

Migration vers l'amont de l'expérience ontarienne: d'une évaluation en temps réel post-marché à une étape de développement de produit pré-marché ?

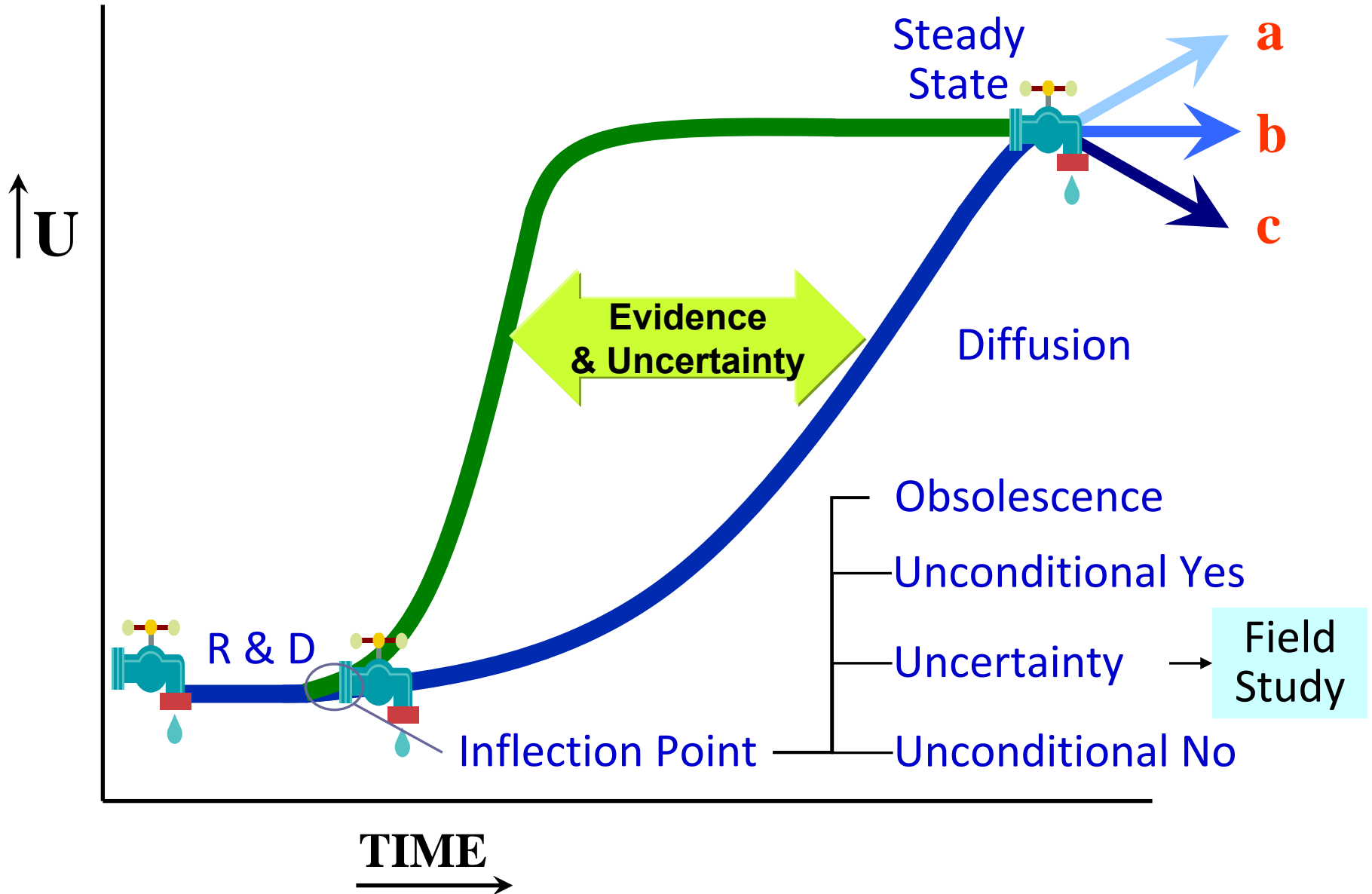
**Technologie De La Santé, De Li'innovation au Marche
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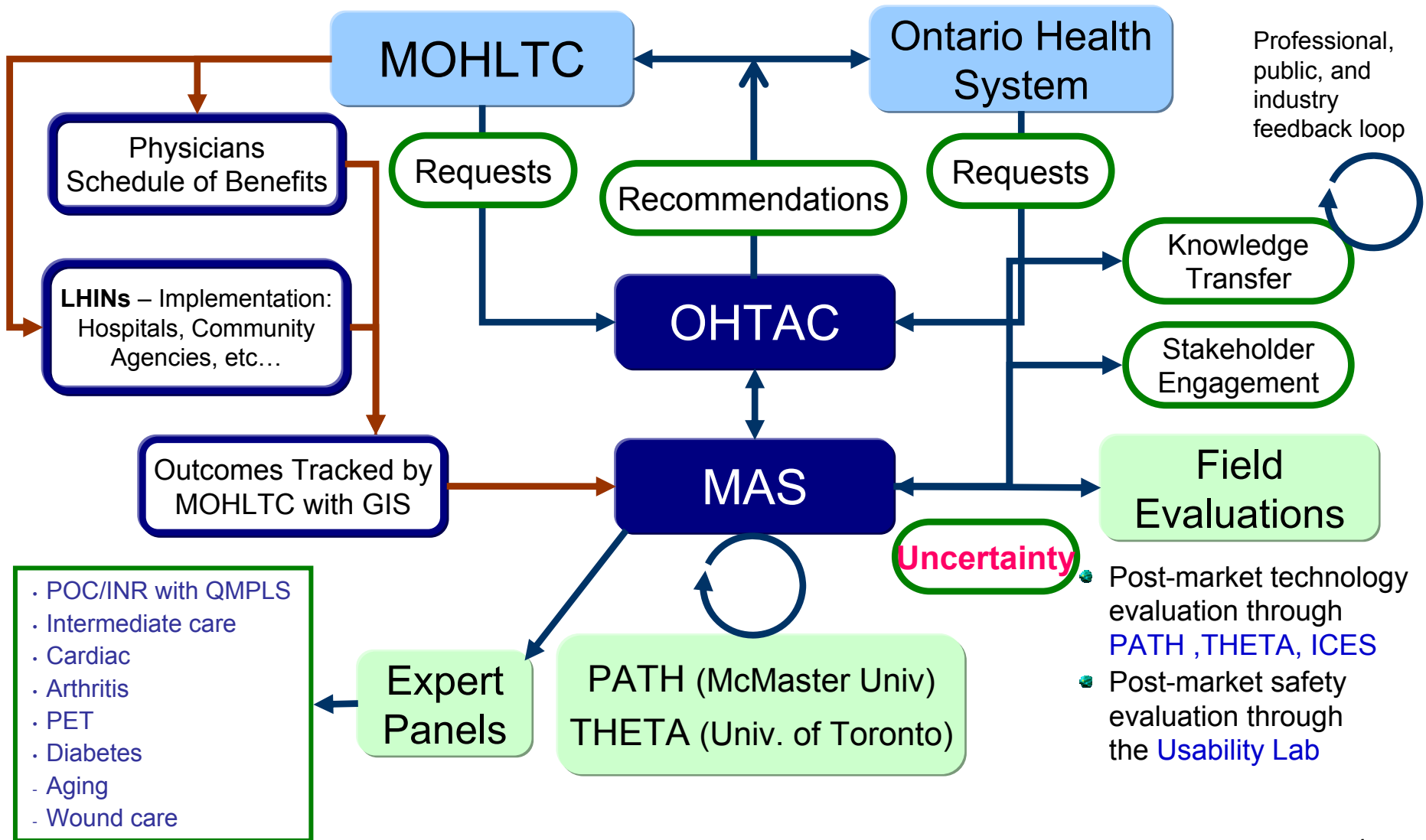
Reality, Evidence and Uncertainty

