Evaluating cost effectiveness of alternative blood safety scenarios:

the search for tools that have traction

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TerumoBCT

Macopharma
Outline

**COST**
- Budget Impact Analysis
- Lifetime Cost Analysis
- Net Monetary Benefits (NMB)

**EFFECTIVENESS**
- Adverse events averted or prevented
- Residual risk
- Number needed to treat (NNT)
  - NNB
  - NNT
- Risk:Benefit ratio
- Net Health Benefits (NHB)
- Utility

**COST : EFFECTIVENESS**
Priority Setting/Decision Making in Health

1) Cost alone
2) Capacity of beneficiaries to pay
3) Cost-effectiveness
4) Horizontal equity (equality)
5) Vertical equity (priority)
6) Adequate demand
7) Public attitudes and expectations
8) Public good?
9) Yields externalities

Muscrove, Health Policy, 1999
Health Economics – ABO RBDM
Consensus Blood Safety Recommendations

Budget Impact Analysis

• Costs that accrue or are expected to accrue when an intervention is implemented
  • Results in terms of the costs incurred or saved by adopting an intervention from the standpoint of the budgeting authority or health care decision-maker.

Cost Effectiveness (Utility) Analysis

• Value gained for resources spent
  • Value for money is assessed in terms of cost per quality-adjusted life-year (QALY) gained or disability-adjusted life-year (DALY) lost.
Cost Analyses

• Many different methodologies

• To implement most new interventions requires additional health care expenditures
  – Rarely a new intervention saves the health care system more than it costs to implement
  • Even in this scenario the issue is one of net savings to the overall health care system and almost never one of direct budget savings to those who implement the intervention

• We should be advocates for interventions that generate net health savings (so long as they have net positive effectiveness)

• Most interventions don’t achieve this so we have to assess if the net effects are worth the cost
Economic Evaluation and Modeling

1) Cost-effectiveness analysis provides the clearest way to promote value for money in health

2) Involves comparative analysis of alternative courses of action

3) Informs key areas requiring additional knowledge/research

5) Assumes scarcity exists and choices have to be made between what to and what not to buy

In blood safety these analyses need reliable data on:

“Real” transmission risks, Epidemiology and recipient characteristics (age, survival, infectious diseases, vaccination, etc), Disease progression, Local treatment costs, etc.
Expressing Effectiveness
Number Needed to Treat (NNT)

- NNT is a measurement of the impact of an intervention. It is the number of patients that need to be treated in order to have an impact on one person.
  \[
  = \frac{100}{\text{Absolute Risk Reduction}} = \text{NNT}
  \]

- NNTB – number needed to treat to benefit or NNB
  - Calculated for something with positive health impact

- NNTH – number needed to treat to harm or NNH
  - Calculated for something with a negative health impact, such as a risk factor for disease or adverse effect of an intervention
Absolute risk reduction (ARR) instead of relative risk reduction (RRR)

90% do not die regardless of intervention

8% die regardless of intervention

2% avoid death

Adapted from http://www.thennt.com/thennt-explained/
NNB Common Clinical Event Rates

**Number Needed to Treat**

Calculates the NNT to prevent one additional adverse outcome

**Study Outcome**

<table>
<thead>
<tr>
<th>Group 1 Incidence (Control Group)</th>
<th>Group 2 Incidence (Experimental Group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 %</td>
<td>.0000 %</td>
</tr>
</tbody>
</table>

**RESULTS**

NNT/NNH 100

On average, 100 patients would have to receive experimental treatment (instead of control treatment) for one additional patient to NOT have the study outcome.

**Equations**

\[
ARR = (Control \ event \ rate) - (Experimental \ event \ rate)
\]

\[
ARR = 0.01 - 1E - 07 = 0.0099999
\]

\[
NNT = 1/ARR = 1/0.0099999 = 100
\]

Number Needed to Treat

Calculates the NNT to prevent one additional adverse outcome

Study Outcome

Group 1 Incidence (Control Group)

Group 2 Incidence (Experimental Group)

On average, 111111.1 patients would have to receive experimental treatment (instead of control treatment) for one additional patient to NOT have the study outcome.

