

# Pre-Market Application of Evidence – the Ontario Experience

Focus the system  
on a common  
quality agenda

Catalyze  
Spread

Build  
Evidence &  
Knowledge

Broker  
Improvement

Evaluate  
Progress

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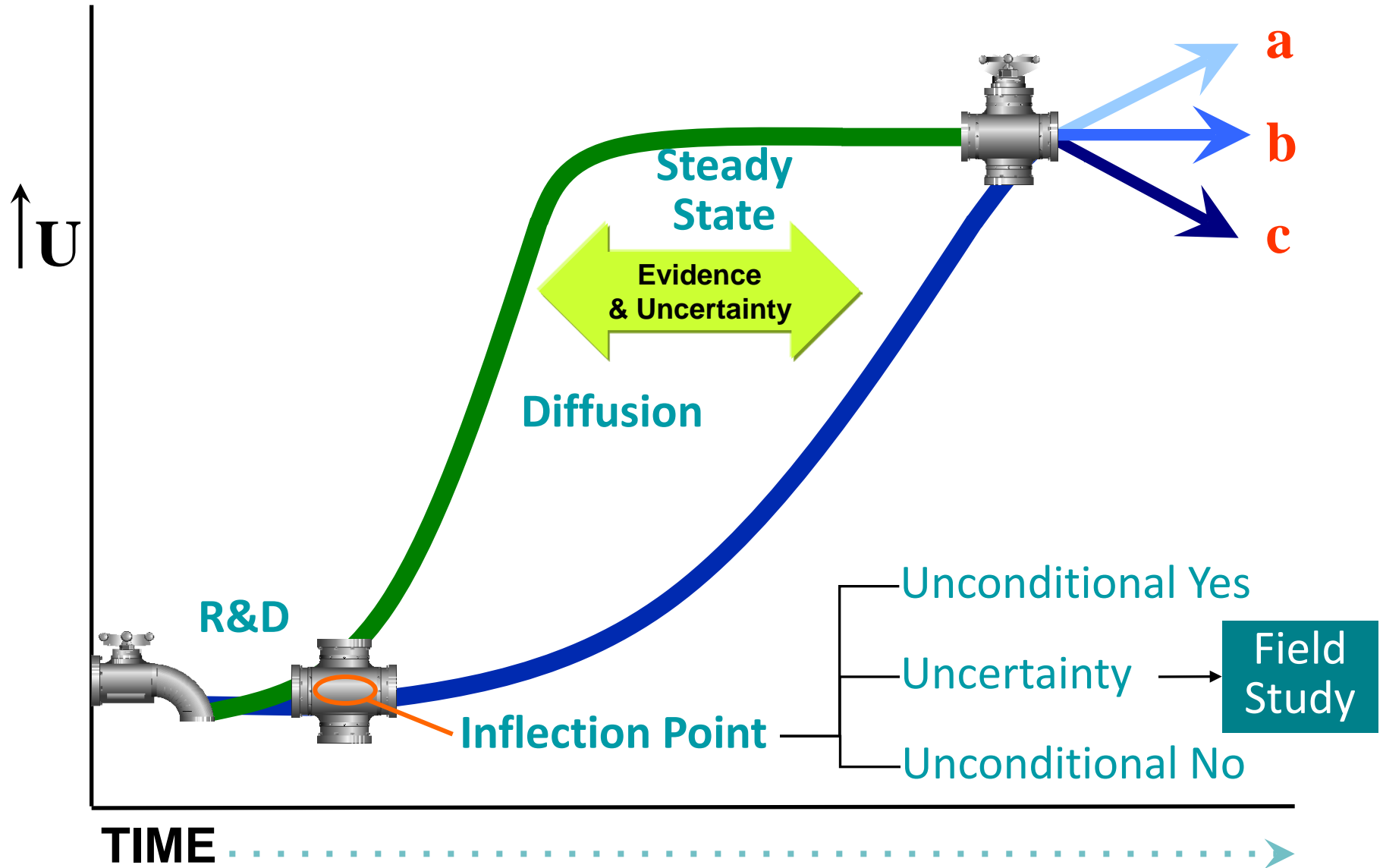
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# Health Technology Life-Cycle Diffusion Curve



