University of Colorado Contributions to ICER Reports; What’s Next for U.S. Value Assessment?

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Outline

• Mathematics warm-up and Motivation
• U of Colorado contributions to Institute for Clinical and Economic Review (ICER) reports
• U.S. Coverage and Reimbursement Patterns
• Can additional quantitative decision aids advance the science of U.S. value assessment?
Mathematical Relationships

• What is the relationship between the area of a perfect square (with side length $= N$, where $N$ is any whole number) and the area of a rectangle with side lengths $N-1$ and $N+1$?

• Claim: The area of the perfect square equals the area of rectangle plus 1.
  – Visual (partial) proof
  – Algebraic proof
Visual Proof

• For illustration purposes, suppose $N = 6$
Visual Proof

- Area of perfect square = \( N \times N = 36 \)
Visual Proof

• How do we manipulate the perfect square to approximate the rectangle with sides N-1 and N+1?
Visual Proof

- The area of the perfect square is one more than the area of the rectangle with sides \(N-1\) and \(N+1\)

\[N - 1 = 5 \quad \text{and} \quad N + 1 = 7\]
Algebra Proof

• Claim: The area of the perfect square (sides N x N) equals the area of the rectangle (sides N-1 x N+1) plus 1.

• Does N x N = (N-1) x (N+1) +1

• \[ N^2 = N^2 + N - N - 1 + 1 \]

• \[ N^2 = N^2 \text{ Q.E.D.} \]
Motivation

• Claim 1. Value = \( \frac{\Delta \text{Cost}}{\Delta \text{QALY}} \) (i.e. traditional cost-effectiveness) alongside a cost-effectiveness threshold

• Claim 2. If value is synonymous with cost-effectiveness in the U.S. and we have value-based system(s), then we should observe a tight clustering of cost-effectiveness for commonly prescribed (and paid) medicines.
Claim 2 does not hold

- Of 25 commonly prescribed CVD drugs, 5 (20%) had cost-effectiveness findings above commonly cited thresholds.

Claim 2 does not hold

- Hazard ratios are flat over time (HRs are less favorable for active comparator trials)
- Annual drug prices increase over time (prices are higher for active comparator trials)
- *Claim 1, value = cost-effectiveness, needs further investigation*

CU Contributions to ICER reports

• Cost-effectiveness evidence for:
  – asthma biologics (2 reviews);
  – rheumatoid arthritis targeted immune modulators;
  – ovarian cancer PARP inhibitors;
  – B-cell malignancy chimeric antigen receptor t-cell (CAR-T) therapies
  – endometriosis (elagolix);
  – and ongoing assessments in secondary prevention of cardiovascular disease
CU Team

• 3 Faculty
  – Jon Campbell
  – R Brett McQueen
  – Mel Whittington

• PhD grad students

• Other staff have included a professional research assistant and post-doctoral fellow
Economic model team contributions to ICER process

- Month 1
  - ICER announces topic; conversations with stakeholders begin
  - Contribute to draft scope
- Month 2
  - Contribute to final scope posted
  - Data requests drafted for manufacturers and others
- Month 3
  - Contribute to model analysis plan
  - Develop model
  - Join stakeholder calls
- Month 4
  - Present preliminary model to manufacturers and join calls with stakeholders
  - Validate model
  - Contribute to draft evidence report
- Month 5
  - Contribute to finalizing draft evidence report and draft model
- Month 6
  - Respond to public comments
  - Revise contributions to report and model
- Month 7
  - Contribute to finalizing report and model
  - Present economic findings at public meeting
- Month 8
  - Contribute to final report and model
<table>
<thead>
<tr>
<th>Disease State</th>
<th>Therapeutic Options</th>
<th>Comparator</th>
<th>Eligible Population</th>
<th>Incr. QALYs</th>
<th>Incr. Cost-Effectiveness Ratio ($/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>Mepolizumab; Nucala®</td>
<td>Standard of care (SoC) alone.</td>
<td>Individuals ages ≥12 with severe eosinophilic asthma</td>
<td>1.53 / 1.63</td>
<td>$385,546 / $344,000</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Targeted immune modulators (Tocilizimab monotherapy; Actemra®)</td>
<td>Adalimumab monotherapy (Humira®)</td>
<td>Adults with moderately-to-severely active RA and inadequate response to conventional DMARDs.</td>
<td>0.4</td>
<td>Cost saving and increased QALYs</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>PARP inhibitors (Olaparib; Lynparza®)</td>
<td>Placebo (i.e. observation only).</td>
<td>Adult women with platinum-sensitive ovarian cancer; with complete or partial response to the most recent regimen and candidates for maintenance therapy.</td>
<td>0.59</td>
<td>$324,116</td>
</tr>
<tr>
<td>B-Cell Lymphoma</td>
<td>CAR-T (Axicabtagene ciloleucel; Yescarta®)</td>
<td>Chemo-therapy (from SCHOLAR-1) for the treatment of DLBCL.</td>
<td>Adults ages ≥18 with relapsed/refractory B-cell lymphoma after two or more lines of systemic therapy.</td>
<td>3.4</td>
<td>$136,078</td>
</tr>
</tbody>
</table>

https://icer-review.org/topics/
Are ICER voting panels basing value votes on cost-effectiveness?

