Better informing decision-making with multiple outcomes cost-effectiveness analysis: case studies in palliative care

Dr Nikki McCaffrey

Palliative Care Clinical Studies Collaborative (PaCCSC)
Flinders Health Economics Group
Flinders University
South Australia
Overview

- Health economics
- Multiple outcome comparison
- Net benefit correspondence theorem
- Analysis in cost-disutility space
- Summary measures
- Implications
Health economics is all about...

- Cutting costs
- Saving $$$

McCaffrey, N & Currow, D 2015
Health economics is really about...

- Maximising patient outcomes,
  improving care for patients
- Within budget-constrained funds
- Making the money go further

Dr Nikki McCaffrey Apr 2015
Health economics is...

‘...concerned with the **optimum use of scarce economic resources** for the care of the sick and the promotion of health, taking into account **competing** use of these resources’

(Mushkin 1958)
Why consider health economics?

McCaffrey, N & Currow, D 2015
Evaluating ‘optimum’ use

\[
\text{Incremental Cost Effectiveness Ratio (ICER)} = \frac{(C_i - C_j)}{(E_i - E_j)}
\]

Dr Nikki McCaffrey Apr 2015
Quality adjusted life year (QALY)

- Quantity AND quality
- Health-related quality of life

- Measuring the ‘Q’
  - EuroQol 5D (EQ-5D)
  - Short Form 6D (SF-6D)
  - Assessment of Quality of Life (AQOL)
  - Health Utility Index (HUI)

Van den Hout WB et al 2006
## Comparison of MAUI domains

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Domains/ dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D</td>
<td>Anxiety; pain; mobility; self-care; usual activities</td>
</tr>
<tr>
<td>SF-6D</td>
<td>Mental health; pain; physical function; role limitation; social function; vitality</td>
</tr>
<tr>
<td>HUI3</td>
<td>Ambulation; cognition; dexterity; emotion; hearing; pain; speech; vision</td>
</tr>
<tr>
<td>AQoL</td>
<td>Coping; independent living; life satisfaction; mental health; pain; relationship; self worth; senses</td>
</tr>
</tbody>
</table>
Palliative Care

‘...improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.’ (WHO)

http://www.who.int/cancer/palliative/en/palliative care

Dr Nikki McCaffrey Apr 2015
Multiple outcomes

Health

Equity

Carers

Dying process

Quality

Access

Cost-consequences analysis

Altman & Bland 2005; Munro 1986; Briggs & O'Brien 2001; Briggs et al 2002;
Rationale

Alternative methods are needed in economic evaluations of interventions with multiple outcome domains to better inform societal decision making under uncertainty.

Net benefit correspondence theorem

1. \( ICER_{ij} = \frac{(C_i - C_j)}{(E_i - E_j)} \)

2. \( INMB_{ij} = \lambda(E_i - E_j) - (C_i - C_j) \)

3. \( INMB_i = (\lambda \times DU_i + C_i) - (\lambda \times DU_\ast + C_\ast) \)

4. \( NL_i = ((\lambda_1 \times DU_{1i}) + (\lambda_2 \times DU_{2i}) + C_i) - ((\lambda_1 \times DU_{1\ast}) + (\lambda_2 \times DU_{2\ast}) + C_\ast) = \)

\( INMB = \) incremental net benefit; \( i = \) strategy 1; \( j = \) strategy 2

\( \ast = \) optimal strategy; \( \lambda = \) threshold value; \( DU = \) disutility; \( C = \) costs

Eckermann 2004; Eckermann et.al. 2008
Cost-effectiveness plane

Incremental cost ($) relative to lowest cost strategy (A)

Incremental pain-free days relative to the lowest cost strategy (A)

Adapted from Eckermann, Briggs & Willan 2008
Cost-disutility plane

Incremental cost relative to the least expensive strategy (A)

Incremental days WITH pain relative to the most effective strategy (D)

Adapted from Eckermann, Briggs & Willan 2008
Palliative Care Extended Packages At Home (PEACH)