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)

### 2010 (to July 2010)

- 64-Slice Computed Tomographic Angiography for the Diagnosis of Intermediate Risk Coronary Artery Disease
- Cancer Screening With Digital Mammography for Women at Average Risk for Breast Cancer, Magnetic Resonance Imaging (MRI) for Women at High Risk: An Evidence-Based Analysis
- Cardiac Magnetic Resonance Imaging for the Diagnosis of Coronary Artery Disease
- Clinical Utility of Vitamin D Testing
- Endovascular Laser Treatment for Varicose Veins
- Extracorporeal Lung Support Technologies - Bridge to Recovery and Bridge to Lung Transplantation in Adult Patients
- Magnetic Resonance Imaging for the Assessment of Myocardial Viability
- Non-Invasive Cardiac Imaging Technologies for the Assessment of Myocardial Viability
- Non-invasive Cardiac Imaging Technologies for the Diagnosis of Coronary Artery Disease
- Population-Based Strategies for Smoking Cessation
- Positron Emission Tomography (PET) for the Assessment of Myocardial Viability
- Single Photon Emission Computed Tomography for the Diagnosis of Coronary Artery Disease
- Solid Organ Transplantation for End Stage Organ Failure in persons with HIV
- Stress Echocardiography for the Diagnosis of Coronary Artery Disease
- Stress Echocardiography with Contrast for the Diagnosis of Coronary Artery Disease
- Use of Contrast Agents with Echocardiography in Patients with Suboptimal Echocardiography

### 2009

- Airway Clearance Devices for Cystic Fibrosis
- Diabetes Strategy Evidence Platform
- Fenestrated Endovascular Grafts for the Repair of Juxtarenal Aortic Aneurysms
- Intracocular Lenses for the Treatment of Age-Related Cataracts
- Intrastromal Corneal Ring Implants for Corneal Thinning Disorders
- Optical Coherence Tomo. for Age-Related Macular Degeneration & Diabetic Macular Edema
- Oral Appliances for Obstructive Sleep Apnea
- Phakic Intracocular Lenses for the Treatment of Low to High Refractive Errors
- Point-of-Care International Normalized Ratio (INR) Monitoring Devices for Patients on Long-term Oral Anticoagulation Therapy
- Prevention and Management of Chronic Pressure Ulcers
- Screening Methods for Early Detection of Colorectal Cancers and Polyps
- Specialized Multidisciplinary Community-Based Care (SMCC) Series
- Ultraviolet Phototherapy Management of Moderate-to-Severe Psoriasis

### 2008

- Aging in the Community
- Aging in the Community: Summary of Evidence-Based Analyses
- Behavioural Interventions for Urinary Incontinence in Community-Dwelling Seniors
- Caregiver- and Patient-Directed Interventions for Dementia
- Limbal Stem Cell Transplantation
- Prevention of Falls and Fall-Related Injuries in Community-Dwelling Seniors
- Social Isolation in Community-Dwelling Seniors
- The Falls/Fractures Economic Model in Ontario Residents Aged 65 Years and Over (FEMOR)

### 2007

- Anal Dysplasia Screening
- Low-Density Lipoprotein Apheresis
- Multidetector Computed Tomography for Coronary Artery Disease Screening in Asym. Pop
- Scintimammography as an Adjunctive Breast Imaging Technology
- Screening Mammography for Women Aged 40 to 49 Years at Average Risk for Breast Cancer

### 2006

- Ablation for Atrial Fibrillation
- Advanced Electrophysiologic Mapping Systems
- Artificial Disc Replacement for Lumbar and Cervical Degenerative Disc Disease
- Coil Embolization for Intracranial Aneurysms
- Energy Delivery Systems for Treatment of Benign Prostatic Hyperplasia
- Enhanced External Counterpulsation (EECP)
- Extracorporeal Photopheresis (ECP)
- Functional Brain Imaging

