Bridging Health Technology Assessment (HTA) with Multi Criteria Decision Analysis (MCDA), Values and Ethics for Complex Decisions: Case Study of Growth Hormone for Turner Syndrome

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Acknowledgments

Panel
- Mary Edwards, Turner Syndrome Society of Canada
- Jack Holland MD, McMaster University
- Philip Jacobs PhD, University of Alberta, Institute of health Economics
- Sheila Kelton RN, British Columbia Children’s Hospital
- Farid Mahmud MD, University of Toronto
- Shayne Taback MD, University of Manitoba
- Guy Van Vliet MD, Ste Justine University Hospital Center

Web prototype
- Peter Melnyk PhD and Patricia Campbell BSc, BioMedCom Consultants

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Context and Framework

- Transparent access to evidence and value judgments on which decisions are made
- Limitations of cost-effectiveness (e.g. disease severity not included)

EVIDEM framework
- consider all components of decision
- inform each component of decision consistently
- communicate decisions transparently

Enhance understanding and implementation of decisions

Tunis SR. Health Affairs. 2007 (26): w500-w515.
Drummond IIJTAHC 2008;9:43.
Components of Decision

Quantifiable (intrinsic value)

Quality of evidence
• Adherence to requirements of decisionmaking body
• Completeness and consistency of reporting evidence
• Relevance and validity of evidence

Disease impact
• Disease severity
• Size of population affected by disease

Intervention
• Clinical guidelines
• Comparative intervention limitations
• Improvement of efficacy/effectiveness
• Improvement of safety and tolerability
• Improvement of patient reported outcomes
• Public health interest (e.g., prevention, risk reduction)
• Type of medical service (e.g., symptom relief, cure)

Economics
• Budget impact on health plan (cost of intervention only)
• Impact on other spending (e.g., hospitalization, disability)
• Cost-effectiveness of intervention

Non-quantifiable (extrinsic value)

Ethical framework
• Goals of healthcare - utility
• Opportunity costs - efficiency
• Population priority & access - fairness

Other components
• System capacity and appropriate use of intervention
• Stakeholder pressures
• Political/historical context

⇒ Extrinsic Value Tool

*Goetghebeur et al. BMC Health Serv Res 2008; 8:270.
Objective

- Test and further develop the framework using a complex case study
- Growth hormone in Turner syndrome

- Used to augment height
- Expensive hormone injections
- Treatment over long time periods

Growth in Turner Syndrome

- Adult women = 163 cm
- Women with Turner Syndrome = 143 cm
Methods

Extrinsic value
Extrinsic Value Tool
Step 3 – Consider impact on value

Intrinsic value
MCDA Value Matrix
Step 1 - Weights
Step 2 - Scores

Validated HTA Report
(web based)

Evidence available
Literature review

Synthesized evidence
Standardized methodology

Quality assessment
Quality Matrix instruments
- Consistent critical analysis (clinical, PRO, economic, epidemiology)

Discussion

Panel of stakeholders

Investigators & experts

- Peer-reviewed literature
- HTA reports
- Registries
- Cochrane reviews
- Disease Association
- Other relevant resources

Validated HTA Report
- Investigators & experts
- Panel of stakeholders

Framework tools available from EVIDEM Collaboration - www.evidem.org
Data Analyses

- **MCDA value estimate**: linear model [sum of value contribution ($V_x$) of combined normalized weights ($W_x$) and scores ($S_x$) for components ($n$) of the matrix]

\[ V = \sum_{x=1}^{n} V_x = \sum_{x=1}^{n} \left( \frac{W_x}{\sum_{x=1}^{n} W_x} \cdot S_x \right) \]

- **Agreement at individual level**: Intra-class correlation coefficients (ICC) between:
  - Test: during panel session
  - Retest: web interface (Tikiwikiv2.0 - MySQL database)
Step 1: Weighting MCDA components

Panelists assess their own values by weighting the relative importance of each component of decision.
## Step 2: Scoring the intervention (MCDA)

Using the HTA report fed into the MCDA Value Matrix, panelists assign scores to each component of decision

### Instructions
- Assign a score to each component based on data available (details and references on web site).

### Step 2: Scoring intervention

<table>
<thead>
<tr>
<th>Components</th>
<th>Highly synthesized information</th>
<th>Scoring of Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quality of evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 Adherence to requirements of decision-making body</td>
<td>Not applicable for case study</td>
<td></td>
</tr>
<tr>
<td>Q2 Completeness and consistency of reporting evidence</td>
<td>Quality scores: Epidemiology: 75% limited statistical information; Clinical data: 75% limited reporting of SE; PRO: 60% incomplete reporting of questionnaire items; Economic evaluation: 75% some model features unclear; Budget impact: 75% no sensitivity analysis reported</td>
<td>Many gaps, inconsistent</td>
</tr>
<tr>
<td>Q3 Relevance and validity of evidence</td>
<td>Quality scores: Epidemiology: 50% study in one Canadian hospital with small sample size; Clinical data: 75% uncertainty on final height gain; high attrition rate in key RCT; PRO: 50% interim analysis of a subset of participants to a non blinded RCT; Economic evaluation: 50% questionable outcomes - cost per cm of final height, no adverse events costs, weak utility data; Budget impact 50% assuming all Canadian girls treated based on prevalence data</td>
<td>Low relevance/validity</td>
</tr>
</tbody>
</table>

