MEDICAL DEVICE REW

a clinician's perspective

INTERNATIONAL MEDICAL DEVICE REGULATORY FORUM (IMDRF) 2017

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Scientist, Sunnybrook Research Institute

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OUTLINE

1. Who am I?
   - Clinician
   - Researcher
   - CADTH
2. What is CADTH?
3. Trans-catheter Aortic Valve Replacement
   - Medical device life-cycle milestones
4. RWE in TAVR – how it happened
5. RWE in TAVR– missed opportunities

Who am I *A. clinician*

- Interventional cardiologist at Sunnybrook Health Sciences Center, University of Toronto, since 2008

Sunnybrook
HEALTH SCIENCES CENTRE

- Clinical practice is restricted to coronary angiography and angioplasty, and TAVR

- TAVR since 2009, with ~150 cases annually (3rd largest in Canada)

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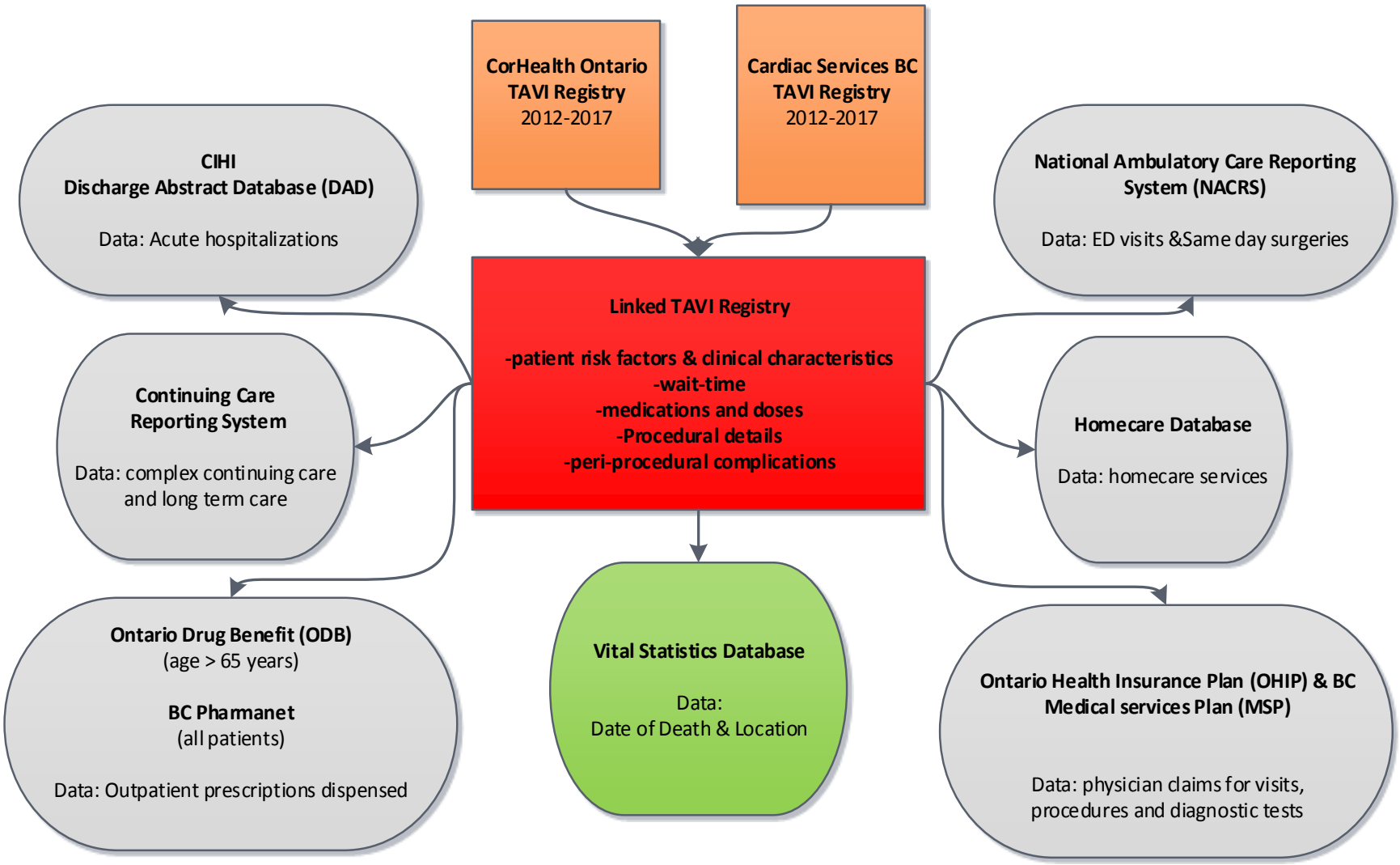
Who am I: *B. researcher*

- Health service researcher at the Institute for Clinical Evaluative Sciences

- Expertise in administrative data for use in health technology assessment
  - Health outcomes
  - Health care costs
  - Integrating these data as inputs in decision analytic economic/policy models

Who I am? *Real World Evidence*



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Who am I: c. CADTH VP

CADTH

is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence about the optimal use of drugs and medical devices.

Our Programs and Services

DRUG REIMBURSEMENT RECOMMENDATIONS

- CADTH Common Drug Review (CDR)
- CADTH pan-Canadian Oncology Drug Review (pCODR)

HEALTH TECHNOLOGY MANAGEMENT PROGRAM

- Rapid Response Service
- Health Technology Assessment Service
- Optimal Use Service
- Environmental Scanning
- Horizon Scanning

OTHER PROGRAMS AND SERVICES

- Scientific Advice

KNOWLEDGE MOBILIZATION AND LIAISON OFFICERS

- Located in jurisdictions across Canada
- Understand the needs and priorities of local decision-makers
- Provide advice and tools to help turn evidence into policy and practice

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PROGRAMS AND SERVICES

HEALTH TECHNOLOGY MANAGEMENT PROGRAMS

- Rapid Response Service
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- Environmental Scanning
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PROGRAMS AND SERVICES

