Early Economic Evaluation of Emerging Technologies: A Systematic Review

Toronto Health Economics and Technology Assessment
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www.theta.utoronto.ca
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Outline

1. Background
2. Objectives
3. Methods
4. Preliminary results
5. Discussion
6. Limitations
7. Next steps
Background
Health System Challenges

- Sustainability
  - Technologies drive cost upward
- Technological innovations can
  - improve health
  - drive economic growth and employment.
Technological Innovations

• Infrequently discovered
  • 1 approved medicine per 5000 screened compounds

• Development process is slow and costly
  • Average ~ 9 years,
  • ~800 million for a new medicine
## Development Plan

<table>
<thead>
<tr>
<th>Phase</th>
<th>Clinical data</th>
<th>Economic Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-clinical studies</td>
<td>Key mechanism of action, biological impacts ➔ Developing the <strong>indication</strong> (e.g., PICO)</td>
<td>Costs and health consequences of the <strong>effectiveness gap(s)</strong> in current practice, maximum attainable price</td>
</tr>
</tbody>
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## Development Plan

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<td>Costs and health consequences of the effectiveness gap(s) in current practice, maximum attainable price</td>
</tr>
<tr>
<td>Clinical research</td>
<td>Phase I: e.g., dose range, side effects&lt;br&gt;Phase II: e.g., dose response, side effects&lt;br&gt;&lt;i&gt;Phase III: clinical benefits, harms&lt;/i&gt;</td>
<td>Phase I-II: Likely cost-effectiveness of the emerging technology</td>
</tr>
</tbody>
</table>
Go/No-Go Decisions

• What is the cost-effectiveness of the emerging technology once it is fully developed?
  • How much would payers be willing to pay for the final product?
• Given what we know now, is it worth investing in the next phase?
Economic Evaluation To Inform Go/No-Go Decisions

- Expected cost-effectiveness ratio of the technology relative to the best alternative.

- Expected monetary value of additional evidence, given what we know now.
Proponents of Early Evaluation

• Assessment **should** be conducted early, and updated often
  • e.g., Ijzerman et al. 2011, Hartz et al. 2008, 2009; Sculpher et al. 1997

• To inform product development
  • By manufacturers, developers, inventors, investors

• To inform policy development
  • When public R&D is used to support technology
    • e.g., Early HTA initiatives from governments or academia
    • e.g. UK, Netherlands, Austria, Ontario
Empirical Questions

• Why is an evaluation needed early?

• Can early evaluation contribute to decision-making for product and policy development?

• When is the optimal timing of early EE?
  • Too early, too much uncertainty
  • Too late, results may not be useful
Objective

• To conduct a systematic review of early economic evaluation of emerging technologies.
Methods
Inclusion Criteria

• Economic evaluation study
  • Compares costs, health outcomes of alternatives
• Regulated health technologies
  • e.g., pharmaceuticals, biologics, high-risk medical devices, biomarkers
• Evaluation must be early
  • Conducted before regulatory approval
• Excluded studies of low-risk medical devices, surgical procedures, health promotion activities.
Systematic Review Conduct

- Literature search of multiple databases
  - MEDLINE, EMBASE, CRD, EconLit.
- Pairs of independent assessors
- Protocol registered with Prospero
  - International Prospective Register of Systematic Reviews
- Protocol submitted to the open-access Journal of Systematic Reviews
Unpublished Studies
Chain-Referral Sampling

Stage 0:
Authors of included studies
Content experts we know
Working in industry
Preliminary Results
## Literature Search Results

<table>
<thead>
<tr>
<th></th>
<th>Medline*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Early EE citations</td>
</tr>
<tr>
<td># EE citations</td>
<td></td>
</tr>
<tr>
<td>Jan. 2010 - March 2013</td>
<td>1,036 (6,804)</td>
</tr>
</tbody>
</table>

**Notes:** EE: economic evaluation.

*We still need to search other databases and unpublished studies.*
Citation Screening