Equations

\[
ARR = (\text{Control event rate}) - (\text{Experimental event rate})
\]

\[
ARR = 1E - 05 - 1E - 06 = 9E - 06
\]

\[
NNT = \frac{1}{ARR} = \frac{1}{9E - 06} = 111111.1
\]

## Explicitly Estimated WTP in Different Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Estimated* or Assumed WTP per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>£23,000*</td>
</tr>
<tr>
<td>Australia</td>
<td>AU$64,000*</td>
</tr>
<tr>
<td>Netherlands</td>
<td>€40,000</td>
</tr>
<tr>
<td>USA</td>
<td>US$62,000*</td>
</tr>
<tr>
<td>Japan</td>
<td>JPY 5 million*</td>
</tr>
</tbody>
</table>

*Health Econ. 2010 Apr;19(4):422-37
Social Value, Expectations and Cost/QALY Willingness to Pay for Health Care Interventions

Higher incremental Cost per QALY

Lower social value

B

Higher social value

A

Lower incremental Cost per QALY

C

B

A

C

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Results Reporting – Cost & Consequences Table

The cost-effectiveness ratio (CER), incremental cost-effectiveness ratio (ICER), cost-effectiveness acceptability curves (CEAC) or other summary measures are final interpretations that only have meaning if disaggregated costs and effects are provided.

Table 3. Costs, effects and incremental cost-utility of competing strategies for PRT in Poland

<table>
<thead>
<tr>
<th></th>
<th>Current screens</th>
<th>Versus P-PRT (reference case)</th>
<th>Versus PP-PRT</th>
<th>P-PRT versus PP-PRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs, PLN</td>
<td>53.69</td>
<td>90.15</td>
<td>113.63</td>
<td></td>
</tr>
<tr>
<td>Total effects, QALY</td>
<td>7.5970195</td>
<td>7.5970339</td>
<td>7.5970610</td>
<td></td>
</tr>
<tr>
<td>Incremental costs, PLN</td>
<td>36.46</td>
<td>59.94</td>
<td>23.48</td>
<td></td>
</tr>
<tr>
<td>Incremental effectiveness, QALY</td>
<td>0.0000143 (7.5)</td>
<td>0.0000414 (21.7)</td>
<td>0.0000271 (14.2)</td>
<td></td>
</tr>
<tr>
<td>ICER, PLN/QALY*</td>
<td>2,595,000</td>
<td>1,480,000</td>
<td>883,000</td>
<td></td>
</tr>
<tr>
<td>95% CI approximation*</td>
<td>1,801,000–3,672,000</td>
<td>1,032,000–2,121,000</td>
<td>621,000–1,238,000</td>
<td></td>
</tr>
<tr>
<td>ICER, EUR/QALY*</td>
<td>610,000</td>
<td>348,000</td>
<td>208,000</td>
<td></td>
</tr>
<tr>
<td>ICER, PPP$/QALY*</td>
<td>1,380,000</td>
<td>787,000</td>
<td>470,000</td>
<td></td>
</tr>
</tbody>
</table>

*ICER values and credible intervals rounded to the nearest thousand.
QALY = quality-adjusted life years (converted to QALM = quality-adjusted life minutes); P-PRT = plasma PRT; PP-PRT = platelets and plasma PRT; PPP$ = adjusted to USD using purchasing power parities index (1.86 for the country of Poland in 2009).
From Cost-effectiveness to Net Benefits

\[
\text{ICER} = \frac{\text{Cost}_A - \text{Cost}_B}{\text{Outcome}_A - \text{Outcome}_B}
\]

