial properties in the cost-disutility plane allows technically simpler identification of dominance and the ability to estimate degree of dominance for replicates just as they do in the expected case. Modelling
uncertainty of the degree of dominance may be particularly important to consider for
the cheapest and most effective strategies given the potential for discontinuities in
their distribution of degree of dominance arising from their extremal position on the
frontier.

**A more complex example – colorectal cancer screening strategies**

In the GERD example, incremental effects were measured as reduction in weeks
without GERD relative to the cheapest strategy and incremental disutility as
additional weeks with GERD relative to the most effective strategy. More generally,
where effects of care are measured in life years or quality adjusted life years (QALYs)
in the incremental cost-effectiveness plane, they simply map to years of life lost or
QALYs lost relative to the most effective strategy in the incremental cost-incremental
disutility plane. For example, consider the expected cost (1998 $US) and life
expectancy of 22 colorectal cancer screening strategies for 50 year old males at
average risk of colorectal cancer in comparison modelled by Frazier [8]. These 22
colorectal cancer screening strategies, the efficiency frontier and comparison of the
net benefit of 2 strategies at a WTP of $50,000 per life year saved are compared on
the incremental cost-effectiveness plane in figure 3 and on the incremental cost
incremental disutility (life years lost relative to most effective strategy) in figure 4.
Figure 3: Colorectal cancer screening expected case on the incremental CE plane

Figure 4: Colorectal cancer screening on the incremental cost-incremental disutility plane
The optimal strategy at a WTP of $50,000 per life year saved is illustrated as the point of tangency between the efficiency frontier and the net benefit line for UFOBT+sig2-10y in figures 3 and 4. That is, at $50,000 per life year saved the strategy of unrehydrated faecal occult blood test and sigmoidoscopy every 10 years followed by colonoscopy in any adenomatous polyp (UFOBT+sig2-10y) lies on a NB line furthest south-east in figure 3 and closest to the origin in figure 4 than that of any other strategy. The amount by which the net benefit of UFOBT+sig2-10y exceeds that of sig2-10y is illustrated by the distance between NB lines on axes as 0.0142 life years (.0389 less .0247 in figure 3 and 0.382 less 0.240 in figure 4) or equivalently $713 ($1947 less $1234 in figure 3 and $1911 less $1198 in figure 4).

Technical efficiency scores for colorectal cancer screening strategies, estimated with DEA in the incremental cost-incremental disutility plane, are reported in table 4 ordered by cost per patient. Strategies on the frontier are simply identified by a technical efficiency of 1, while the degree to which other strategies are dominated can be estimated as 1-technical efficiency.
Table 4: Degree of dominance (technical inefficiency) on the incremental cost-incremental disutility plane of 22 colorectal cancer screening strategies in 50 year old males at average risk