- New interventions account for 60-70% of incremental health costs
- Evidence is a transparent, fair, and defensible basis for making tough choices
- Uncertainty can lead to uncontrolled passive diffusion
- Post market field evaluation to address uncertainty is needed prior to multi-million dollar, multi-year commitments
- Mega analysis is relevant to prioritize technologies around disease conditions. Direct investments that optimize cost-effective outcomes

Life-Cycle Diffusion Curve



MAS/OHTAC Associated Structures & Linkages



Health Technologies Reviewed by OHTAC Based on Analyses by MAS, PATH & THETA (85% Conversion to Policy)

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
- Intraocular 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 Intraocular 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 Hylan 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

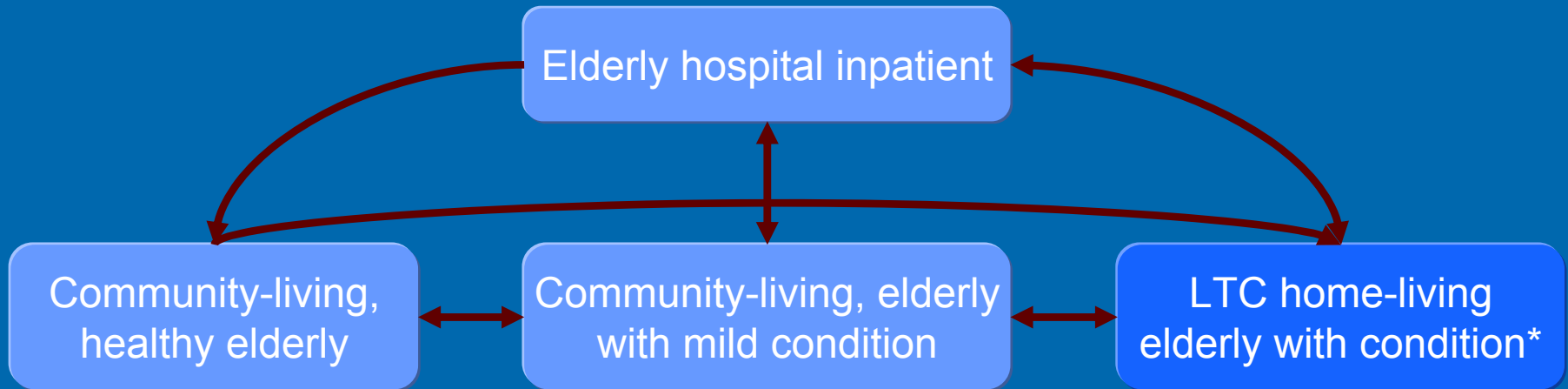
Mega-Analysis and Economic Modeling

- Mega-analysis - disaggregation of technologies around a disease condition or health state with re-aggregation for comparative analysis
- Mega-analyses to date:
 - Osteoarthritis of the knee MAS (2005)
 - Cardiac viability MAS (2005)
 - **Aging in the community MAS/PATH (2008)**
 - Colon cancer screening MAS/PATH (2008)
 - **Diabetes MAS/PATH (2009)**
 - Intermediate care MAS/THETA (2009)
 - Wound care prevention MAS/THETA (2009)
 - Cardiac diagnostic tests MAS/THETA (2010)
 - **COPD MAS/PATH (2010)**
- Robust micro-economic policy decision models
 - Ontario Diabetes Economic Model (PATH) (2006)
 - Ontario Cardiovascular Model (THETA) (2009)
 - Ontario Wound Prevention and Care Models (THETA) (2009)
 - Ontario Arthritis Model (PATH) (Commenced October 2009)
 - Ontario COPD Model (PATH) (Commenced April 2010)
- Turn-around time ~ 6-8 months

DIABETES MEGA-ANALYSIS

	Multidisciplinary Program	Insulin Pumps for Type 2	Behavioural Interventions	Bariatric Surgery
Δ HbA1c	-1.02%	-0.14%	-0.44%	-2.70%
Δ Costs (in billions)	\$5.623	\$8.010	\$0.212	\$1.573
Δ QALYs	290,424	4,222	5,957	100,196
\$/QALY gained	\$19,869/QALY	\$1.9M/QALY	\$36,226/QALY	\$15,697/QALY
Δ IHD	15,265	201	446	2,757
Δ MI	40,882	562	521	13,839
Δ Heart Failure	8,563	462	595	31,137
Δ Stroke	14,074	361	372	8,957
Δ Amputation	13,180	201	372	2,997
Δ Blindness	6,180	281	521	4,179
Δ Renal Failure	819	-8	74	17