- Gastric Electrical Stimulation
- Hydrophilic Catheters
- In Vitro Fertilization and Multiple Pregnancies
- Intravascular Ultrasound to Guide Percutaneous Coronary Interventions
- Metal-on-Metal Total Hip Resurfacing Arthroplasty
- Midurethral Slings for Women with Stress Urinary Incontinence
- Nanotechnology
- Negative Pressure Wound Therapy
- Optimum Methadone Compliance Testing
- Polysomnography in Patients with Obstructive Sleep Apnea
- Portable Bladder Ultrasound
- Routine Eye Exams
- Ultrasound Screening for Abdominal Aortic Aneurysm
- Utilization of DXA Bone Mineral Densitometry in Ontario

### 2005


- Bariatric Surgery
- Deep Brain Stimulation in Parkinson's Disease and Other Movement Disorders
- Sacral Nerve Stimulation For Urinary Urge Incontinence, Urgency-Frequency, Urinary Retention, and Fecal Incontinence
- Spinal Cord Stimulation for Neuropathic Pain
- Multi-Detector Computed Tomography Angiography for Coronary Artery Disease
- Osteogenic Protein-1 for Long Bone Nonunion
- Intrathecal Baclofen Pump for Spasticity
- Physiotherapy Rehabilitation After Total Knee or Hip Replacement
- Total Knee Replacement
- Intra-Articular Viscosupplementation With Hyal G-F 20 To Treat Osteoarthritis of the Knee
- Hyperbaric Oxygen Therapy for Non-Healing Ulcers in Diabetes Mellitus
- Arthroscopic Lavage and Debridement
- Biventricular Pacing (Cardiac Resynchronization Therapy)
- Implantable Cardioverter Defibrillators (ICD)
- Technologies for Osteoarthritis of the Knee
- Positron Emission Tomography for the Assessment of Myocardial Viability
- Air Cleaning Technologies
- Endovascular Repair of Descending Thoracic Aortic Aneurysm
- Automated External Defibrillators

### 2004 (and prior)

- Balloon Kyphoplasty
- Bispectral Index Monitor
- Bone Anchored Hearing Aid (BAHA)
- Bone Morphogenetic Proteins and Spinal Surgery for Degenerative Disc Disease
- Computed Tomographic Colonography
- Computer-Assisted Hip and Knee Arthroplasty: Navigation and Robotic Systems
- Computer-Assisted Surgery Using Telemanipulators
- Endovascular Repair of Abdominal Aortic Aneurysm
- Functional Cardiac Magnetic Resonance Imaging in the Assessment of Viability and Perfusion
- Gamma Knife
- Intracoronary Radiation: An Evidence-Based Analysis
- Islet Transplantation
- Left Ventricular Assist Devices
- Neonatal Screening of Inborn Errors of Metabolism Using Tandem Mass Spectrometer
- Patient Monitoring System for MRI [PDF]
- Primary Angioplasty for the Treatment of Acute ST-Segment Elevated Myocardial Infarction
- Pyrocarbon Finger Joint Implant
- Radio Frequency Ablation for Primary Liver Cancer
- Repetitive Transcranial Magnetic Stimulation for the Treatment of Major Depressive Disorder
- Small Bowel Transplant
- Thermal Balloon Endometrial Ablation for Dysfunctional Uterine Bleeding (TBEA)
- Video Laryngoscopy for Tracheal Intubation
- Wireless Capsule Endoscopy