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Incremental cost relative to cheapest strategy ($US 1998/patient)</th>
<th>Reduction in Life expectancy (years) relative to most effective strategy</th>
<th>Technical efficiency</th>
<th>Degree dominated (technical inefficiency)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>$0</td>
<td>0.0629</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>Sig1 @ 55 y</td>
<td>$18</td>
<td>0.0478</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>Sig2 @ 55 y</td>
<td>$43</td>
<td>0.0456</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>DCBE @ 55 y</td>
<td>$148</td>
<td>0.0525</td>
<td>0.898</td>
<td>0.102</td>
</tr>
<tr>
<td>Sig1-10y</td>
<td>$166</td>
<td>0.0378</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>Sig2-10y</td>
<td>$236</td>
<td>0.0335</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>Col @ 55y</td>
<td>$260</td>
<td>0.0350</td>
<td>0.974</td>
<td>0.026</td>
</tr>
<tr>
<td>Sig1-5y</td>
<td>$386</td>
<td>0.0304</td>
<td>0.959</td>
<td>0.041</td>
</tr>
<tr>
<td>DCBE-10y</td>
<td>$462</td>
<td>0.0423</td>
<td>0.832</td>
<td>0.168</td>
</tr>
<tr>
<td>Sig2-5y</td>
<td>$484</td>
<td>0.0244</td>
<td>0.973</td>
<td>0.027</td>
</tr>
<tr>
<td>UFOBT</td>
<td>$532</td>
<td>0.0209</td>
<td>0.985</td>
<td>0.015</td>
</tr>
<tr>
<td>UFOBT + Sig1-10y</td>
<td>$752</td>
<td>0.0106</td>
<td>0.984</td>
<td>0.016</td>
</tr>
<tr>
<td>UFOBT + Sig2-10y</td>
<td>$758</td>
<td>0.0088</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>DCBE-5y</td>
<td>$820</td>
<td>0.0184</td>
<td>0.807</td>
<td>0.193</td>
</tr>
<tr>
<td>RFOBT</td>
<td>$944</td>
<td>0.0109</td>
<td>0.892</td>
<td>0.108</td>
</tr>
<tr>
<td>UFOBT+Sig1-5y</td>
<td>$971</td>
<td>0.0069</td>
<td>0.951</td>
<td>0.049</td>
</tr>
<tr>
<td>Col-10y</td>
<td>$976</td>
<td>0.0051</td>
<td>0.850</td>
<td>0.150</td>
</tr>
<tr>
<td>UFOBT+Sig2-5y</td>
<td>$982</td>
<td>0.0044</td>
<td>1.000</td>
<td>0</td>
</tr>
<tr>
<td>RFOBT+Sig1-10y</td>
<td>$1,152</td>
<td>0.0045</td>
<td>0.928</td>
<td>0.072</td>
</tr>
<tr>
<td>RFOBT+Sig2-10y</td>
<td>$1,174</td>
<td>0.0032</td>
<td>0.969</td>
<td>0.031</td>
</tr>
<tr>
<td>RFOBT+Sig1-5y</td>
<td>$1,376</td>
<td>0.0019</td>
<td>0.939</td>
<td>0.061</td>
</tr>
<tr>
<td>RFOBT+Sig2-5y</td>
<td>$1,396</td>
<td>0.0000</td>
<td>1.000</td>
<td>0</td>
</tr>
</tbody>
</table>

Sig1 = Sigmoidoscopy followed by colonoscopy in high risk polyps only
Sig2 = Sigmoidoscopy followed by colonoscopy in any adenomatous polyp
DCBE = Double contrast barium enema
FOBT = Faecal occult blood test (UFOBT= unrehydrated, RFOBT= rehydrated)
Col = Colonoscopy
5y = every 5 years
10y = every 10 years
@ 55y = at 55 years of age

Table 5 reports ranges of WTP over which screening strategies on the frontier (technical efficiency of 1 in table 4) maximise net benefit calculated back solving between adjacent technically efficient strategies with equation 6.
Table 5: WTP regions for colorectal cancer strategies ($/life year saved)

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Incremental cost per patient relative to cheapest strategy</th>
<th>Average life years lost relative to the most effective strategy</th>
<th>WTP region of preferred (NB maximising) strategy (1998 US$ per life year saved)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>$0</td>
<td>0.0629</td>
<td>0 to $1,192</td>
</tr>
<tr>
<td>Sig1 @ 55 yrs</td>
<td>$18</td>
<td>0.0478</td>
<td>$1,193 to $11,363</td>
</tr>
<tr>
<td>Sig2 @ 55 yrs</td>
<td>$43</td>
<td>0.0456</td>
<td>$11,364 to $15,769</td>
</tr>
<tr>
<td>Sig1-10years</td>
<td>$166</td>
<td>0.0378</td>
<td>$15,770 to $16,279</td>
</tr>
<tr>
<td>Sig2-10years</td>
<td>$236</td>
<td>0.0335</td>
<td>$16,280 to $21,336</td>
</tr>
<tr>
<td>UFOBT + Sig2-10y</td>
<td>$758</td>
<td>0.0088</td>
<td>$21,337 to $50,909</td>
</tr>
<tr>
<td>UFOBT+Sig2-5y</td>
<td>$982</td>
<td>0.0044</td>
<td>$50,910 to $94,090</td>
</tr>
<tr>
<td>RFOBT+Sig2-5y</td>
<td>$1396</td>
<td>0</td>
<td>$94,091 or more</td>
</tr>
</tbody>
</table>