MAS Transition Model: Aging in the Community



Four Factors Driving Patients Along Pathway (Left to Right)

Repeat Falls

Incontinence


Dementia

Social Isolation

Uncertainty

- Uncertainty if the HTA is inconclusive
- May be caused by e.g.:
 - Low quality evidence
 - ? Incremental net benefit
 - ? Generalizability
 - Safety issues
- Compounded by:
 - Less rigorous pre-market assessment & licensing
 - Narrow time lines for market exclusivity
 - Early adoption to profile innovation
- For uncertainty in incremental net benefit there is (an option) value to delaying decisions and waiting for further evidence (Eckerman and Willan, 2006)

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	Certainty  Uncertainty
Moderate	Likely	
Low	Very likely	
Very Low	Any estimate of effect is very uncertain	

Delayed Open Diffusion to Address Uncertainty Through Post-Market Assessment

- CMS - Coverage with Evidence Development (CED)
- NICE - Only-In-Research program
- MSAC – Interim funding e.g. capsular endoscopy
- Ad Hoc e.g. BCBS sponsored RCT to assess high dose chemo with bone marrow support in breast cancer
- Ontario's Field Evaluation Program informs decision making through post-market assessments (Goeree and Levin 2004, Levin et al 2010)

Summary of Ontario Field Evaluations (FE)

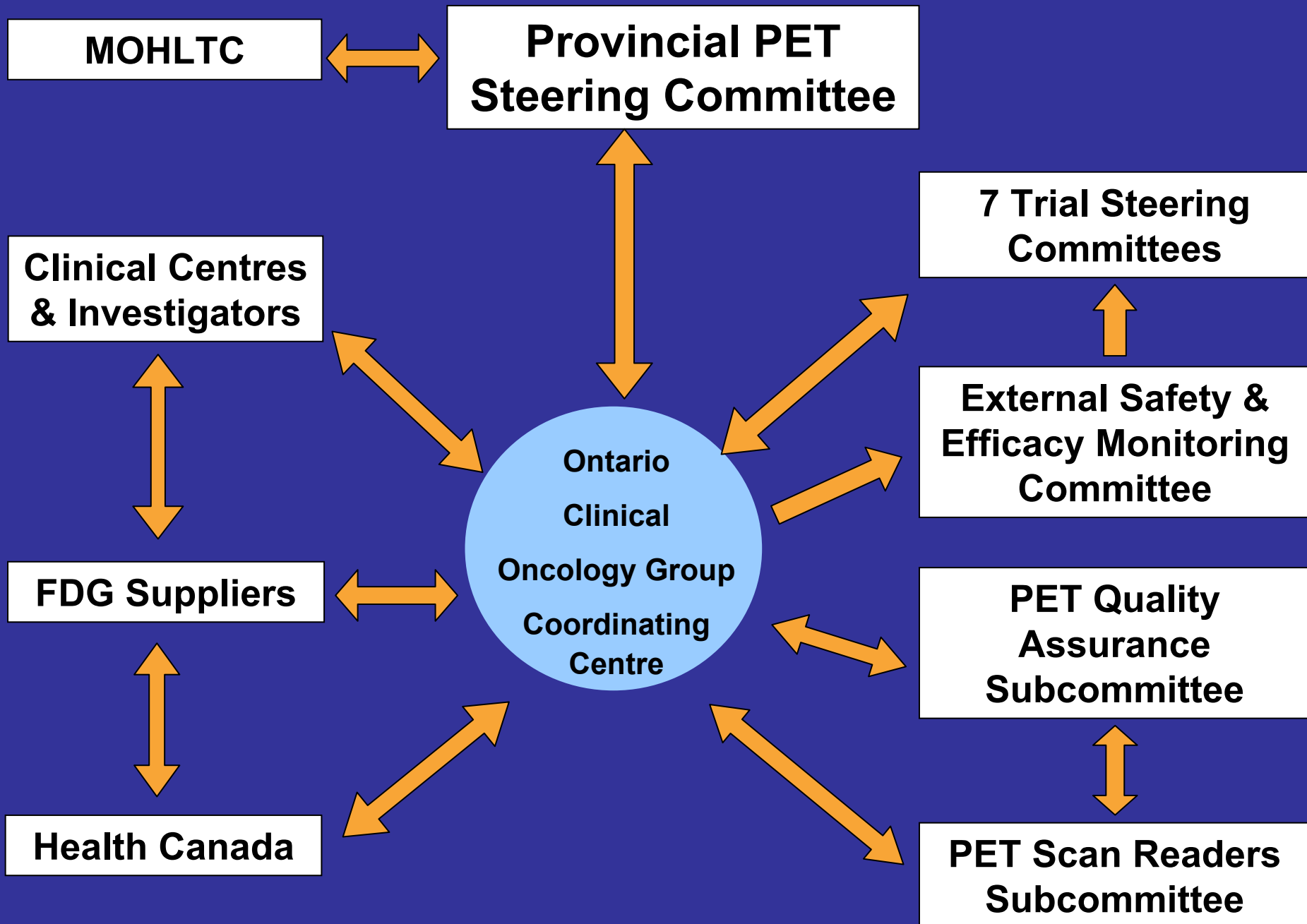
- 38 since 2003:
 - 8 RCTs
 - 17 observational
 - 7 registries
 - 2 polls
 - 4 decision analytic models
 - 10/19 (53%) of completed studies and 10/19 (53%) of studies in progress are CED

19 Completed Ontario Field Evaluations

- 10 CEDs
- Significantly affected decision-making in 88%
- Shaped diffusion curve in 11/13 (85%)
 - accelerated 50%
 - slowed 44%
 - withdrawal in 6%
- Safety alerts from 3 FEs
- Published in peer-reviewed journals in 8/13 (62%) (data undergoing analysis in additional 3)
- Contributed to >\$500M cost avoidance

