Pre-Market Application of Evidence – the Ontario Experience

Focus the system on a common quality agenda
Build Evidence & Knowledge
Broker Improvement
Catalyze Spread
Evaluate Progress

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Health Technology Life-Cycle Diffusion Curve

- **R&D**: Research and Development
- **Diffusion**: The process of technology adoption
- **Steady State**: A phase where the technology adoption rate stabilizes
- **Evidence & Uncertainty**: Indicating areas of further study
- **Inflection Point**: A critical point in the technology adoption curve
- **Unconditional Yes**: Positive adoption
- **Unconditional No**: Negative adoption
- **Uncertainty**: Areas with ambiguous adoption status
- **Field Study**: Further research needed
What’s wrong with the post market evaluation process?
Barriers to Adoption

Poor pre-market quality clinical trial produce uncertainty

- Accuracy versus clinical utility for diagnostic tests
- No prospective economic analysis
- Research failed to address health system perspectives
- Me-too technologies
- Lack of generalisability
- Inadequate trial design e.g. randomization, concealment, ITT – leading to low quality evidence

Policy including non-affordability, competing pressures
>110 Single Technology Analyses by EDS/MAS, PATH & THETA
92% Conversion to Policy (48% Rejection Rate)
## Uncertainty Drove Field Evaluation Studies

### Recognizing Uncertainty – Effect of GRADE

<table>
<thead>
<tr>
<th>GRADE (Quality of Evidence Following Systematic Review)</th>
<th>Will Further Research Change Confidence in the Estimate?</th>
<th>Level of Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Very unlikely</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>Likely</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Very Likely</td>
<td></td>
</tr>
<tr>
<td>Very Low</td>
<td>Any estimate of effect is very uncertain</td>
<td></td>
</tr>
</tbody>
</table>

**Certainty**

**Uncertainty**
Dealing with Uncertainty – Field Evaluation Studies

- Post-market assessment of technology performance in the real world through primary data gathering
- Improves decision making prior to long-term commitment through appropriate adoption
- Designed to inform policy and funded by government
- Alternative is passive diffusion and intuitive decision making
- Completed 19 and 19 ongoing. Ten CEDs significantly impacted policy decision making and published in peer reviewed journals
Post Market Field Studies – Unpredictability for Policy When Considering Pre-Market Alone

• Inconsistencies between pre and post market performance of certain technologies e.g.
  – CT angiography
  – PET
  – Drug eluting stents

• Consistencies for other technologies e.g.
  – Heart failure clinics
  – Endovascular aortic aneurysm repair
  – Turning q 4 hourly v 2 hourly on alternate foam mattresses

• Is post-market EBA becoming increasingly time-consuming – could this stifle innovation?
Expedited Evidence Processes

- EU – intent to collect clinical evidence before licensing to expedite HTA processes and decisions after licensing. RFP closing June 2013
- FDA priority review - device evaluation prioritized with additional review resources, as needed for devices
  - 1. intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition, and
  - 2. meets at least one of the following:
    - a. breakthrough technology that provides a meaningful advantage over existing technology
    - b. no approved alternative treatment or diagnosis exists
    - c. availability is in the best interest of patients
“Something is Rotten in the State of Denmark”
– Hamlet Act 1, Scene 4

• Does HTA cover the full spectrum of evidence required to inform decision making? (Is HTA passé?)

• How to deal with generalizability/external validity?

• How to deal with low quality evidence from pre-market evaluation of non-drug technologies

• Is there an alternative to post market evaluation of non-drug health technologies?
What is Early HTA?
(Ijzerman and Steuten, 2011)

- Very early HTA:
  - Basic research on mechanisms
- Early HTA
  - Targeting for specific products
  - Proof of principle
  - Prototype product development
  - Phase 1 clinical trials
- Mainstream and Horizon Scanning
  - Phase 2 and 3 clinical trials
  - Coverage and adoption

Pre-Market
Post-Market
Examples of Early HTA (Ijzerman, 2011)

• **Clinical Case Analysis in translational research**
  – Lab-on-a chip technology in current and future healthcare settings (Grob *et al*, 2011).