If the incremental cost is positive and the incremental effect is negative (NW quadrant), the intervention is unequivocally not cost-effective (it is dominated, achieving poorer outcomes at higher cost).

\[
\lambda = \frac{\Delta \text{Cost}}{\Delta \text{Outcomes}}
\]

If the incremental cost is negative and the incremental effect is positive (SE quadrant), the intervention is unequivocally cost-effective (it is dominant, achieving better outcomes at lower cost).
From Cost-effectiveness to Net Benefits

If both the incremental cost and the incremental effect are negative (SW quadrant) or both the incremental cost and the incremental effect are positive (NE quadrant) no unequivocally statements can be made.

Determining whether the intervention is cost-effective depends on a threshold value ($\lambda$), defined as the maximum amount society is willing to pay for an incremental health gain or, equivalently, as the minimum amount society is willing to accept for foregoing an incremental health gain.

Net Monetary Benefits (NMB) = $\lambda \times \Delta \text{Outcomes} - \Delta \text{Cost}$

Net Health Benefits (NHB) = $\Delta \text{Outcomes} - \frac{\Delta \text{Cost}}{\lambda}$

The incremental net benefit (regardless of the scale) provides an unambiguous decision rule, although this implies knowledge of the threshold value ($\lambda$), which has been a subject of considerable debate.
## Net Monetary Benefits

<table>
<thead>
<tr>
<th>NMB (€)</th>
<th>Δ Effectiveness</th>
<th>Threshold Value (λ)</th>
<th>Δ Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>400</td>
<td>0.01</td>
<td>50000</td>
<td>100</td>
</tr>
<tr>
<td>-97.5</td>
<td>0.00005</td>
<td>50000</td>
<td>100</td>
</tr>
<tr>
<td>-50</td>
<td>0.00005</td>
<td>10000000</td>
<td>100</td>
</tr>
<tr>
<td>4900</td>
<td>0.005</td>
<td>10000000</td>
<td>100</td>
</tr>
<tr>
<td>4995</td>
<td>0.005</td>
<td>10000000</td>
<td>5</td>
</tr>
</tbody>
</table>
# Net Health Benefits

<table>
<thead>
<tr>
<th>NHB (QALYs)</th>
<th>– Δ Costs</th>
<th>Threshold Value (λ)</th>
<th>Δ Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0075</td>
<td>-100</td>
<td>500000</td>
<td>0.01</td>
</tr>
<tr>
<td>-0.00195</td>
<td>-100</td>
<td>500000</td>
<td>0.00005</td>
</tr>
<tr>
<td>-0.00005</td>
<td>-100</td>
<td>10000000</td>
<td>0.00005</td>
</tr>
<tr>
<td>0.004900</td>
<td>-100</td>
<td>10000000</td>
<td>0.005</td>
</tr>
<tr>
<td>0.004995</td>
<td>-5</td>
<td>10000000</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Net Monetary Benefits for PRT

Willingness to Pay (€/QALY)

-15,000 € - 10,000 € - 5,000 € 0 € 5,000 € 10,000 € 15,000 € 20,000 € 25,000 € 30,000 €

40,000 250,000 500,000 750,000 1,000,000

PLSM v CS  PLT&PLSM v CS  PLT&PLSM v PLSM

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Net Benefits Framework

• Willingness to pay: Using the ICER method the role of WTP is often opaque. Using the NMB method the analysis is entirely descriptive and allows the decision maker to identify their preferred option based on their own explicit WTP threshold.

• Impact of cost and effect on uncertainty: NMB analysis reveals that costs have a relatively larger impact on CE results at low WTP values (due to the NMB line shifting up or down). However, at high WTP values changes in effectiveness have a relatively larger impact on CE results (due to the magnified effect of changes in slope on NMB at high WTP values).
Objective: To compare the cost-utility of HIV, HBV and HCV donation screening in a list of countries with similar HDIs.