# Uncertainty Drove Field Evaluation Studies

## Recognizing Uncertainty – Effect of GRADE

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



# 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)

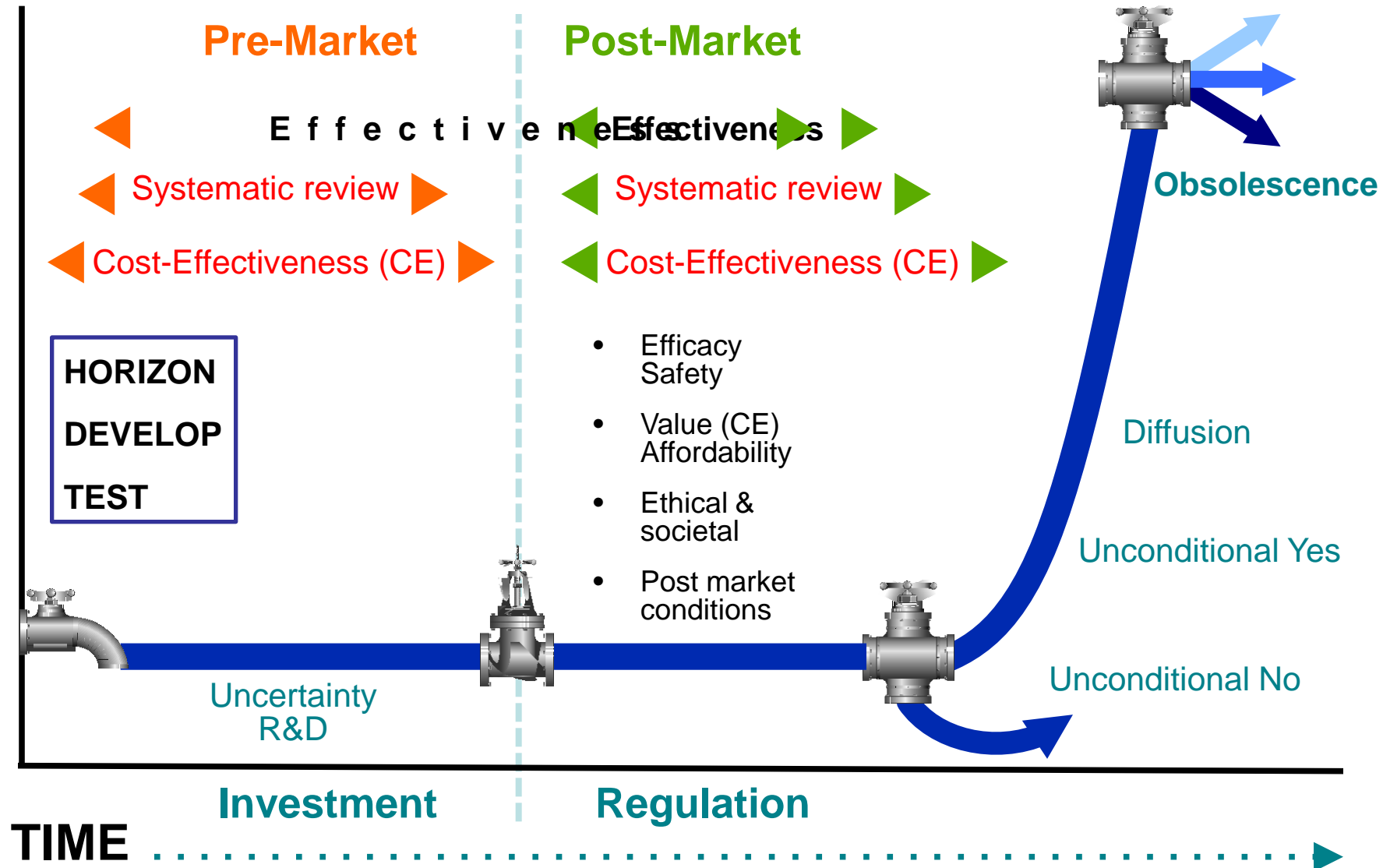
# Analytic Hierarchy Process (AHP) to Elicit User Needs (Pecchia and M. P. Craven, 2012)