TECHNOLOGY (N)	OVERSEEN BY	TYPE OF STUDY	REASON FOR FE	RESULT	POLICY DECISION
Drug eluting stents (DES) (21,000)	PATH, with ICES,	Prospective pragmatic registry-based	Generalisability of RCT evidence and cost effective analysis	Only effective in patients at high risk for restenosis	Funded 30% conversion from bare-metal to DES (90% in U.S.A.)
Endovascular abdominal aortic aneurysm repair (EVAR) (160)	PATH and single AHSC	Prospective observational	Safety assessment of endoleak	No endoleak. CE only for high surgical risk	Funded for high but not low surgical risk
Multifaceted primary care diabetes program	PATH, with Oxford University,	Before-after study using micro simulation economic model	Prioritize investments following systemic review of diabetes strategy.	Most CE were bariatric surgery, MDT. Least CIIP for type 2	Bariatric funded and additional funding for MDT. No Insulin infusion pumps for type II
64-slice CT angiography (CTA) v coronary angiography (CA) (175)	PATH, with cardiologists, radiologists, selected AHSCs	Patients for CA also underwent CTA	Uncertainty re-indications for use, CE and QA parameters	Sensitivity lower than reported, reducing CE	OHTAC recommended slow diffusion until sensitivity issue resolved

TECHNOLOGY (N)	OVERSEEN BY	TYPE OF STUDY	REASON FOR FIELD EVALUATION	RESULT	POLICY DECISION
PET to stage locally advanced NSCLC (310)	OCOG	RCT	Clinical utility	Terminated by efficacy & safety cmtee	PET insured for this indication
PET to stage early NSCLC (322)	OCOG	RCT	Resolve inconsistencies to inform decision	PET reduces futile thoracotomy rates	PET insured for this indication
PET to stage breast cancer (320)	OCOG	Prospective cohort	Compare PET to sentinel lymph node biopsy	No utility in staging	Not insured
PET for colon cancer metastatic to liver (400)	OCOG	RCT	Clinical utility in decision for metastatectomy	Accrual completed February/10	Awaiting results
PET for head and neck cancer (400)	OCOG	Prospective cohort	Clinical utility pre surgery following radiation therapy	No clinical utility	Likley will not be insured
Extracorporeal photopheresis (EP) (120)	PATH with AHSC	Prospective observational	Basis for decision re-funding for GvH and Sezary	Effective in GvH. Inconclusive for Sezary	Insured for GvH. Inconclusive for Sezary - small vol. after backlog dealt with



Bringing Together Mega-Analysis and Field Evaluation - CT Angiography

- Field Evaluation (FE) (2007-2009)

Hospitals replacing CT scanners with 64-slice including software for CT angiography (CTA)

 - FE at 4 academic centres with quality controls under PATH (2007-2009)
 - CTA not insured until results from FE available
- Mega-Analysis (2009)

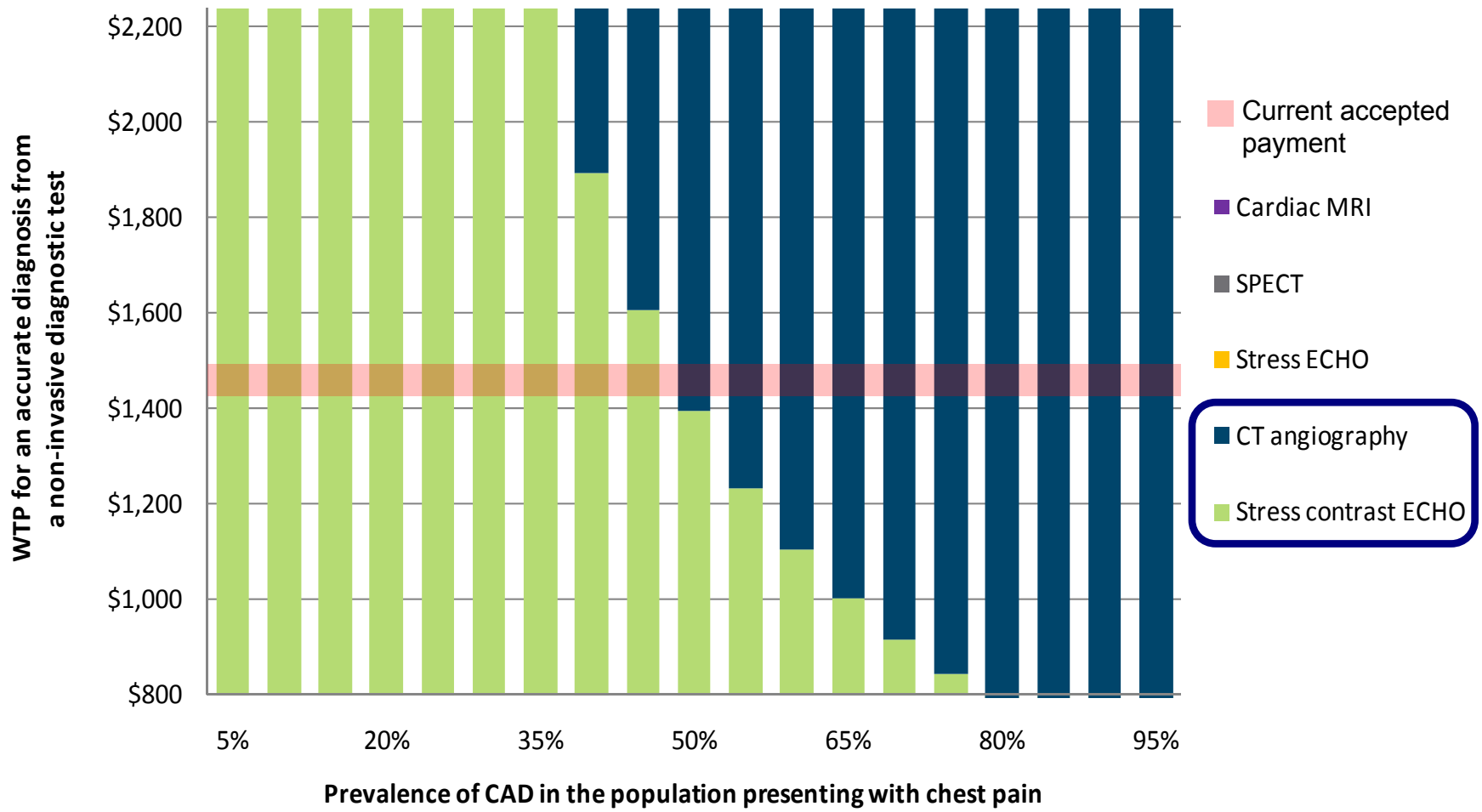
MAS/THETA mega-analysis of cardiac imaging with coronary angiography (CA) as gold standard to determine the most effective and cost-effective technologies pre-CA
- MAS analysis and CTA FE completed in 2010