• **Decision support in product development & market access**
  – Added value of Photoacoustic Mammoscope in breast cancer diagnosis (Hilgerink *et al*, 2011)

• **Patient preferences in medical product development**
  – Next generation neural prosthesis to restore bladder function (Sanders *et al*, 2011)
Analytic Hierarchy Process (AHP) to Elicit User Needs (Pecchia and M. P. Craven, 2012)

- Decision-making method to solve complex problems.
- Quantifies user opinions, based on personal experiences, to design a consistent decision framework.
- Defines a hierarchy of elements prioritized by questionnaires based on pair-wise comparisons.
- Elicits relative importance of each need within its category, the relative importance of each category and of each need compared to all the other individuated.
Life-Cycle Diffusion Curve
(Pre-Market Evidence Based Analysis)

Pre-Market
- Systematic review
- Cost-Effectiveness (CE)

Post-Market
- Systematic review
- Cost-Effectiveness (CE)

R&D
- Efficacy
- Safety
- Value (CE)
- Affordability
- Ethical & societal
- Post market conditions

Uncertainty

Diffusion
Obsolescence

Uncertainty R&D

Efficiency

Unconditional Yes
Unconditional No

HORIZON
DEVELOP
TEST

TIME

Regulation
Key Steps in the EXCITE Process

1. SME and MNE Technologies
2. Apply
3. Review by OHTAC subcommittee
4. Prioritization and Selection by EXCITE Board

- Relevance
- Disruptive potential
- Identify obsolescence
- Magnitude of effect on patient outcomes and system efficiencies
- OHTAC recommendations
- Potential economic benefit
- Stage of readiness
- Feasibility
- Capacity
Key Steps in the EXCITE Process

- SME and MNE Industry
- Review by OHTAC subcommittee
- Prioritization and Selection by EXCITE Board
- *Evaluation by EXCITE Methodological Centres
- MOHLTC and Broader Health System
- Communication re - accrual, safety, and recommendations for improvement
EXCITE Evaluations

Core Evidentiary Bundle:
• Safety + Effectiveness
• Systematic Review
• Economic Analysis

Optional Additional Analyses:
• Assess usability/human factors
• Develop education system for training end users
• Investigate patient preferences
• Analyze factors influencing of uptake
• Develop a registry for tracking post-adoption effectiveness + long-terms safety
• Knowledge transfer

Completed by:
Methodological Centres

Completed by:
Specialized Methodological Centres
EXCITE’s Realities

✓ Increased likelihood of adoption/market uptake
✓ Access to a vast, coordinated network of medical expertise experienced in evaluation of health technologies
✓ Early feedback provides insight during formative stage
✓ Single, harmonized pre-market process

• Duration and cost depends on complexity
• 12-30 months to complete
• Company pays the cost which range from C$1-3 million
• Consideration for defining conditions of adoption pre-market
The EXCITE Scientific Collaborative

Methodological Centres and specialized expertise

CAHO: 24 Academic Hospitals

Ottawa Hospital Research Institute (OHRI)

University of Toronto
Toronto Health Economics and Technology Assessment (THETA)

St. Michael's Hospital:
Academic Health Research Centre, Li Ka Shing Knowledge Institute

Institute for Clinical Evaluative Sciences (ICES)

McMaster University:
- Program for the Assessment of Technologies in Health (PATH)
- Ontario Clinical Oncology Group (OCOG)
  - Dr. Marshall (patient preferences)

University Health Network
- Health Technology Safety Research Team (HTSRT)
- Centre for Innovation in Complex Care (CICC)
EXCITE - Progress in Year One

- Endovascular renal nerve-ablation
- Home based apnoea diagnostic
- Predictive RNA disruption to predict chemotherapy response
- IV infusion delivery not gravity dependent; does not run on electricity or battery
- Rapid recovery from stroke in hand/upper limb
- RTMS system for treatment of refractory depression
- Hand held device to detect pneumothorax and ? Fluid
- Alignment and length of limb following hip replacement
- Fluorescence to detect wound infection at POC
- Remote induced ischemia in treatment of ischemic conditions
EXCITE Leadership Through Partnership

MaRS Board
Richard Ivey (Chair)
Ilse Treurnicht,

EXCITE Chief Scientific Officer
Dr Leslie Levin

Industry: MEDEC (MNEs)
Brian Lewis, Peter Robertson
HTX (SMEs)
John Soloninka, Peter Goodhand

Government: MOHLTC, ADM Vasanthi Srinivasan
MEDI
ADM Bill Mantell

Health System: OHTAC
Charles Wright

Academia: Council of Academic
Karen Michell, Catherine Zahn
Hospitals of Ontario (CAHO)