BMJ Supportive & Palliative Care.
doi:10.1136/bmjspcare-2012-000361
<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>PEACH (n=23)</th>
<th>Usual care (n=8)</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total number of days at home</td>
<td>13.09 (8.52, 17.65)</td>
<td>12.13 (5.88, 18.38)</td>
<td>0.96 (-6.79, 8.64)</td>
</tr>
<tr>
<td>Proportion of home deaths (%)</td>
<td>56.25 (31.25, 80.00)</td>
<td>80.00 (33.33, 100)</td>
<td>-23.75 (-63.16, 25.00)</td>
</tr>
<tr>
<td><strong>Cost (AUS$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEACH package</td>
<td>$3,489 ($2,170, $4,943)</td>
<td>0</td>
<td>$3,489 ($2,170, $4,943)</td>
</tr>
<tr>
<td>Inpatient stay</td>
<td>$2,603 ($1,205, $4,147)</td>
<td>$5,053 ($2,084, $8,139)</td>
<td>-$2,450 (-$5,843, $957)</td>
</tr>
<tr>
<td>Total costs</td>
<td>$6,452 ($4,469, $8,586)</td>
<td>$5,425 ($2,404, $8,531)</td>
<td>$1,027 (-$2,612, $4,738)</td>
</tr>
<tr>
<td>Threshold value above which the mean INB becomes positive</td>
<td></td>
<td></td>
<td>$1,068 (-$6,627, $6,578)</td>
</tr>
</tbody>
</table>
Results: Incremental costs & outcomes framed from a disutility perspective

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PEACH (n=23)</th>
<th>UC (n=8)</th>
<th>PEACH</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of inpatient days</td>
<td>14.91 (10.35, 19.48)</td>
<td>15.88 (9.63, 22.13)</td>
<td>0# (0, 6.78)</td>
<td>0.96# (0, 8.64)</td>
</tr>
<tr>
<td>Proportion of inpatient deaths (%)</td>
<td>43.75 (20.00, 68.75)</td>
<td>20.00 (0, 66.67)</td>
<td>23.75# (0, 63.16)</td>
<td>0# (0, 25.00)</td>
</tr>
<tr>
<td>Total costs, mean</td>
<td>$6,452 ($4,469, $8,586)</td>
<td>$5,425 ($2,404, $8,531)</td>
<td>$1,027$ (0, $4,738)</td>
<td>$0$ (0, $2,612)</td>
</tr>
</tbody>
</table>

# relative to the most effective model of care ($DU_{1i} - DU_{1*}$);  
$ relative to the cheapest model of care ($C_i - C*$)
Cost-disutility plane

Incremental cost relative to the least expensive strategy (A)

Incremental days WITH pain relative to the most effective strategy (D)

Adapted from Eckermann, Briggs & Willan 2008
Efficiency frontier

INB improves contracting to the vertex

Additional number of inpatient days over 28 days relative to the most effective model of care

A
usual care
(0.96 days, 0%, $0)

B
PEACH
(0 days, 23.8%, $1,027)

Additional proportion of inpatient deaths over 28 days relative to the most effective model of care
Threshold regions

Threshold value for one extra day at home over 28 days ($\lambda_1$)

Threshold value per additional home death ($\lambda_2$)

usual care is the preferred strategy

PEACH is the preferred strategy

McCaffrey et al. 2011, 2015
Summary measures

- Threshold regions: combinations of values over which strategies maximise ENB
  - Expected Net Loss (ENL) planes
  - ENL contour
  - Cost Effectiveness Acceptability Plane (CEAP)

Bootstrapping the \((\Delta DU_1, \Delta DU_2, \Delta C)\) distribution
Expected net loss (ENL) plane

McCaffrey et al. 2011, 2015
Expected net loss contour (ENLC)

- PEACH minimises the ENL
- usual care minimises the ENL

Threshold value per additional home death over 28 days ($k_2$):
- $0
- $2,000
- $4,000

Threshold value per extra day at home over 28 days ($k_1$)

Eckermann et al. 2007, 2008; McCaffrey et al. 2011, 2015
Expected net loss (ENL) planes

McCaffrey et al. 2011, 2015
Expected net loss contour (ENLC)

- PEACH minimises the ENL
- usual care minimises the ENL

Threshold value per additional home death over 28 days ($k_2$)
- $0
- $2,000
- $4,000

Threshold value per extra day at home over 28 days ($k_1$)

Eckermann et al. 2007, 2008; McCaffrey et al. 2011, 2015
The ENLC and EVPI

- The loss of $3,004 per participant could be avoided by picking the optimal service model in each realisation with perfect information.

- The expected value of perfect information is the loss from a bad decision that could be avoided with perfect, rather than current information.

- Hence, the ENLC represents the EVPI per patient of adopting the strategy minimising ENL given current uncertainty as a function of threshold values for multiple effects.