Cardiac Testing for Intermediate Risk IHD

Overall Results on Diagnostic Accuracy

Technology	Number of Studies (patients)	Sensitivity	Specificity	AUC	DOR
CT Angio	8 (1,635)	0.96	0.81	0.96	108.6
Cardiac MRI (perfusion)	23 (1,993)	0.91	0.80	0.93	38.1
Stress ECHO with contrast (wall motion)	15 (1,689)	0.84	0.80	0.90	21.6
Stress ECHO (exercise + pharma)	127 (13, 035)	0.79	0.84	0.89	20.6
AC SPECT	12 (1,238)	0.86	0.82	0.91	28.5
Gated SPECT	19 (2,710)	0.84	0.78	0.89	18.8
Traditional SPECT	63	0.86	0.71	0.88	15.4

THETA Economic Analysis: Cost per Accurate Diagnosis by Coronary Angiography

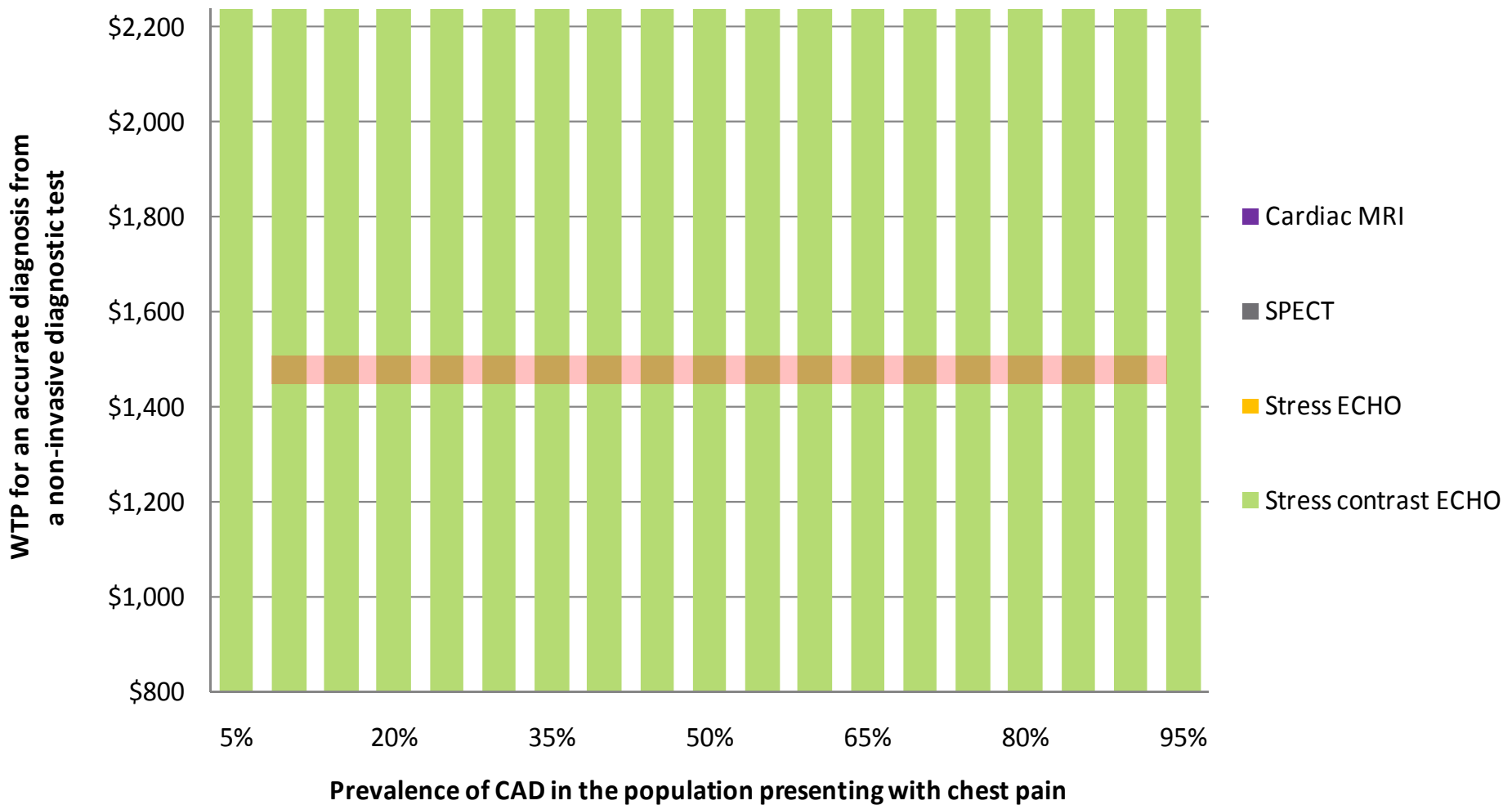


Comparison of CTCA Diagnostic Accuracy ($\geq 50\%$ stenosis)

	Raff (2005) (N=70)	Budoff (2008) (N=230)	Meijboom (2008) (N=360)	Miller (2008) (N=291)	PATH OMCAS Study (2010) (N=169)
Sensitivity	95 (88, 98)	95 (85, 99)	99 (98, 100)	85 (79, 90)	81 (71, 89)
Specificity	90 (80, 94)	83 (76, 88)	64 (55, 73)	90 (83, 94)	93 (86, 98)
Positive Predictive Value	93 (79, 98)	64 (53, 75)	86 (82, 90)	91 (86, 95)	92 (82, 97)
Negative Predictive Value	93 (76, 99)	99 (96, 100)	97 (94, 100)	83 (75, 89)	85 (76, 91)
Number of centres	1	16	3	9	4
Multiple vendors	No	No	Yes	No	Yes

Cost per Accurate Diagnosis by CA

CTA Cost-Effectiveness from Field Evaluation (THETA)