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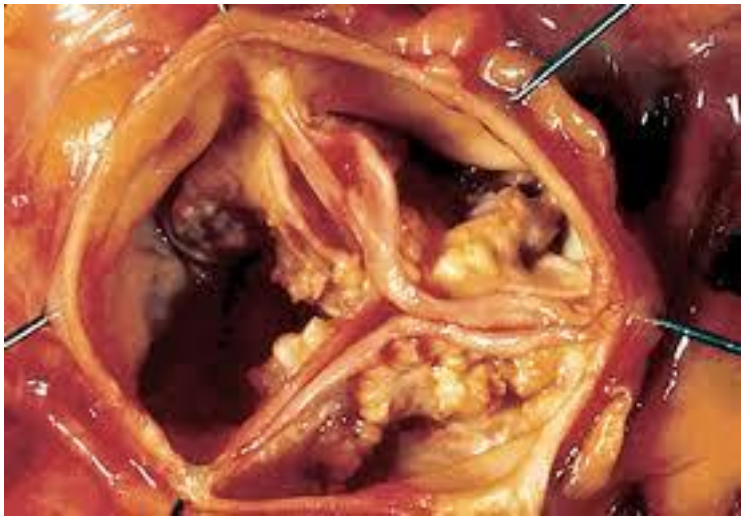
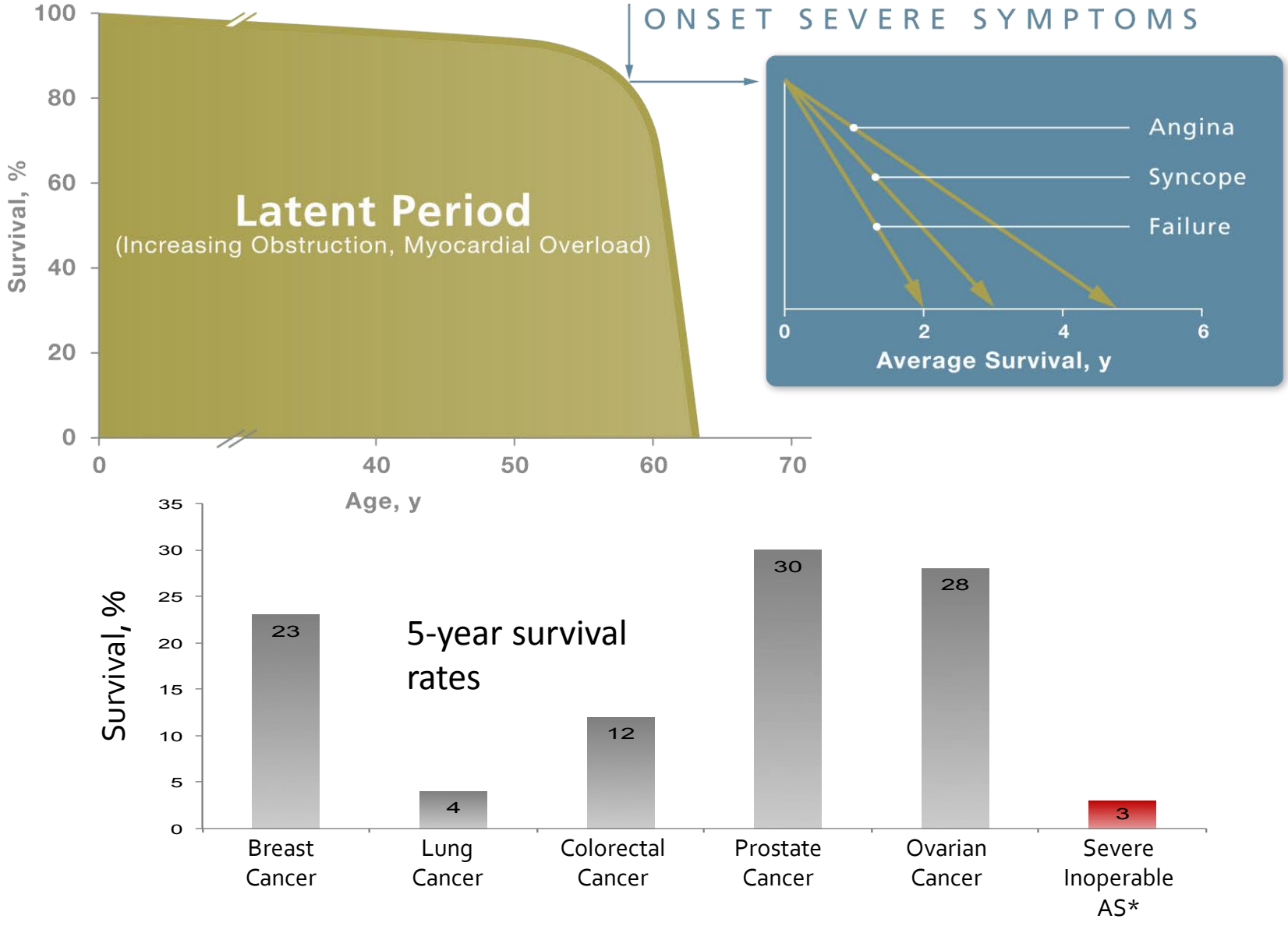
was created to build Canada's capacity to use evidence as the basis for sound health care decisions. This strategic imperative remains a cornerstone of our work.

Aortic Stenosis Background

- Degenerative valve disease
  - Prevalence of 13.2% in patients >75 years
  - Next cardiovascular epidemic in developed countries
  - Severe aortic stenosis (AS) is the most common valvular condition that requires intervention




ONSET SEVERE SYMPTOMS
Survival, %
100
80
60
40
20
0
Latent Period
(Increasing Obstruction, Myocardial Overload)
0
40
50
60
70
Age, y
Angina
Syncope
Failure
0
2
4
6
Average Survival, y
Survival, %
35
30
25
20
15
10
5
0
5-year survival rates
23
4
12
30
28
3
Breast Cancer
Lung Cancer
Colorectal Cancer
Prostate Cancer
Ovarian Cancer
Severe Inoperable AS*

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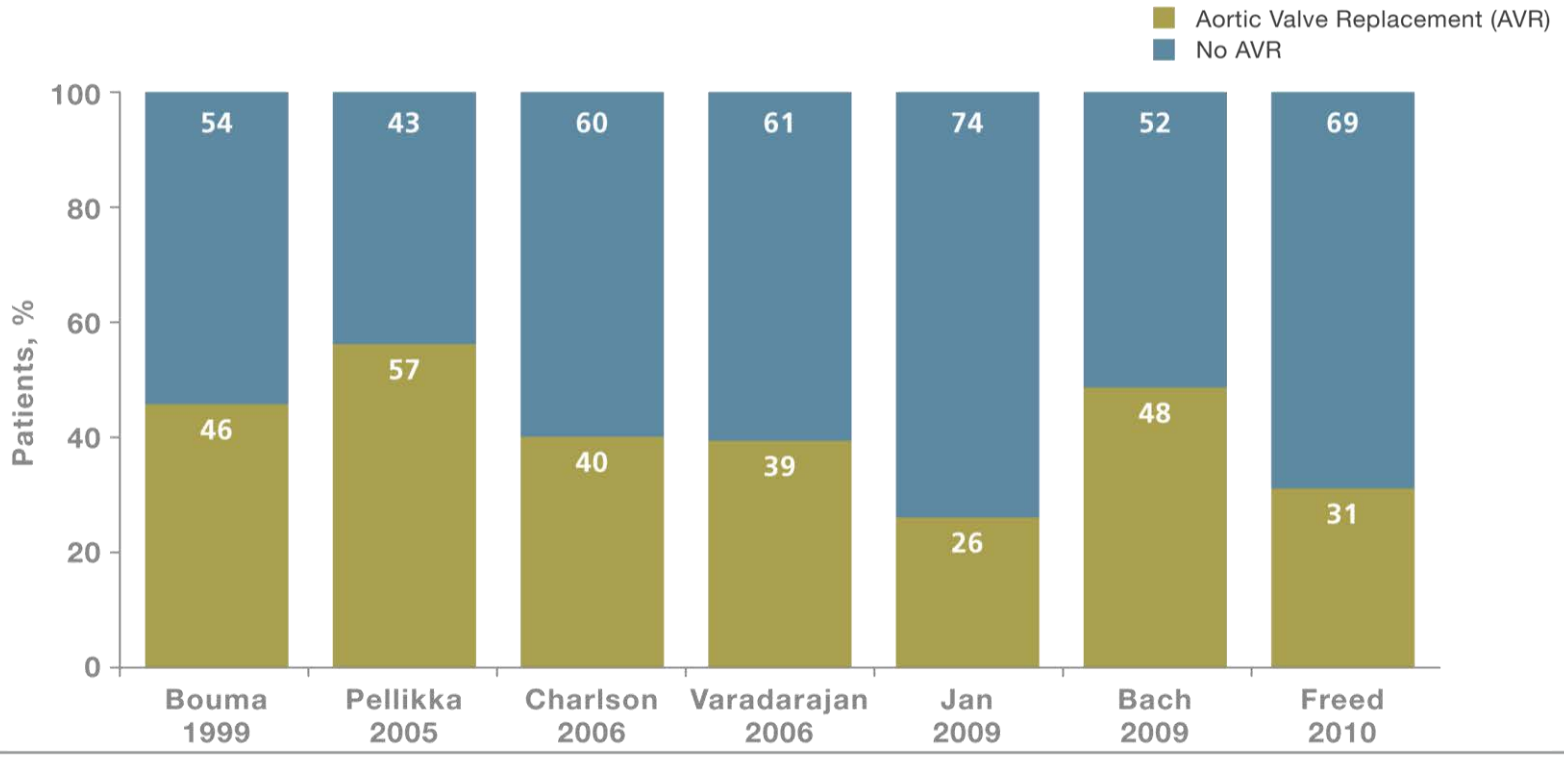
Therapeutic Need