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• ICER devotes a section of their reviews to “Potential Other Benefits and Contextual Considerations” including domains with yes/no votes from the panel

• Criteria influencing value votes include:
  – cancer
  – ultra-rare diseases
  – reduced caregiver burden
  – improved productivity
  – disease severity
  – lack of evidence
  – uncertain benefits compared to alternatives
  – safety concerns

Should we tinker with the threshold rather than incremental analyses?

Value-Based Pricing for Emerging Gene Therapies: The Economic Case for a Higher Cost-Effectiveness Threshold

Louis P. Garrison, PhD; Tristen Jackson, PharmD, MS; Douglas Paul, PharmD, PhD; and Mike Kenston, BS, MBA

• Health Technology Assessment
  – Ultra-rare, value of statistical life (up to $500k/QALY)
• Method Approaches
  – Opportunity cost, 3x GDP ($20k to $180k/QALY)
• Technology Examples (wide range)

Garrison LP et al. J Manag Care Spec Pharm. Published online February 19, 2019
What about U.S. coverage and reimbursement patterns?

- Summarize the U.S. coverage of therapies CU team has contributed to ICER reviews and compare coverage with cost-effectiveness
  - Preferred (with or without prior authorization or step therapy)
  - Covered but not preferred (with or without prior authorization or step therapy)
  - Not covered
Mepolizumab; Nucala®

$344,000/QALY

Insurance Type

Percent of Plans

CATEGORY
- PREFERRED
- PREFERRED (PA/ST)
- COVERED
- COVERED (PA/ST)
- NOT COVERED
Tocilizumab; Actemra®
Dominates Humira® (lower cost and higher QALY)
Adalimumab; Humira®
Dominated by Actemra® (higher cost and lower QALY)
Olaparib; Lynparza®

$324,000/QALY
Axicabtagene ciloleucel; Yescarta®

$136,000/QALY
Claims Revisited

• Health systems that strive to achieve good value will be more efficient
• Coverage heterogeneity across plans suggests different evidence weights
  – U.S. Coverage decisions are evidence-based, but what evidence and what weights?
• Cost-effectiveness is not synonymous with U.S. view of value but is a good starting point
  – $5,000/QALY vs. $50,000/QALY vs. $500,000/QALY vs. $5,000,000/QALY
Hypothesis

• Additional quantitative decision aids, namely multicriteria decision analysis (MCDA), will advance the science of value assessment to guide coverage and reimbursement decision making.
  – MCDA explicitly evaluates multiple (conflicting) criteria in decision making.
  – MCDA offers a promising compliment to traditional value assessment by explicitly weighting and including multiple value components outside the cost-per-QALY metric.
pValue Center of Excellence collaborators, objectives, and outreach

**Collaboration**
- Syreon Research Institute
- Real Endpoints
- Data Science to Patient Value

**pValue Objectives**
- Advance understanding of therapy value with MCDA and stakeholder engagement

**Methods**
- Multicriteria decision analysis
- Stakeholder engagement
- Traditional cost-effectiveness analysis

**Deliverables**
- MCDA methods review paper
- US MCDA pilot tool
- Payer case value rankings
- Plan member case rankings

**Outreach**
- Value Assessment Frameworks
- Health Plans (Payers)
- Plan Members

**Advances**
- Multicriteria decision analysis
- Stakeholder engagement
- Traditional cost-effectiveness analysis

**Deliverables**
- MCDA methods review paper
- US MCDA pilot tool
- Payer case value rankings
- Plan member case rankings
Conclusions

• Cost-effectiveness is not the full picture of value but remains a starting point for value assessment
  – Math continues to help us solve problems
  – Definitions and intent of analyses are critical for interpretation and use

• ICER and others are working to advance the field of value assessment through CEA modifications and CEA compliments

• Let us be constructive in our critiques and continue to test possible solutions
Acknowledgements

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  – Syreon Research Institute
  – Real Endpoints

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