Uncertainty Due to Safety and *Human Factors

- Human factors analysis examines interactions between end-users and technologies
- Undertaken for OHTAC by the Usability and Human Factors Laboratory at University Health Network
- Examples to date include evaluations on:
 - *Error rates on smart infusion pumps
 - *Error rates on multiple infusion lines
 - *Automated external defibrillators
 - Radiation exposure and safety issues for CT scans
 - Placement of in-room air filtration units and use in pandemic

Rapid Diffusion of New Technology e.g. Robotic Laparoscopic Surgery

- MAS systematic review for prostate and GYN cancer surgery –
 - reduces hospital stay
 - reduces blood loss
 - reduces incontinence and erectile dysfunction in prostatic cancer

(All low quality evidence)
- Increasing demand.
 - NEJM August 2010 (Borbash and Glied)
 - 80,000 procedures world-wide in 2007 and 205,000 in 2009
 - # units in U.S. ↑ 75% (800-1400) 2005-2008
 - 60% ↑ prostate cancer surgery in U.S. 2005-2008 despite ↓ incidence
- OHTAC recommended August 2010:
 - restrict diffusion to 4 existing centres
 - prospective data collection in hospitals with and without robotic surgery by linked data set analysis for ~12 months

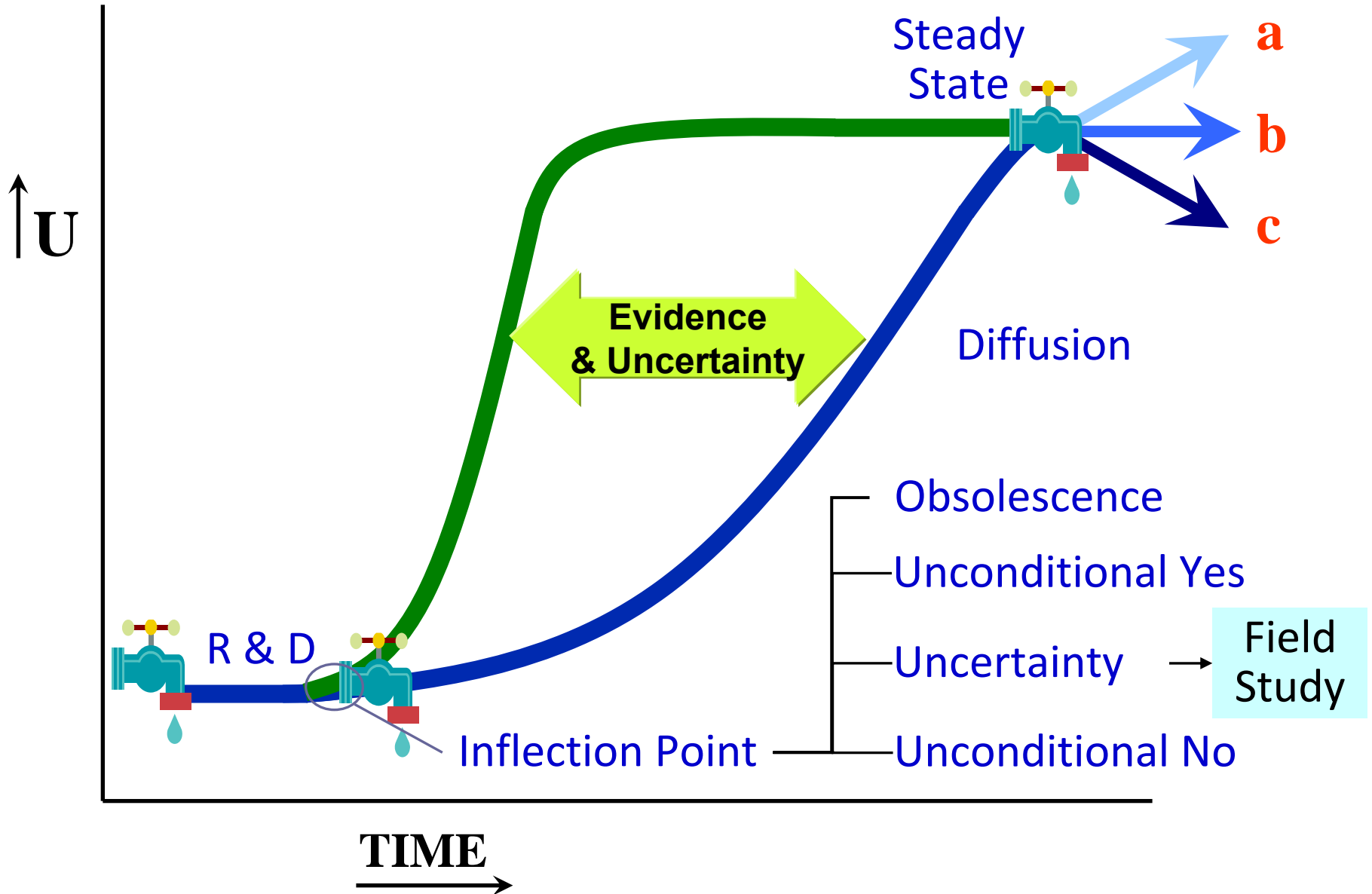
Lessons from Post-Market Field Evaluations

- RCT outcomes not necessarily reproducible under real world conditions. Funding implications
- Ignoring collection of adequate data prior to definitive funding decisions leads to:
 - Passive diffusion
 - Potential wastage
 - Intuitive decision making
- Study designs should not restrict access, and be of short duration while maintaining high quality
- Engaging end-users results in greater confidence
- IT IS EASIER TO SHAPE A DIFFUSION CURVE THAN TO BEND A DIFFUSED CURVE
- Given issues of generalizability, which new technologies should be exempt from post-market assessment?
- The current division between pre-and post-market assessments could lead to greater difficulties in decision-making e.g. genomics,