- Surgical Aortic Valve Replacement (SAVR)
  - Traditionally ~ 50% of AS patients ineligible due to excessive peri-operative risk



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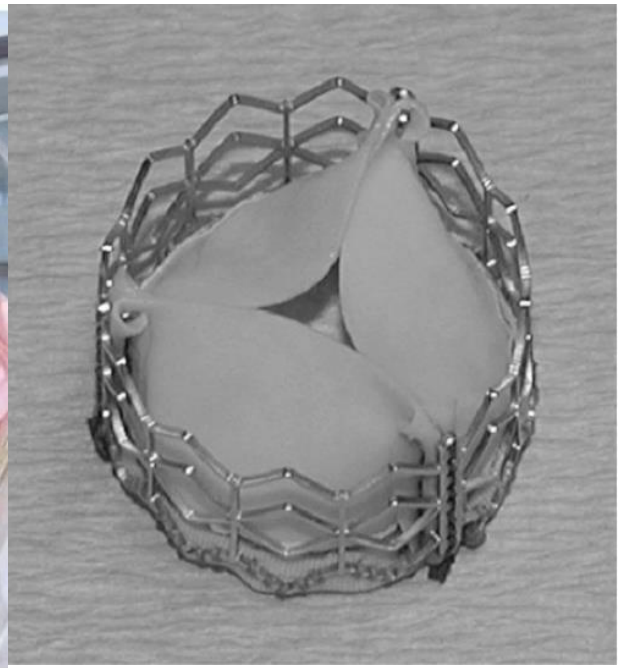
Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis

First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD



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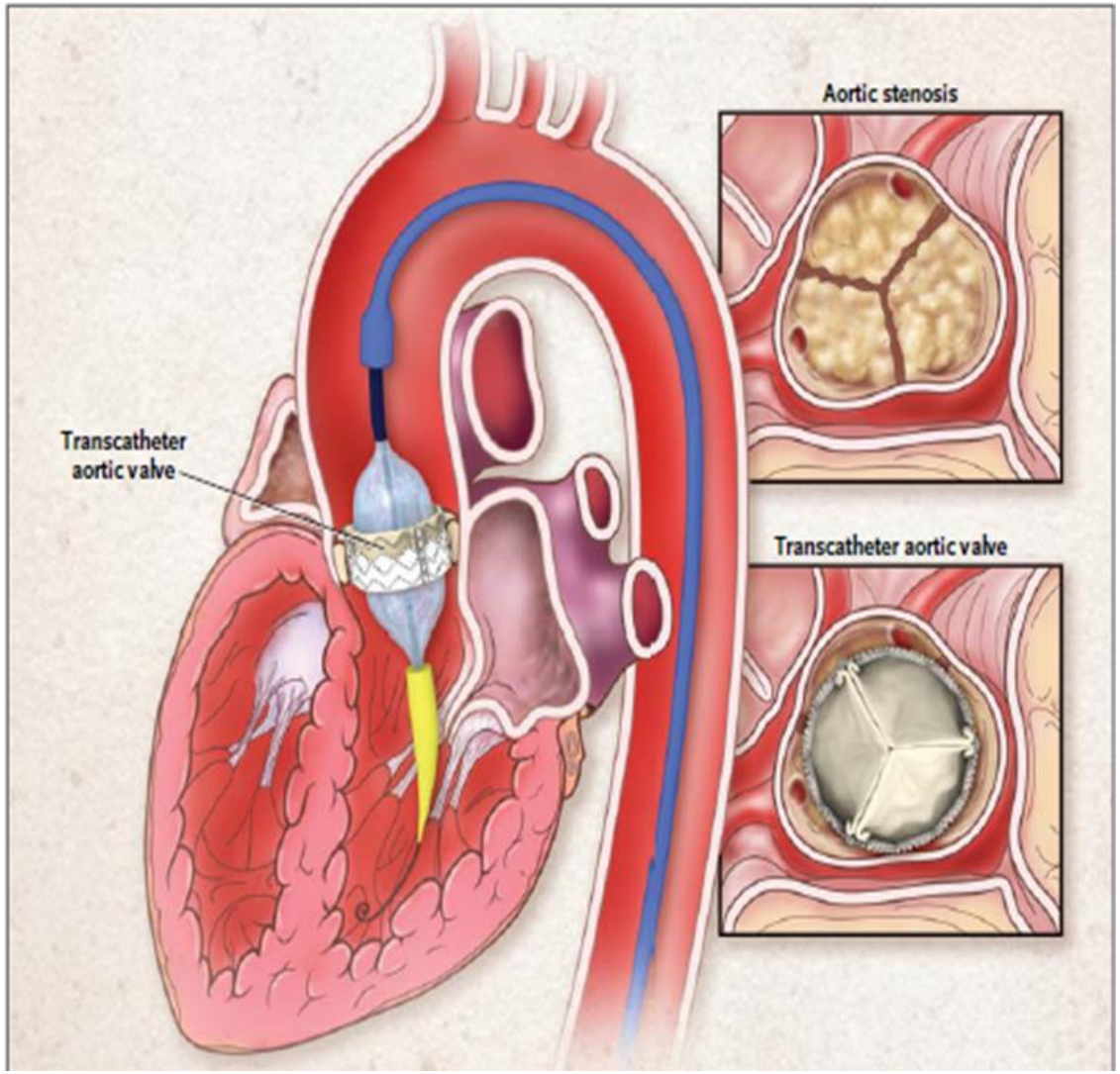
TAVR



- Majority are awake
- Fully percutaneous
- Median Length of hospital stay
  - 2 days