- 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



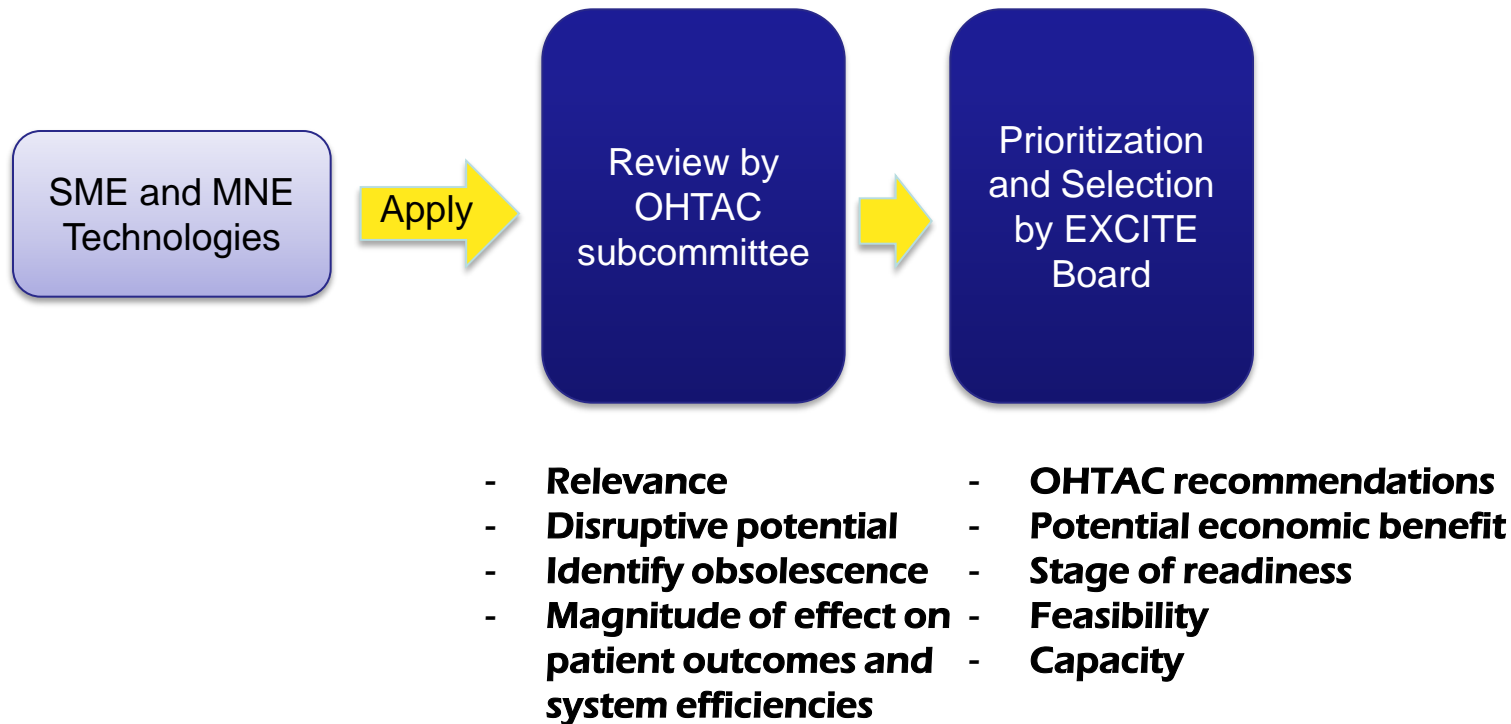
# Life-Cycle Diffusion Curve (Pre-Market Evidence Based Analysis)