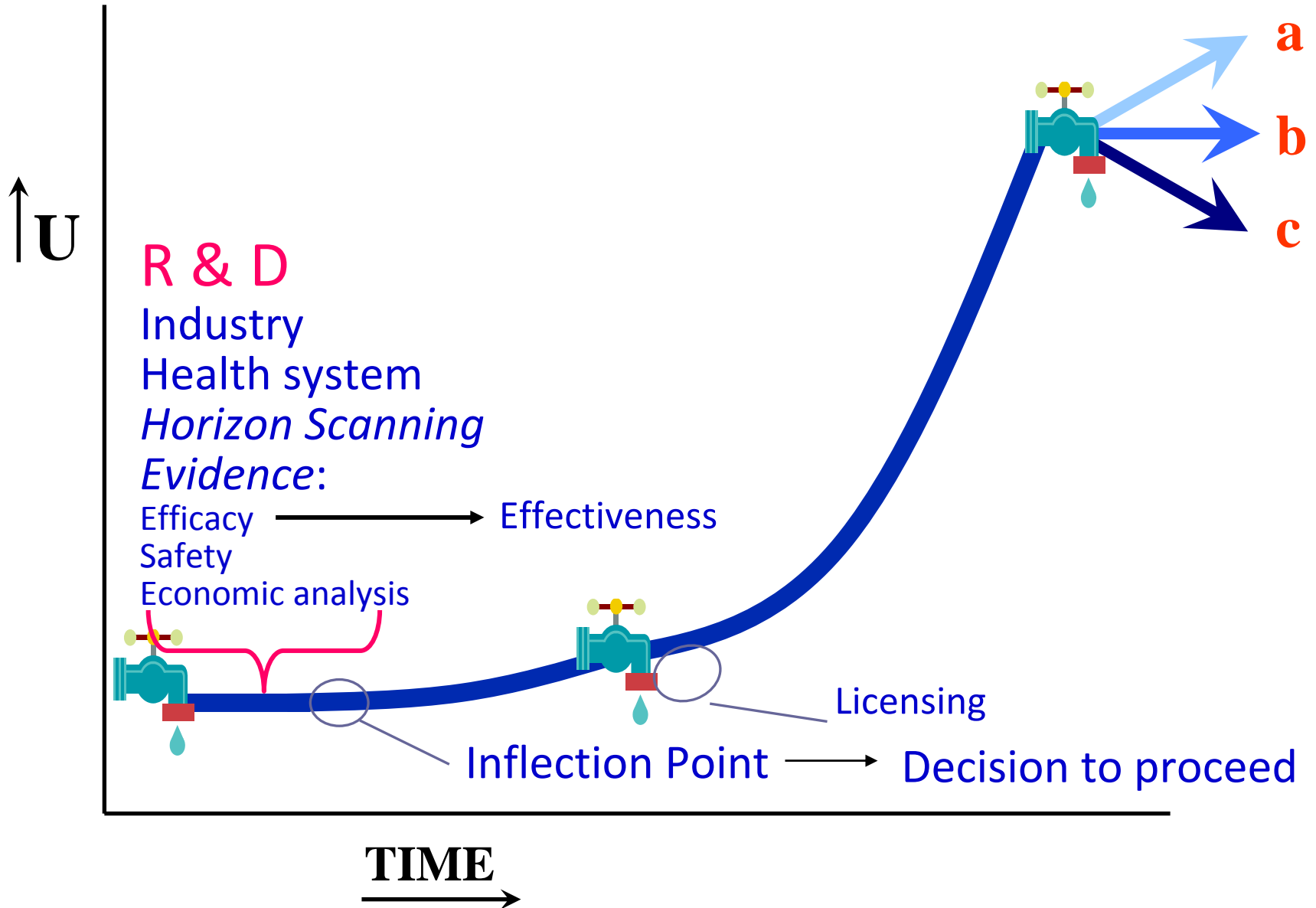
Problems With Where We Have Arrived

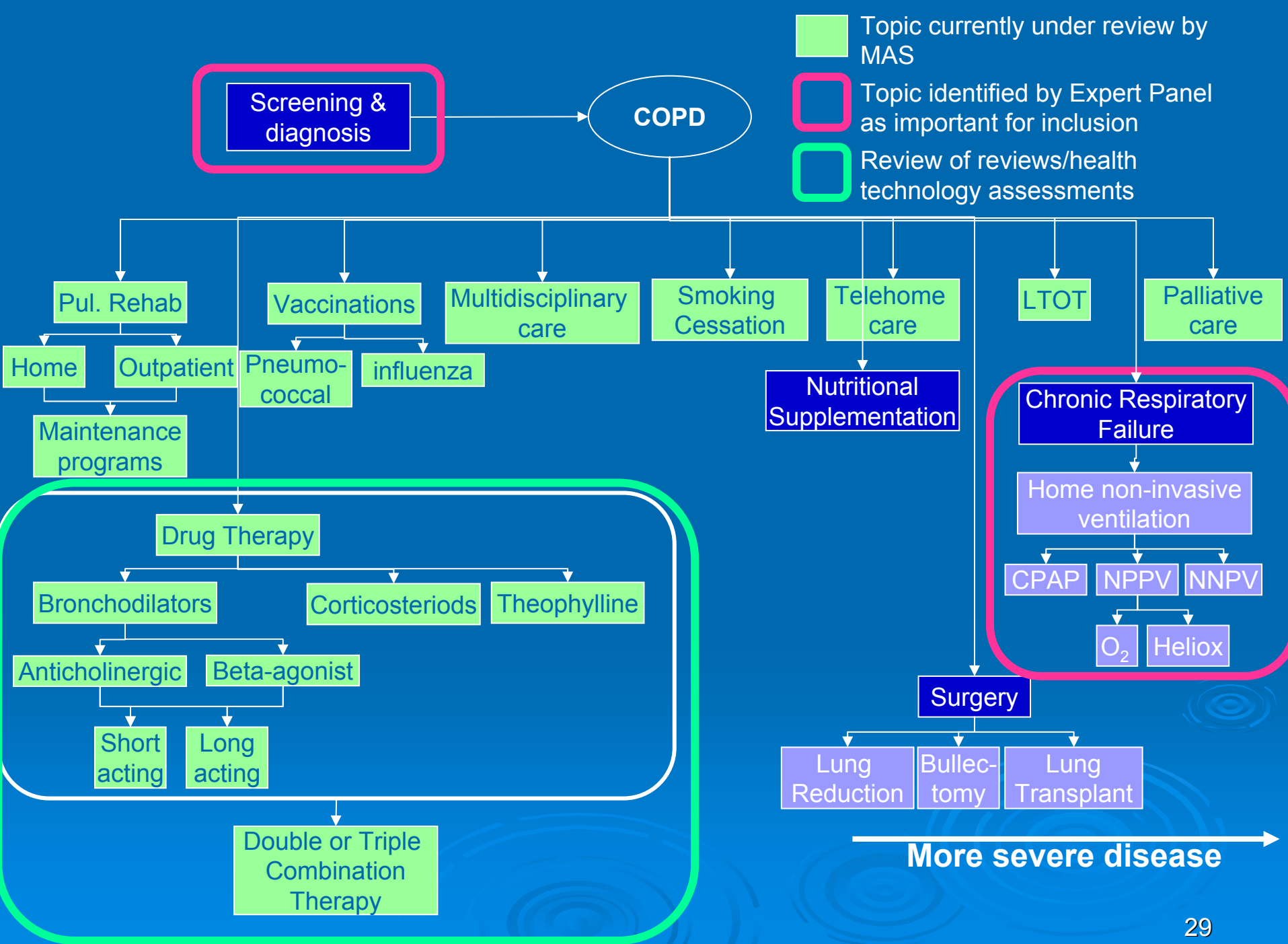
- Evidence obsession might lead to:
 - Better decisions
 - Log-jams
 - Stifled innovation through increase risk and limited market exclusivity
 - By-passing established processes
 - Division between industry and health systems
- Industry is the Research and Development part of health systems and the following changes might be considered:
 - HTA should be conducted pre-market, including comparative effectiveness and economic analysis
 - Health systems should engage industry pre-market to
 - define relevance and conduct joint horizon scanning of health systems needs
 - provide time to prepare for uptake and obsolescence
 - negotiate post-market conditions
 - Pre-market evaluation should harmonize regulatory and health system requirements.
 - To achieve the above, methodologies should combine phase 3/4 studies to:
 - expedite market penetration of effective technologies
 - test effectiveness under real world conditions as part of the adoption strategy and ? licensing process.