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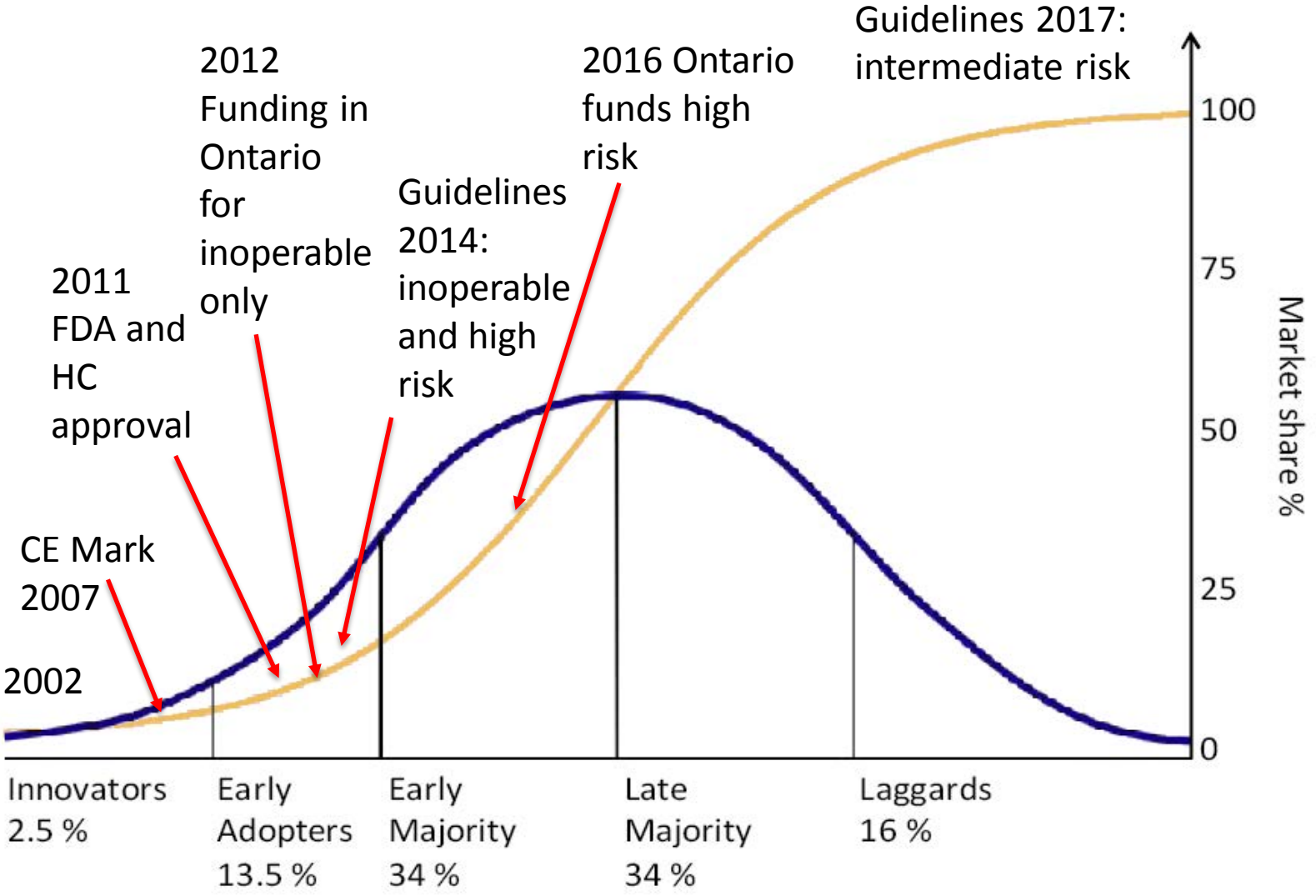
Life Cycle of TAVR



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RWE in TAVR: how it happened

- Pre-regulatory
  - None
  - Regulatory approval delayed till publication of landmark PARTNERs trials

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Oct, 2010

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

June, 2011

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RWE in TAVR: how it happened

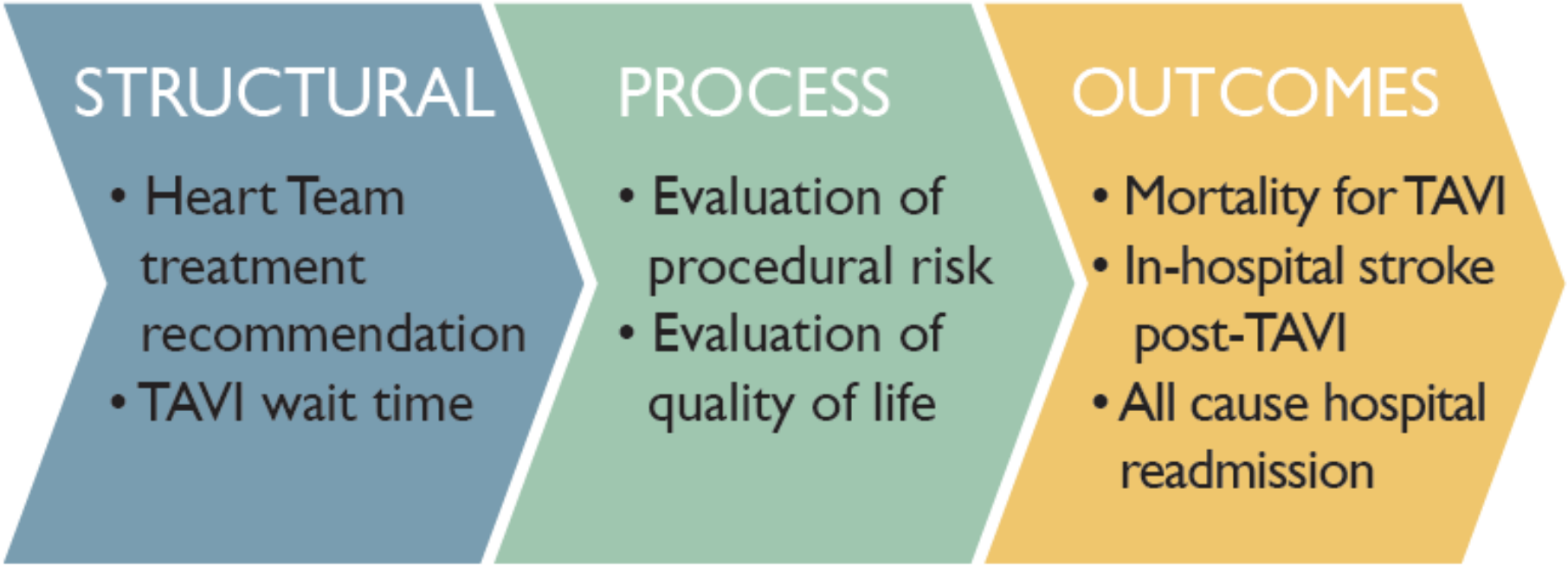
- Pre-regulatory programs had initiated with foundation funds
- 10 programs in Ontario
- First in 2007

RWE in TAVR: how it happened

- Post-Regulatory
  - Funding 2012
    - No RWE used in decision
    - Mandated that precondition for funding would be mandatory data entry into clinical registry to be held by CorHealth Ontario (CCN)
    - However,
      - No clear a priori objective for data
      - No direction on data elements
      - No funding for data collection

RWE in TAVR: how it happened

- Canadian Cardiovascular Society (CCS) developed quality indicators for TAVR



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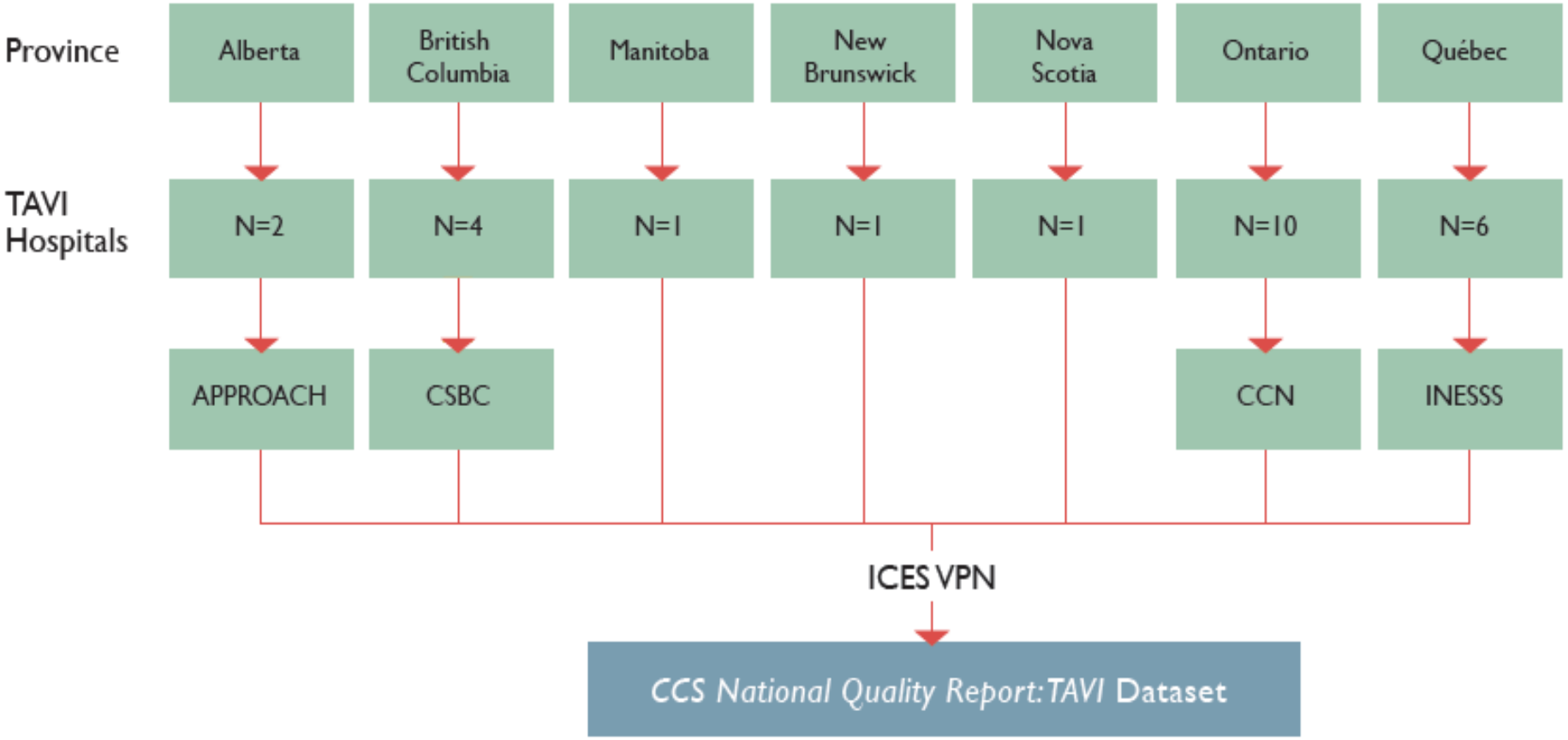
RWE in TAVR: as it happened