MaRS EXCITE

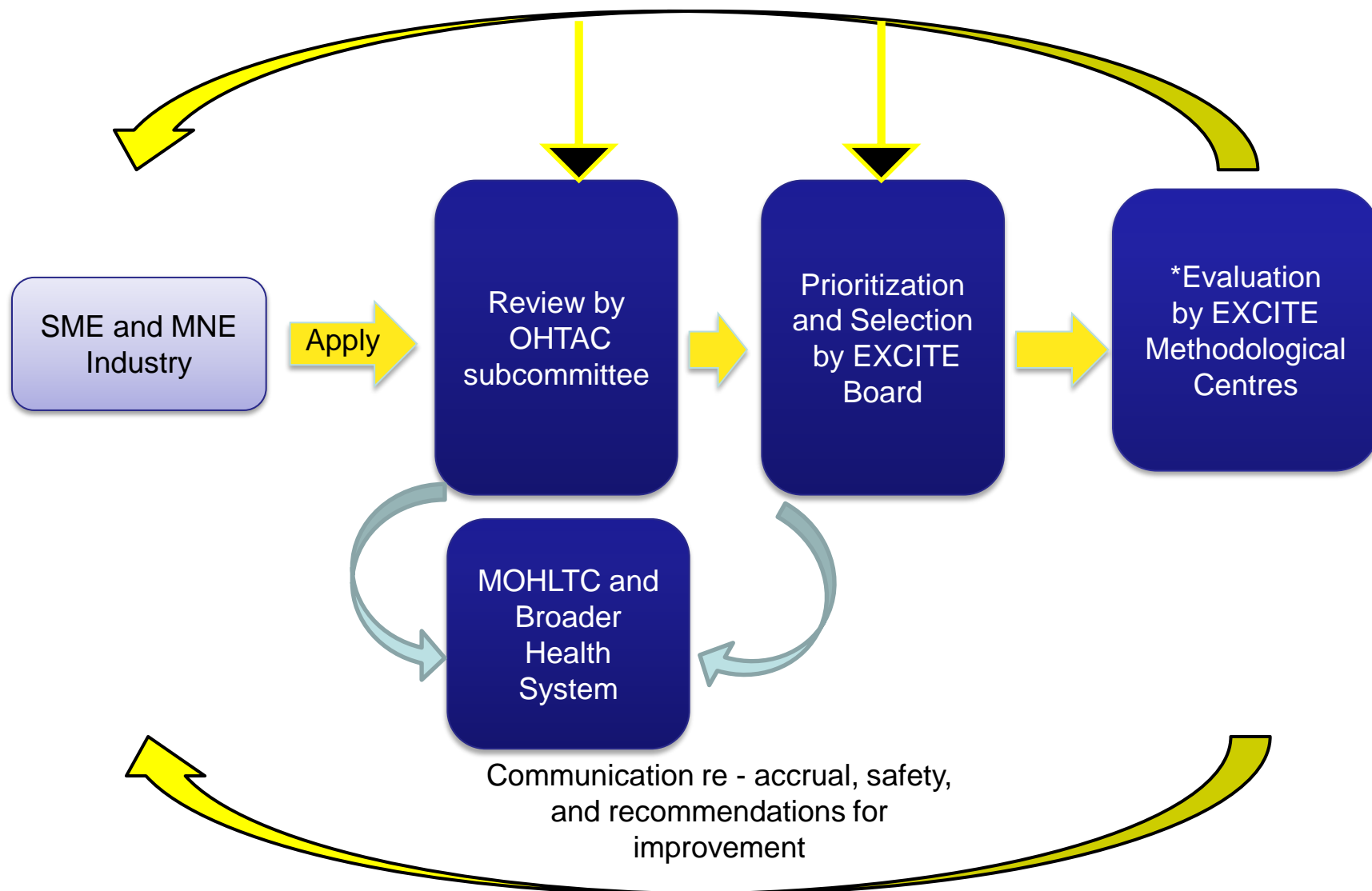




# Key Steps in the EXCITE Process



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# EXCITE Evaluations

## **Core Evidentiary Bundle:**

- **Safety + Effectiveness**
- **Systematic Review**
- **Economic Analysis**

**Completed by:  
Methodological  
Centres**