Eckermann et al. 2007, 2008; McCaffrey et al. 2011, 2015
Cost-effectiveness acceptability plane (CEAP)

Eckermann et al. 2008; McCaffrey et al. 2011, 2015
Robust presentation & summary measures

- **Threshold regions:** combinations of values over which strategies minimise NL (maximise NB)
- **Expected Net Loss (ENL) planes:** differences in ENL
- **ENL contour:** strategy minimising ENL & EVPI with current evidence
- **Cost Effectiveness Acceptability Plane (CEAP):** probability the strategy minimises ENL
Conclusions

Limitations of current methods

– Cost-consequences analysis deterministic
– QALYs have limited coverage of palliative care domains

Advantages of proposed approach

– Jointly allows for uncertainty & explicit weights across multiple domains or outcomes
– ENL planes & contour identify optimal strategies & value of information
Better informing decision making with multiple outcome cost-effectiveness analysis under uncertainty in cost-disutility space

McCaffrey N, Agar M, Harlum J, Karnon J, Currow D, Eckermann S

doi:10.1371/journal.pone.0115544

Dr Nikki McCaffrey May 2015
THANKS

nicola.mccaffrey@flinders.edu.au
References


McCaffrey, N, Agar, M, Harlum, J, Karnon, J, Currow, D & Eckermann, S 2013, 'Is home-based palliative care cost-effective? An economic evaluation of the Palliative Care Extended Packages at Home (PEACH) pilot', BMJ Supportive & Palliative Care, doi:10.1136/bmjspcare-2012-000361


# Cost-consequences analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Capecitabine</th>
<th>Mayo Clinic</th>
<th>De Gramont</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival without relapse (months)</td>
<td>35.00</td>
<td>33.73</td>
<td>33.73</td>
</tr>
<tr>
<td><strong>Grade 3/4 adverse event rates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>11%</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>17%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Alopecia</td>
<td>2%</td>
<td>26%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Mean costs (Euros)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td>43.46</td>
<td>153.37</td>
<td>62.29</td>
</tr>
<tr>
<td>Total</td>
<td>3,697</td>
<td>10,635</td>
<td>7,266</td>
</tr>
</tbody>
</table>

Douillard JY et al 2008
Farrell’s production possibilities frontier with two inputs and one output
Preferred model of care?

The preferred option is the model of care minimising NL

Rearranging terms,

\[ NL_i = (C_i - C_*) + \lambda_1(DU_{1i} - DU_{1*}) + \lambda_2(DU_{2i} - DU_{2*}) \]

\[ NL_{PEACH} = $? + \lambda_1 ? + \lambda_2 ? = ? \]

\[ NL_{UC} = $? + \lambda_1 ? + \lambda_2 ? = ? \]
Results: Incremental costs & outcomes framed from a disutility perspective

<table>
<thead>
<tr>
<th>Outcome</th>
<th>PEACH (n=23)</th>
<th>UC (n=8)</th>
<th>PEACH</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of inpatient days</td>
<td>14.0 (10.4, 19.4)</td>
<td>15.9 (9.5, 21.9)</td>
<td>0# (0, 6.8)</td>
<td>0.96# (0, 8.6)</td>
</tr>
<tr>
<td>Proportion of inpatient deaths (%)</td>
<td>43.8 (13.0, 52.2)</td>
<td>20.0 (0, 63.2)</td>
<td>23.8# (0, 63.2)</td>
<td>0# (0, 25.0)</td>
</tr>
<tr>
<td>Total costs, mean</td>
<td>$6,452 ($4,469, $8,586)</td>
<td>$5,425 ($2,404, $8,531)</td>
<td>$1,027$ (0, $4,738)</td>
<td>$0$ (0, $2,612)</td>
</tr>
</tbody>
</table>

# relative to the most effective model of care ($DU_{1i} - DU_{1*}$);

$ relative to the cheapest model of care ($C_i - C*$)
Preferred model of care?

\[
$1,027 + 0\lambda_1 + 0.24\lambda_2 = \$1,027 + 0.24\lambda_2 \quad \text{PEACH}
\]

\[
$0 + 0.96\lambda_1 + 0\lambda_2 = 0.96\lambda_1 \quad \text{Usual Care}
\]

\[
0.96\lambda_1 = \$1,027 + 0.24\lambda_2
\]

\[
\lambda_1 < 0.25\lambda_2 + \$1,068 \quad \text{Usual care}
\]

\[
\lambda_1 > 0.25\lambda_2 + \$1,068 \quad \text{PEACH}
\]

McCaffrey et al. 2011, 2015
Efficiency frontier in cost-disutility space

Incremental cost relative to the cheapest strategy (AUS$)

Placebo (52.2%, 0%, $0)

Dexamethasone (0%, 17.0%, $25.20)

Megestrol (6.8%, 12.8%, $291.50)

Additional proportion of patients without appetite improvement relative to the most effective strategy (%)

Additional proportion of patients with oedema relative to the most effective strategy (%)
Threshold regions

- Placebo is the preferred option when \( \lambda_2 = $13,357 \)
- Megestrol is the preferred option
- Dexamethasone is the preferred option when \( \lambda_1 = $4,398 \)