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RWE Data in TAVR: findings

- Data quality:

	Ontario	Québec	British Columbia	Alberta - Calgary Site	Alberta - Edmonton Site	Manitoba	New Brunswick	Nova Scotia
Heart Team Recommendation	●	■	♦	♦	♦	♦	♦	♦
Wait time 1	■	●	♦	♦	♦	♦	♦	♦
Wait time 2	■	●	♦	♦	♦	♦	♦	♦
Total wait time	♦	●	♦	♦	♦	♦	♦	♦
STS score	♦	♦	♦	♦	♦	♦	♦	♦
Quality of life pre and 1-year post	●	●	■	●	♦	●	■	●
30-day mortality	♦	♦	♦	♦	♦	■	♦	♦
1-year mortality	♦	■	♦	♦	♦	■	♦	♦
In-hospital stroke	♦	♦	♦	♦	♦	♦	♦	♦
30-day readmission	♦	●	♦	■	♦	■	♦	♦
1-year readmission	♦	●	♦	■	♦	■	♦	♦

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RWE in TAVR: findings

- ACCESS

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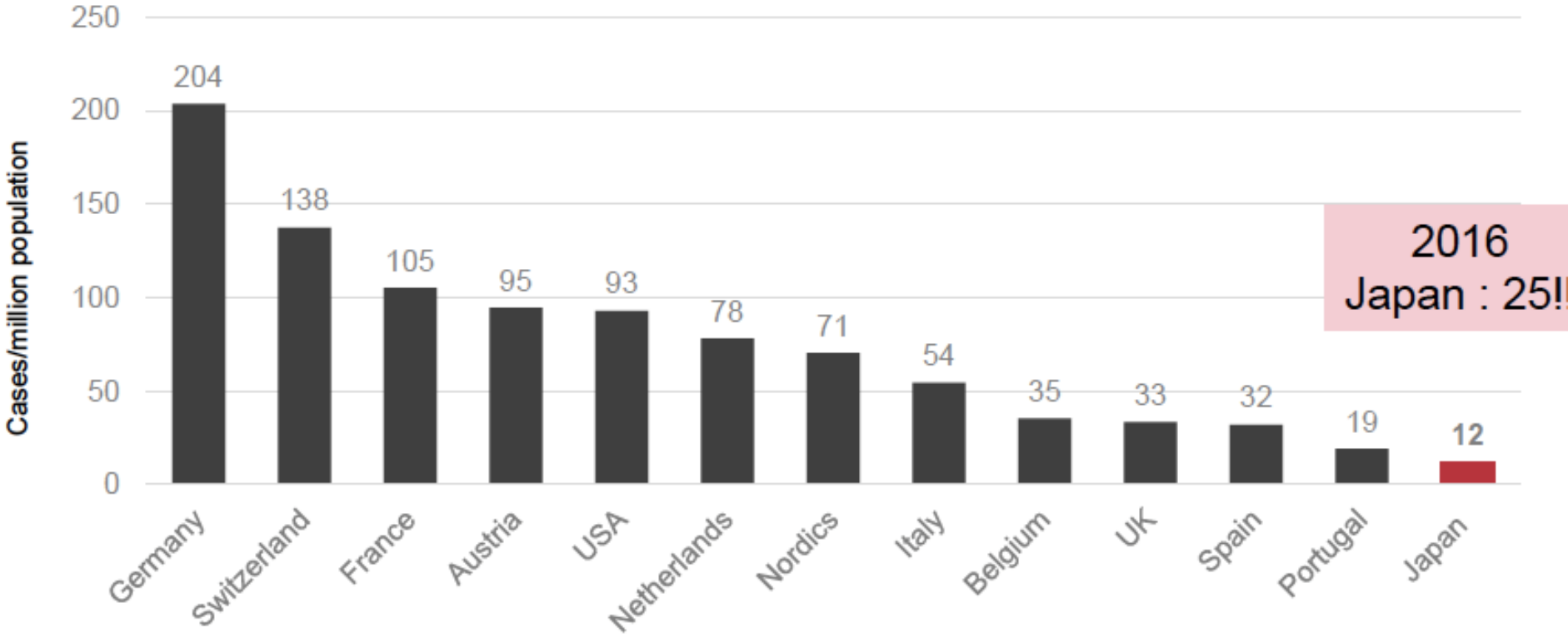
ACCESS