Participants: Australia, Canada, Denmark, Finland, France, Netherlands, UK, USA

- Are patterns of similar cost-effectiveness/utility ratios evident?
- What aspects may exhibit substantial differences?
- Are there broader patterns with respect to blood safety for HIV, HBV, and HCV that can be discerned?
## ABO Project Results: Cost and Consequences

<table>
<thead>
<tr>
<th>Country</th>
<th>QALYs gained</th>
<th>Net Costs ($ x 1000)</th>
<th>Cost-utility ratio ($ x 1000 per QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sero</td>
<td>Sero + NAT</td>
<td>Sero</td>
</tr>
<tr>
<td>Country A</td>
<td>1.37</td>
<td>1.38</td>
<td>178</td>
</tr>
<tr>
<td>Country B</td>
<td>2.97</td>
<td>2.98</td>
<td>-23</td>
</tr>
<tr>
<td>Country C</td>
<td>3.14</td>
<td>3.16</td>
<td>223</td>
</tr>
<tr>
<td>Country D</td>
<td>3.62</td>
<td>3.63</td>
<td>160</td>
</tr>
<tr>
<td>Country E</td>
<td>3.74</td>
<td>3.75</td>
<td>65</td>
</tr>
<tr>
<td>Country F</td>
<td>4.73</td>
<td>4.75</td>
<td>78</td>
</tr>
<tr>
<td>Country H</td>
<td>6.88</td>
<td>6.89</td>
<td>-52</td>
</tr>
<tr>
<td>Country G</td>
<td>9.03</td>
<td>9.08</td>
<td>1</td>
</tr>
</tbody>
</table>
Net Health Benefits of Combined Serology + NAT per 100,000 Donations Screened

- Country A
- Country B
- Country C
- Country D
- Country E
- Country F
- Country G
- Country H

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COST : EFFECTIVENESS

• Small adverse event rates are best assessed by number needed to treat

• The WTP for blood safety interventions in any setting remains unanswered by formal assessment

• Costs of interventions are most relevant near traditional WTP threshold values

• Small adverse event rates drive cost-effectiveness at higher WTP values
Summary

• CEA contributes information for blood safety decision making by establishing a common denominator
  • Across diseases ★
  • Across settings (much harder to achieve because of different WTP thresholds)
• Can be used to choose between competing alternatives
  • There remain no good examples for this in blood safety
  • Analyses are usually seen (in error) as independent from one another
• The ICER model may not be the appropriate analytical perspective for blood safety
  • Budget Impact
  • Net Benefits Framework and WTP
Thank you for your attention

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Economic Evaluation and Modeling

- Basic model comparing 2 interventions

$$\text{ICER} = \frac{\text{Cost}_A - \text{Cost}_B}{\text{Outcome}_A - \text{Outcome}_B}$$

- Cost-Effectiveness and Utility vs. Cost-Benefit

- Threshold considerations
  - US$50,000/quality-adjusted life year
  - WHO suggests: 3 x GDP ($120k/QALY for US)
  - Interaction between cost-effectiveness, disease burden, available funds, and other factors

- Capturing influential parameters and uncertainty
  - 1-way
  - Probabilistic (Monte Carlo simulation)
Net Benefits Framework

• Decision making: The net benefit method simplifies the decision making process by rendering it a simple maximization problem. This makes identifying the cost-effective option conceptually more straightforward than under the ICER method where a decision maker must identify the greatest ICER with a value below their WTP threshold.

• Multiple comparator analyses: There is no need to rank order options or to eliminate dominated and extendedly-dominated options in conducting a CE analysis. With the net benefit method, a CE analysis consists of calculating NMB for all options plotted across a range of reasonable WTP values.

• Ability to rank CE of options: The NMB method allows options to be easily ranked at a given WTP threshold from most cost-effective to least cost-effective. This may be particularly useful when some options included in an analysis are not available in a particular geographic region or when it is necessary to offer providers and patients treatment alternatives.