### Disease impact

<table>
<thead>
<tr>
<th>D1 Disease severity</th>
<th>Prevalence: 1 in 25,000 female adults</th>
<th>Very severe: GHD treatment is considered</th>
<th>Very severe: Not severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2 Size of population</td>
<td></td>
<td></td>
<td>0 □ 1 □ 2 □ 3 □</td>
</tr>
</tbody>
</table>

### Intervention

| I1 Clinical guidelines | | | |
|------------------------|-------------------|-------------------|
| | International guidelines: Consider GHD treatment as seen as growth failure is demonstrated and potential side effects have been discussed with patient/family. Treatment until satisfactory height is reached | Not recommended | Strong recommendation 0 □ 1 □ 2 □ 3 □ |
| I2 Comparative interventions | There is no other therapeutic intervention indicated to treat short stature in Turner syndrome | No or very minor | Major limitations 0 □ 1 □ 2 □ 3 □ |
Step 2: Scoring the intervention (MCDA)

Scores reflect the performance of the intervention for each component of decision

Scoring of Intervention

Q1  Adherence to requirements of decisionmaking body
Q2  Completeness and consistency of reporting evidence
Q3  Relevance and validity of evidence
D1  Disease severity
D2  Size of population affected by disease
I1  Clinical guidelines
I2  Comparative interventions limitations
I3  Improvement of efficacy/effectiveness
I4  Improvement of safety & tolerability
I5  Improvement of patient reported outcomes
I6  Public health interest
I7  Type of medical service
E1  Budget impact on health plan
E2  Cost-effectiveness of intervention
E3  Impact on other spending

Not available for workshop

Mean Score (±SD)

Scoring of intervention

Low  High
**MCDA Value Estimate**

Combination of weights and scores provides a comprehensive evaluation of the intervention

For an intervention to achieve close to 100% on this scale, it would have to cure a severe endemic disease, demonstrate a major improvement in safety, efficacy and PRO compared to limited existing approaches, and result in major healthcare savings.

An intervention that scores low would be for a rare disease that is not severe, with limited data showing small improvement in efficacy & major safety and PRO issues over existing alternatives, & resulting in major increases in healthcare spending.

Retest data  
**MCDA estimate: 40%**  
Good agreement at individual level (ICC: 0.687)
Step 3: Consideration of extrinsic components

Using the HTA report fed into the Extrinsic Value Tool, panelists assess the impact of each component on the value of intervention.

### Step 3: Consider impact of extrinsic components

<table>
<thead>
<tr>
<th>Ethical framework*</th>
<th>Highly synthesized information*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goals of healthcare — utility*</td>
<td>Goal of healthcare is to maintain normal functioning which may be impaired by very short stature. Goals of GH treatment are to promote growth and improve psychosocial adaptation of individual with short stature. However, psychosocial functioning of individuals with short stature is largely indistinguishable from their peers.</td>
<td></td>
</tr>
<tr>
<td>Opportunity cost—efficiency*</td>
<td>Considering maximizing impact on health for a given level of resources at; Patient level: resources allocated to GH treatment may be more beneficial if allocated to other interventions such as psychological support to cope with condition overall (not just short stature); Society level: Significant cost/benefit but small population.</td>
<td></td>
</tr>
<tr>
<td>Population priority &amp; access — fairness*</td>
<td>Prioritize worst off: applicable to patients with Turner Syndrome but maybe not to the short stature part of the disease, daily but probably not improved with daily injections for several years, but maybe as adult with less short stature than without treatment. Treat like cases similarly: should we treat differently short stature due to disease or due to genes? Access to care/treatment easier in big cities where specialists are available</td>
<td></td>
</tr>
</tbody>
</table>

### Other components

| System capacity and appropriate use of intervention | Optimal age for initiation of treatment has not been established. Appropriate follow up requires the intervention of skilled healthcare professionals. In Canada, any physician can prescribe GH; some of the provinces that reimburse GH require it be prescribed by an endocrinologist. | |
| Stakeholder pressures | Potential pressures from parents, from insurance, industry? Social pressure on short stature? | |
| Political/ historical context | | |
| Other components to consider | | |

*Ethical framework based on three principles: when conflicting principles, clearly identify trade-offs and legitimize decision by engaging a broad range of stakeholders & explaining decision; legitimizing decision is key to provide accountability for reasonableness.
Step 3: Consideration of extrinsic components

- **Negative impact on value**
  - Weak evidence linking increased height and personal gain (utility)
  - More value may be derived from other interventions (efficiency)
  - Risk of inappropriate use in toddlers
  - Stakeholder pressure

- **Positive impact on value**
  - Prioritize worst off patients (fairness)

  **Overall value:** Striking a balance
Outcomes

- Systematization of judgment
- Identification of bias
- Defining research questions
- Transparency (evidence and values)
- Comprehensive measure of intervention (step beyond cost-effectiveness)
- Web access to validated, synthesized information

Applications

- Decision-making/priority setting
- Knowledge transfer
- Communication
- Planning
Future Developments

- Collaborative studies
  - Field testing
  - Methodological validation

- Web collaborative registry (long term)
- Interactive prototypes

Optimize resources, decisions and health

Thank you