Procedures / million inhabitants in 2015



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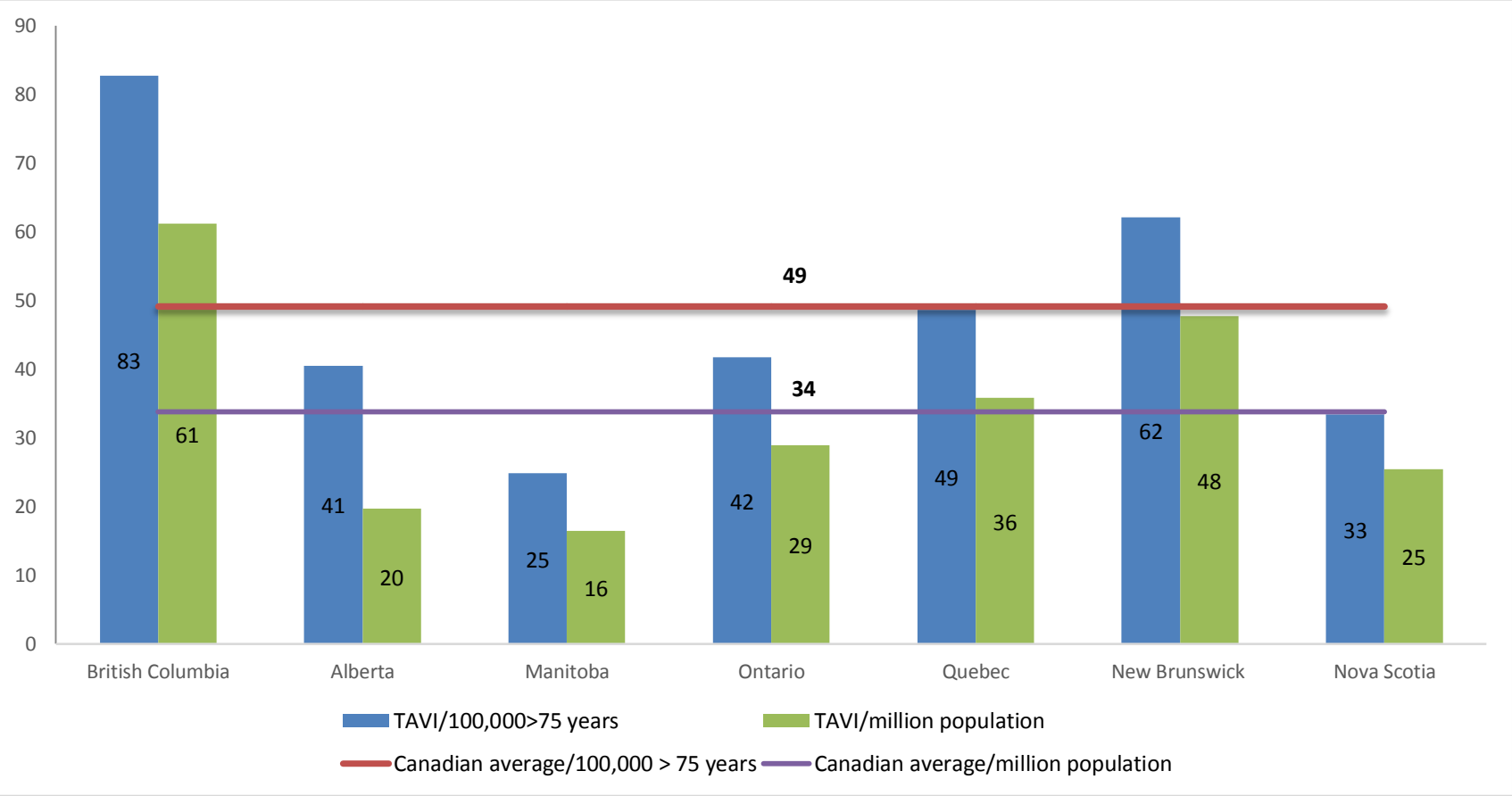
Canada

- April 1st 2013- March 31st 2014: 1,136 cases



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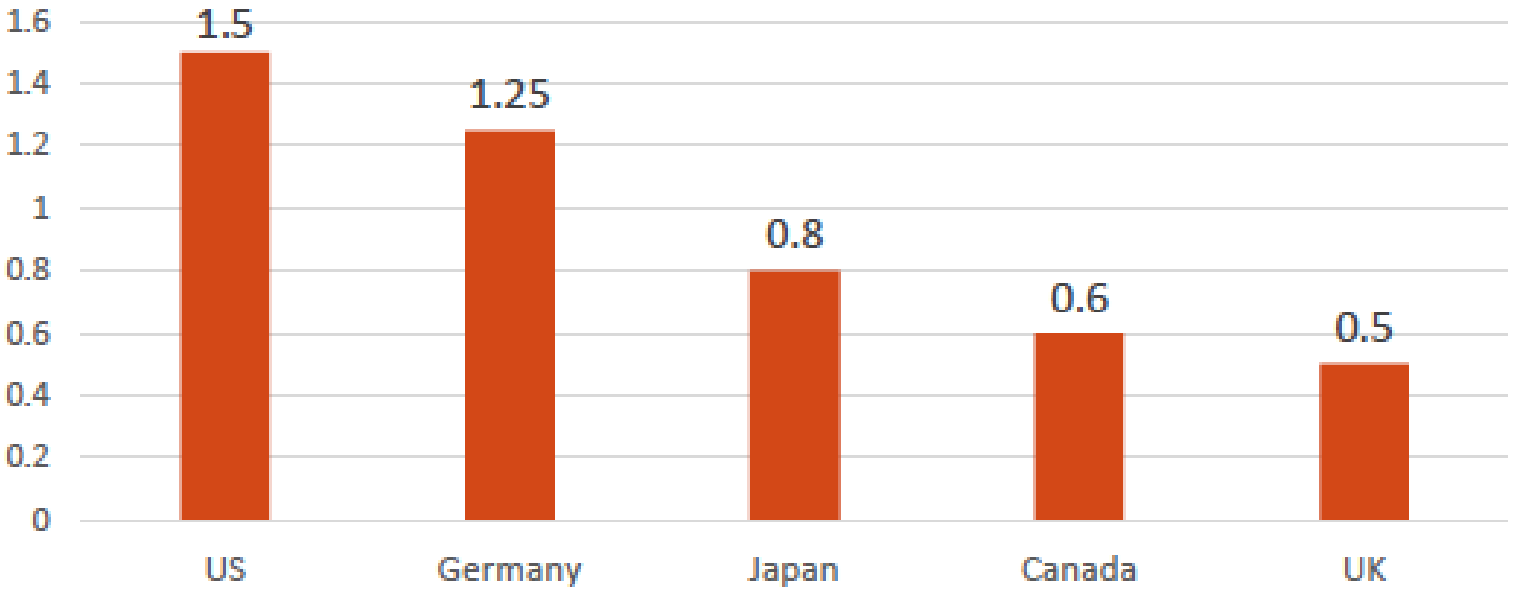
Valve Centers/Million Population



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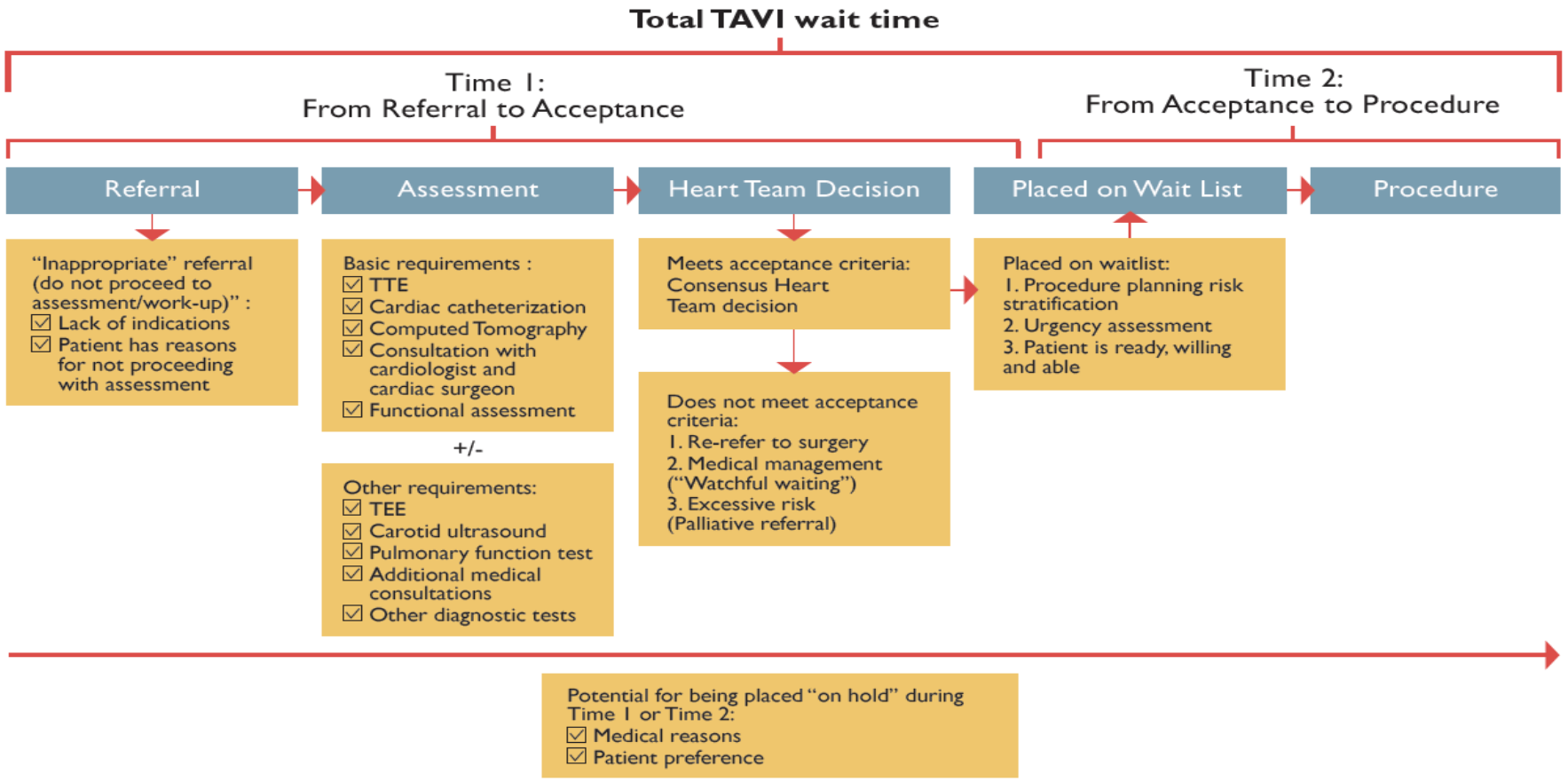
RWE: Access