## **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**

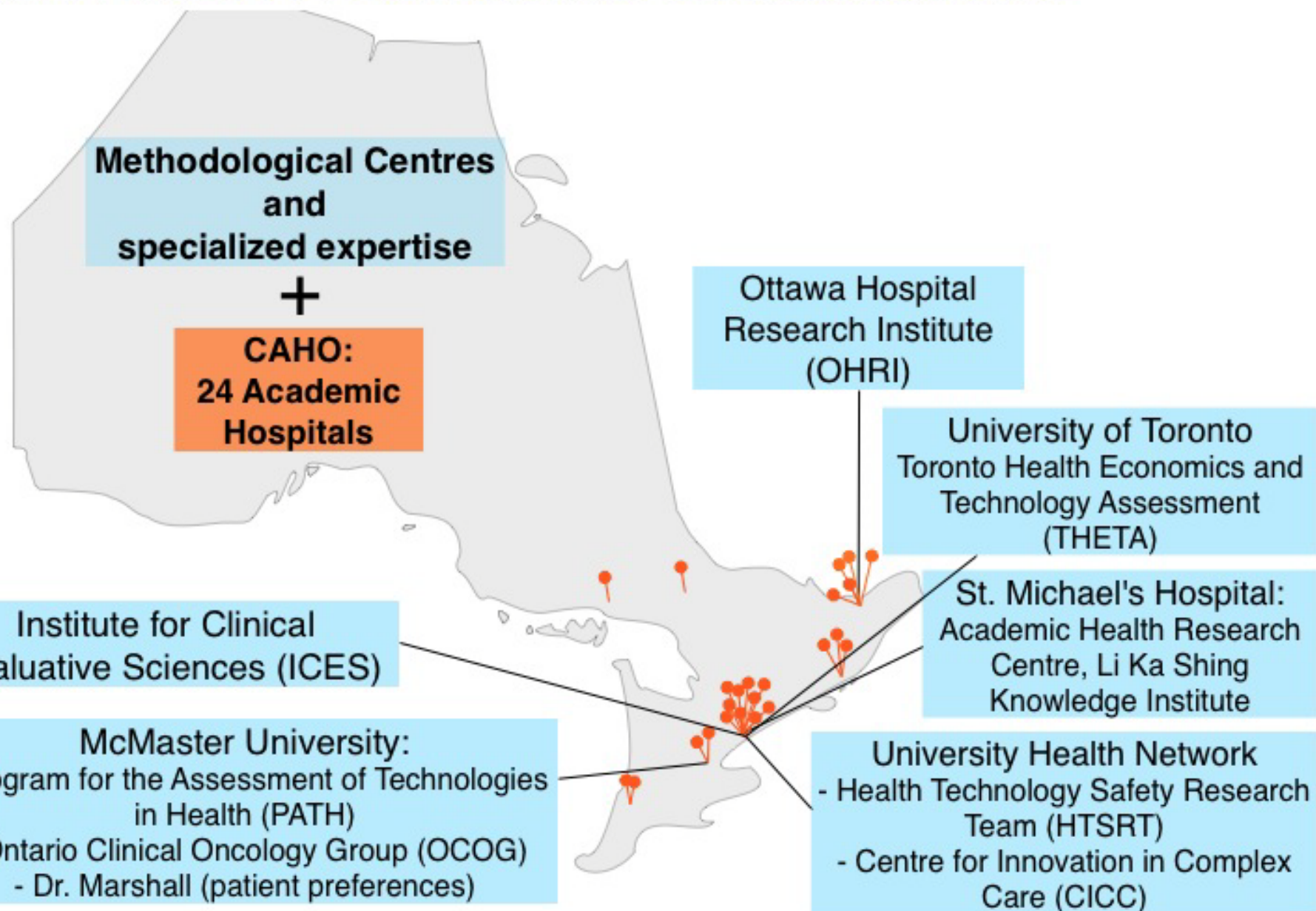
**Completed by:  
Specialized Methodological  
Centres**



# 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



## 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  
Hospitals of Ontario (CAHO)

Karen Michell, Catherine Zahn



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