Medline 2010-Current Search n=1036 citations

Economic evaluation?
Not EE: 450

Regulated medical products?
No: 219

Early evaluation?
Not early: 297

Full-text retrieval n=70

Included studies n=14
Searching reference lists n=2
Total included studies: 16
Decision Context

• Who initiated the evaluation?
• Who was the primary target audience?
• Why was an evaluation needed now?
• Answers are not explicitly stated in the included studies.
Characteristics – Funding Sources
(n=16 studies)
Study Characteristics – Country
(n=16 studies)
Health Technologies
(n=16 studies)

- Vaccine
- Therapeutic devices
- Biomarkers
- Pharmaceuticals
- Diagnostic devices

Chart showing the distribution of studies for each category.
Timing of Early Evaluation
(n=16 studies)

Phase I or II trials
Post-marketing (ex-post early evaluation)
Pre-clinical trial
Evaluation Type
(n=16 studies)
<table>
<thead>
<tr>
<th>1st Author</th>
<th>Data Sources</th>
<th>Likely effectiveness estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soares</td>
<td>Literature review, expert opinions, a pilot RCT</td>
<td>Estimate derived from multiple data sources</td>
</tr>
<tr>
<td>Nagelkerke</td>
<td>Related RCT</td>
<td>Estimate derived from related RCT data</td>
</tr>
<tr>
<td>Gaultney</td>
<td>Related RCT</td>
<td>Estimate derived from related RCT data</td>
</tr>
<tr>
<td>Pink</td>
<td>Related RCT</td>
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<tr>
<td>Dempsey</td>
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<tr>
<td>Gold</td>
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</tr>
<tr>
<td>Multinghe</td>
<td>Genetic association studies</td>
<td>Estimates from genetic association studies</td>
</tr>
<tr>
<td>Retel</td>
<td>Selected studies</td>
<td>Estimates from small validation studies</td>
</tr>
<tr>
<td>Biasutti</td>
<td>Selected studies</td>
<td>Estimates from studies of “similar” indication</td>
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<tr>
<td>Postmus</td>
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</tr>
<tr>
<td>Meijboom</td>
<td>Basic research</td>
<td>Estimates based upon immunological characteristics</td>
</tr>
<tr>
<td>Bartha</td>
<td>Literature review</td>
<td>Estimates from studies of “similar” indication</td>
</tr>
<tr>
<td>Lu</td>
<td>Content experts</td>
<td>Estimates from clinical or expert opinions</td>
</tr>
<tr>
<td>Garrison</td>
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</tr>
<tr>
<td>Carrasco</td>
<td>Not reported</td>
<td>Stated estimates without justifications</td>
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Uncertainty-Related Analyses
(n=16 studies)
Can the results address the main study question or objective? (n=16 studies)

Notes: Results are reasonably similar according to • authors • reviewers
Discussion
Key Findings

- < 1% of published EE studies are early evaluation.
  - Early EE may be conducted for internal use only.
- Early evaluation may contribute to decision making, but the decision context is unknown.
Suggestions for Product Development

• Better understanding the decision context of early evaluation
  • Drugs, biologics, medical devices, biomarkers
  • Early evaluation is routine practice for vaccines

• There may be room for better uptake of analytical approaches to early evaluation.
  • Iterative economic evaluation
Suggestions for Policy Development

- Explore the use of early evaluation in public investment decisions
  - Select technologies for early evaluation
  - Design research program to evaluate the new technologies.
Next Steps

• Completing the systematic review
• Chain-referral sampling of content experts working in industry.
  • To obtain unpublished studies, if possible.
  • To survey responders regarding the decision context of early evaluation.
Next Steps

• Conducting a methodological review of decision analytic modeling for early economic evaluation.
  • Collaborating with authors of published studies
Limitations

- Preliminary results
- Final results may be different
  - Unpublished studies
  - Studies from other timeframes
  - Studies from other databases
    - (e.g., European CEA studies in EMBASE)
Questions and Comments
Thank you!