- Exponentially increasing demand with limited capacity



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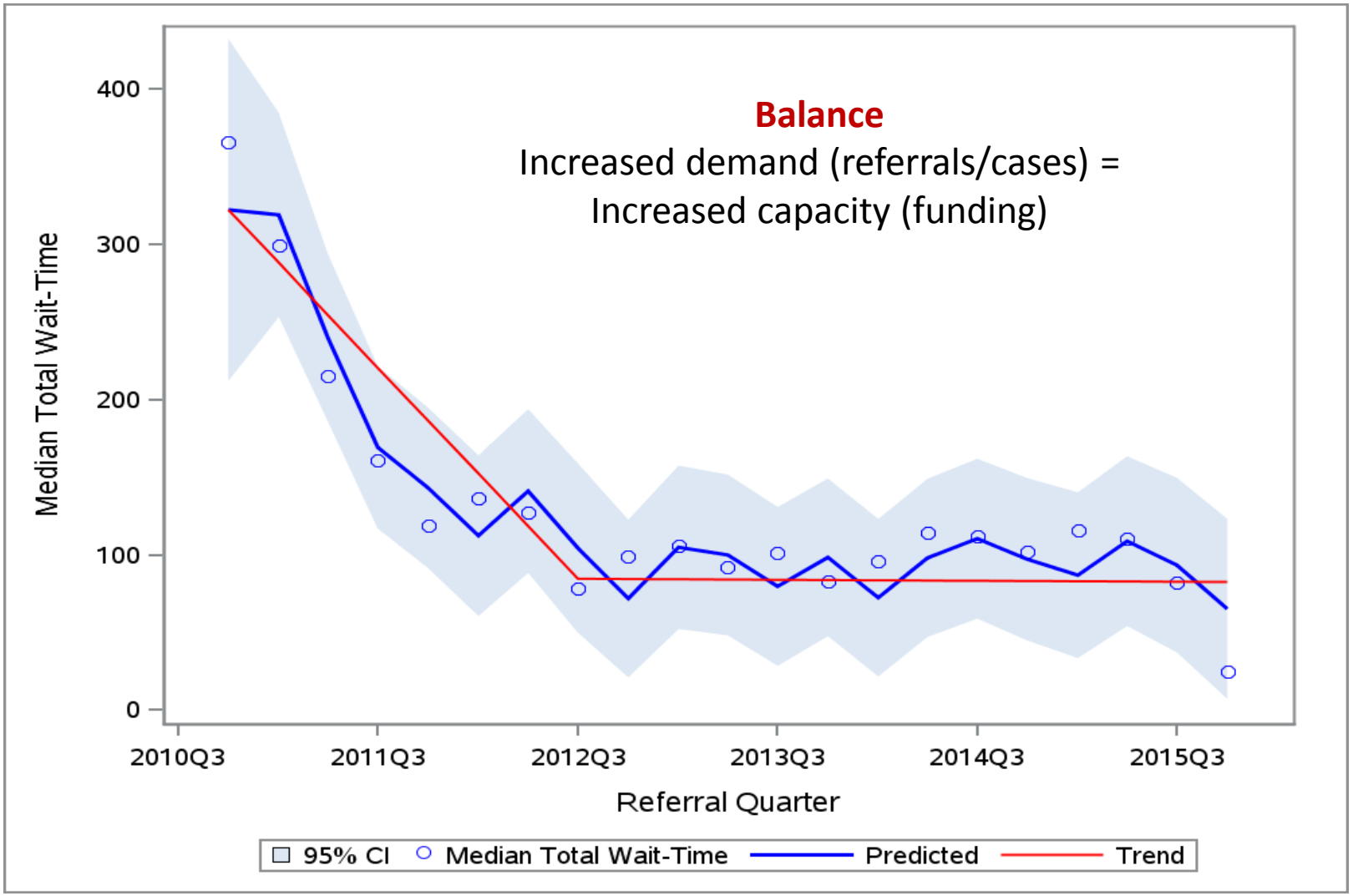
RWE: Wait-times

TAVI WAIT TIME					
	Ontario (N=396)	Québec (N=294)	British Columbia (N=270)	Alberta, Manitoba, New Brunswick, Nova Scotia (N=162)	Canada (N=1,122)
Total Wait Time (median and IQR, days)	105 (58-183)	n/a	91 (57-139)	145 (79-219)	106 (59-172)
Missing data (%)	0.2	100	0	0	26.3

- Canadian Wait-Time Alliance:
  - Maximum recommended wait-times for surgical aortic valve replacement
    - 14 days for urgent cases
    - 42 days for elective cases