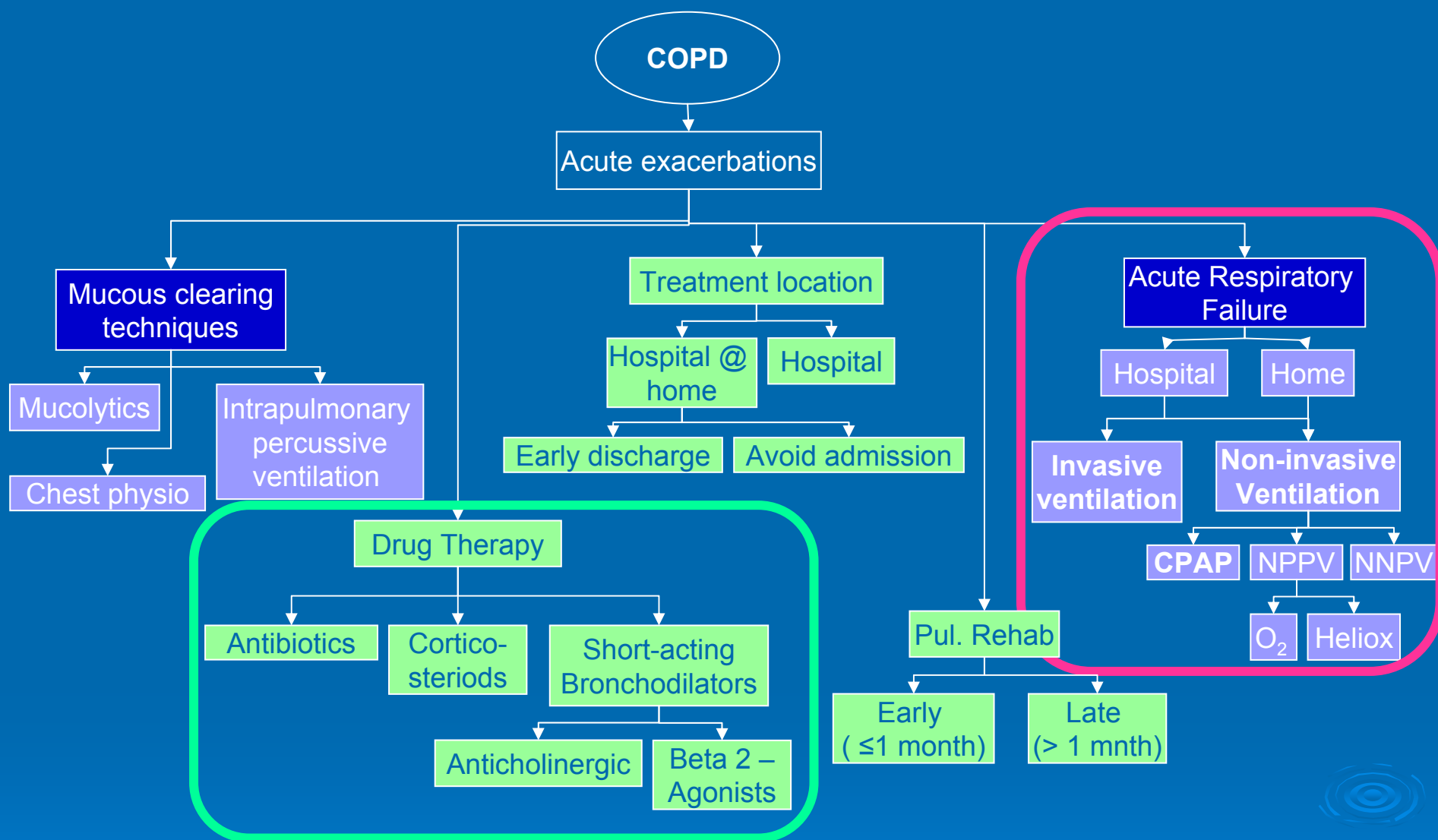
Life-Cycle Diffusion Curve



Life-Cycle Diffusion Curve







- Topic currently under review by MAS
- Topic identified by Expert Panel as important for inclusion

- Review of reviews/health technology assessments
- CPAP, continuous positive airway pressure; NPPV, noninvasive positive pressure ventilation; NNPV, noninvasive negative pressure ventilation