Allowing for WTA greater than WTP

Where strategies have negative expected effect relative to current practice, loss aversion under prospect theory [20] predicts that willingness to accept loss will be greater than willingness to pay for gain for some endowment. In the case of health care, O’Brien, Gersten, Willan and Faulkner [21] found empirical evidence of a 2-3 fold greater value for WTA health loss than WTP for equivalent health gain. Willan, O’Brien and Leyva [22] suggested that where the origin in the incremental cost effectiveness plane represents current practice, acceptance and rejection regions between current practice and an alternative strategy could be modelled in the incremental cost effectiveness plane with a kink at the origin. This kink would result from a greater slope of the threshold line for health losses (WTA) than gains (WTP), relative to the current endowment. When comparing multiple strategies, net benefit lines could similarly be kinked at the expected effect of current practice with a slope equivalent to WTA for effects representing losses relative to current practice and WTP for effects which were gains relative to current practice. Figure 5 illustrates
such a kink in net benefit curves in comparing colorectal cancer screening strategies in the incremental cost-incremental disutility plane, where current practice is assumed to be unrehydrated faecal occult blood test (UFOBT), the WTP for health gain $50,000 per life year saved and WTA health loss $100,000 per life year lost.

In comparison with figure 4, the distance between net benefit curves for UFOBT+sig-2 and sig-2 increases from $767 to $1243 on the vertical axis in figure 5 ($2541-$1198). This reflects the greater value of health losses than gains relative to current practice (assumed UFOBT). In general, figure 5 illustrates how a kink in the threshold reduces the likelihood of preference for strategies with reduction in effect relative to current practice. It also clarifies that there will still be a unique optimal strategy given convexity of the efficiency frontier, and concavity of kinked net benefit curves.
Discussion

Comparison of multiple HTA strategies in the cost-disutility plane has been shown in this paper to have distinct advantages over current comparison in the incremental cost-effectiveness plane. Radial properties in the cost disutility plane, which are absent in the incremental cost effectiveness plane have been illustrated to allow:

(i) A simpler and more intuitive construction of frontiers;
(ii) The ability to estimate degree of dominance and;
(iii) A closed mathematical form in comparing net benefit of strategies.

The net benefit correspondence theorem underlying comparison of performance in the cost-disutility plane also provides a more explicit theoretical framework for comparison of strategies. Correspondence conditions of comparability and coverage establish the theoretical requirement for randomized control trial evidence with adequate coverage of relative effects and length of follow up. The common comparison condition also supports principles such as the use of stratified randomization to minimise potential differences in risk by chance and adjustment for differences when they occur by chance in practice. The proposed approach of comparison under the net benefit correspondence theorem in the cost-disutility plane therefore has clear theoretical and technical advantages in comparing more than two strategies, over that currently adopted in the incremental cost effectiveness plane.

However, where comparison is between two strategies only, an argument can still be made for using the incremental cost-effectiveness plane. For such comparisons there are no frontiers or extended dominance and hence there are no advantages of radial properties in comparison relative to a frontier in the cost disutility plane. Where only two strategies are compared acceptance regions in the incremental cost effectiveness
plane allow simple identification of decision making consistent with maximising net benefit. For the set of HTA economic evaluations where effects are reported with a generic measure such as QALYs, and comparison is restricted to a new strategy and current practice the incremental cost-effectiveness plane with the origin representing current practice permits simple global comparison. Representing all such bilateral comparisons in the incremental cost-effectiveness plane could be used similar to QALY league tables in addressing questions of allocative efficiency of alternative new treatments relative to current practice. Such comparison across different economic evaluations is not possible in the incremental cost-incremental disutility plane, where the origin does not represent current practice.

The incremental cost-effectiveness plane may therefore be preferred where the objective is to consider allocative efficiency across multiple health technology assessments based on a bilateral comparison and a generic measure of effect such as QALYs. However, even in this case, principles of coverage of effects and a common comparator in the net benefit correspondence theorem underlying comparison of strategies in the cost-disutility plane should still be considered in the incremental cost-effectiveness plane. These principles are currently implicit in undertaking appropriate evidence-based comparison of costs and effects of strategies on the incremental cost-effectiveness plane. Their explicit consideration in applying the net benefit correspondence theorem to health technology assessment in the cost-disutility plane provides a robust theoretical framework while not imposing any additional requirements for analysis than should already be undertaken.
More generally, common comparator and coverage conditions of the correspondence theorem provide a robust evidence-based theoretical framework for comparison of performance. In HTA this framework supports principles of comparing strategies based on RCT evidence with adequate follow-up, adequate coverage of the scope of costs and effects, and adjusted analysis where chance differences in prognostic factors occur. In comparing efficiency of health care providers in practice, risk factor adjustment is required to avoid cream skimming and satisfy the common comparator assumption, while data linkage is required to avoid cost and event shifting incentives and satisfy the coverage of effects condition. Provided these conditions are satisfied, relative performance can be compared in the cost-disutility plane consistent with maximising net benefit, as discussed in Eckermann [17]. The proposed approach therefore provides a robust framework for comparing performance of technologies and providers in practice, which allows advantages of radial properties from efficiency measurement in HTA and advantages of an appropriate objective function in comparison of providers.

**Conclusion**

Comparison of multiple health technology strategies in the cost-disutility plane has been demonstrated in this paper to have conceptual and technical advantages over that in the incremental cost-effectiveness plane. Both methods allow identification of the efficiency frontier, dominance and net benefit maximisation at a decision makers’ threshold value for effects. However, the property of radial contraction in the cost-disutility plane permits the analyst simpler construction of efficiency frontiers using existing methods such as data envelopment analysis. In explaining relative performance of providers, the property of radial contraction also allows a more
intuitive identification of dominance, estimation of degree of dominance and a closed form in representing differences in net benefit. In applying the proposed method a standardised approach has been suggested in comparing strategies in the cost disutility plane with disutility events measured relative to most effective and costs relative to least expensive strategy. This retains advantages of a framework with incremental comparison [18], while preventing slacks in estimating degree of dominance.

Uncertainty in degree of dominance has been shown to be important to consider given potential discontinuities in degree of dominance for the cheapest and most effective strategies at the extremity of the efficiency frontier. While in the base case such strategies lie on the frontier, they can be dominated to a large degree if dominated under uncertainty.

While there are technical advantages in comparing performance in the cost-disutility plane, the robust structural framework provided by the net benefit correspondence theorem underlying this method also provides conceptual advantages. In HTA, common comparison and coverage conditions of the correspondence theorem provide explicit support for principles of common comparison and coverage of effects currently implicit in the incremental cost-effectiveness plane. Principles explicitly supported by these conditions include: double-blind randomisation, stratification and risk factor adjustment in satisfying the comparability condition and; adequate scope of effects included and follow-up in satisfying the coverage condition.

The general performance measurement framework illustrated in this paper can also be used to compare efficiency of providers consistent with maximising net benefit, with
correspondence conditions providing a robust framework to prevent incentives for
cream-skimming and cost-shifting [17]. The broader advantages of the proposed
method may therefore be seen in providing a robust framework for comparing relative
performance of technologies or provider efficiency consistent with maximising net
benefit. The link between the radial properties of efficiency measurement and the
objective of net benefit maximisation allows advantages of an appropriate underlying
objective in comparison of providers and technically simpler efficiency measurement
methods such as DEA in HTA when comparing multiple strategies.

References

   for the Pharmaceutical Industry on Preparation of Submissions to the
   Pharmaceutical Benefits Advisory Committee including major submission
   involving economic analyses
   2002].

   Manufacturers and Sponsors on Making a Submission to a Technology Appraisal.


4. Anderson JP, Bush JW, Chen M, Dolenc, D. Policy space areas and properties of


6. Charnes A, Cooper RC, Rhodes E. Measuring the Efficiency of Decision Making

7. Briggs AH, Goeree R, Blackhouse G, O'Brien BJ. Probabilistic analysis of cost-
   effectiveness models: choosing between treatment strategies for gastroesophageal


Appendix 1: Data Envelopment Analysis and HTA

In undertaking HTA in the incremental cost- incremental disutility plane the constant returns to scale form of DEA (Charnes Cooper and Rhodes, 1978) can be applied to identify technical efficiency and the efficiency frontier (technical efficiency of 1). For n strategies with inputs of incremental cost per patient relative to the cheapest strategy \(x_1\) and incremental disutility (e.g. weeks of GERD or life year lost) relative to the most effective strategy per patient \(x_2\) and output of 1, the preferred formulation is simply:

\[
\min_{\theta, \lambda} \theta \\
\text{s.t.} \\
\lambda \geq 1 \\
\theta x_1 - X \lambda \geq 0
\]

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 efficiency score for the ith strategy. It will lie between 0 and 1, with 1 indicating it lies on the frontier, and more generally one minus this technical efficiency score representing the equi-proportional reduction in inputs possible to a convex combination of other strategies of degree of dominance. To undertake DEA, The DEAP computer package developed by Professor Tim Coelli and associated manual is available free at http://www.uq.edu.au/economics/cepa/deap.htm.