Wait-times



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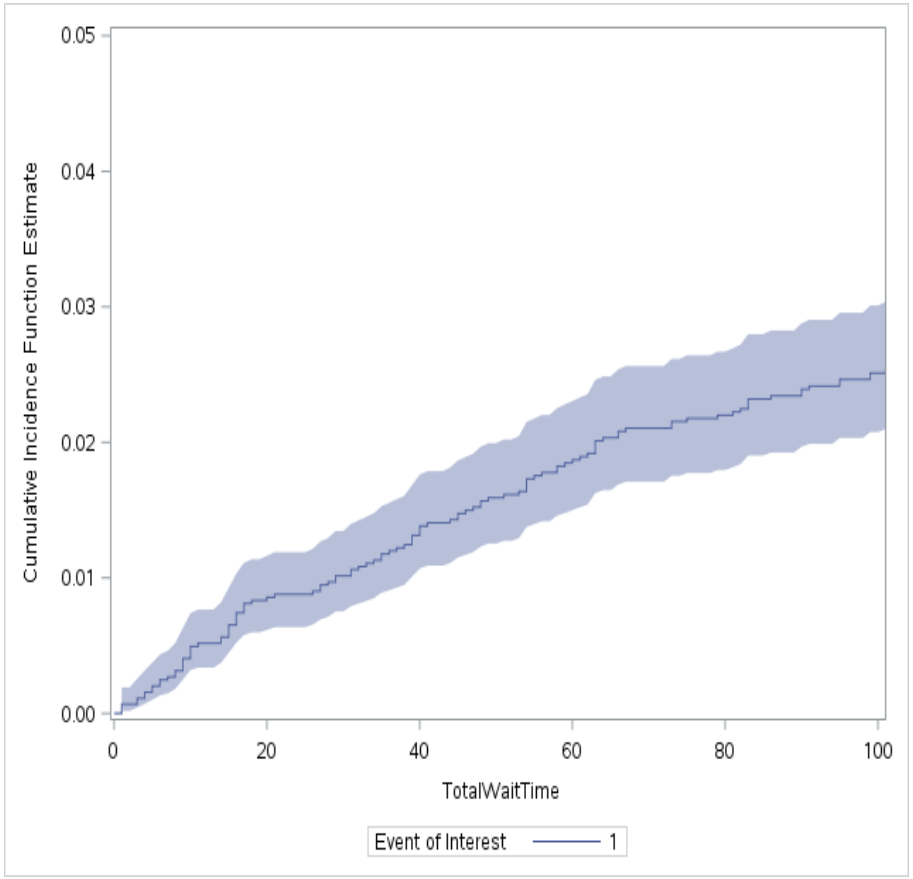
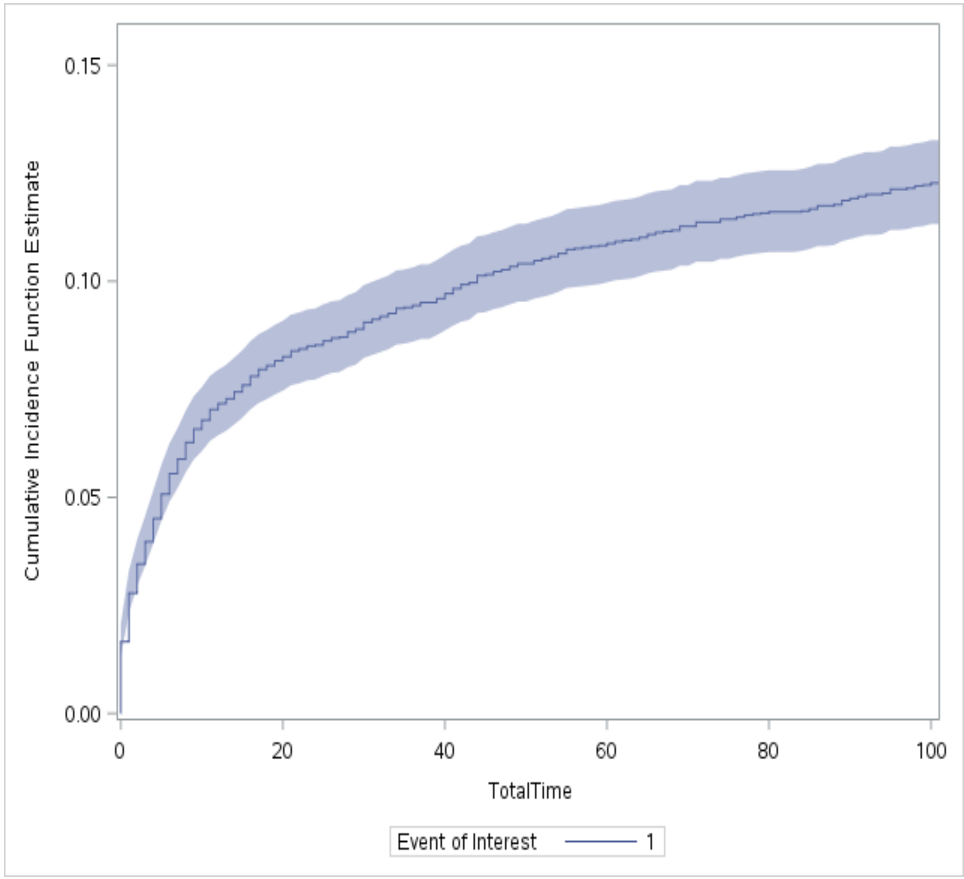
Wait-time consequences





Wait-time mortality: ~4.5%

Wait-time hospitalization for heart failure: ~15%

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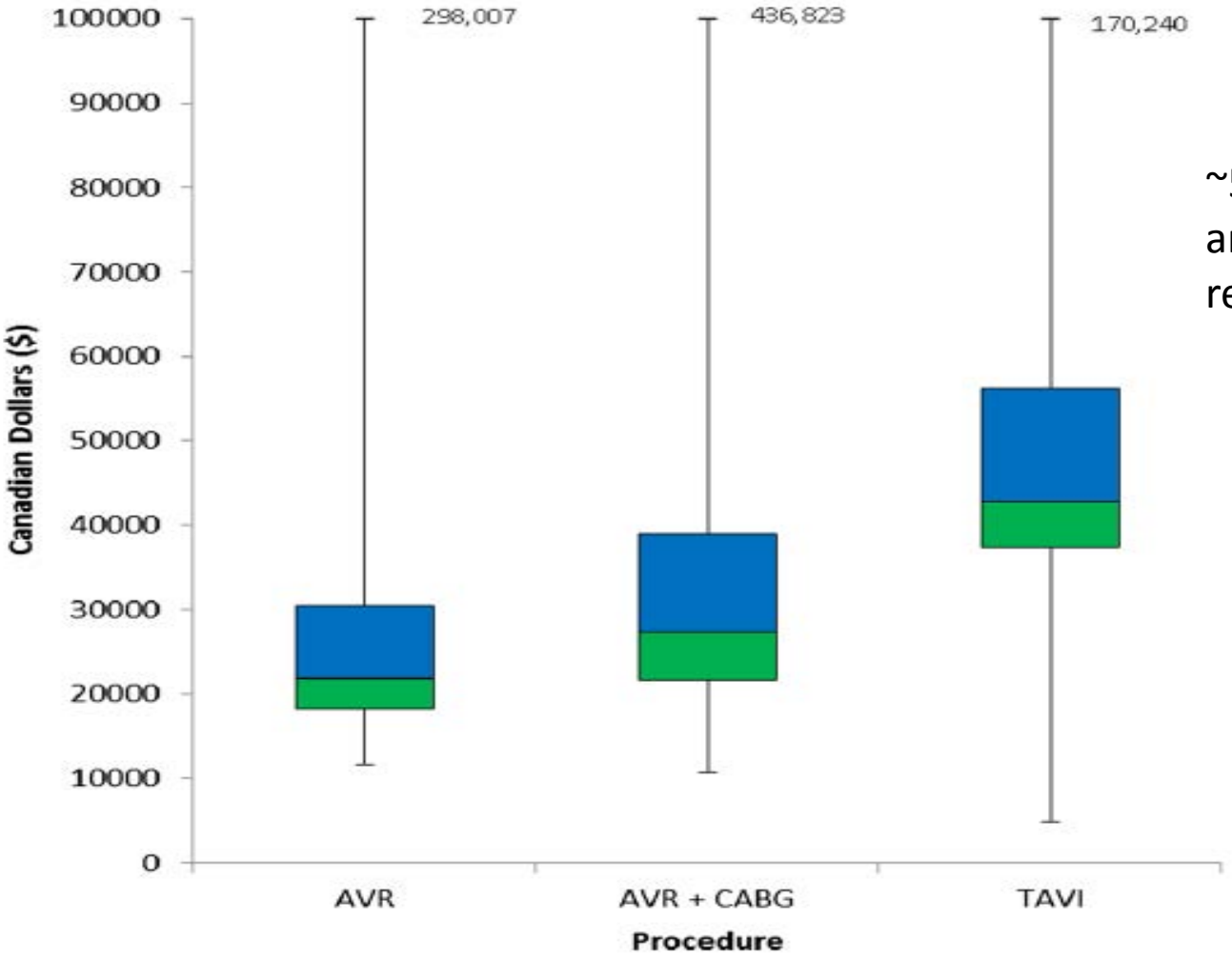
Canada



~50% of costs are device related

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Modifiable Drivers of Costs

Factor	Rate Ratio	P-value
Non-transfemoral	1.31 (1.18-1.45)	<0.001
Length of stay >3 days	1.42 (1.14-1.78)	<0.001
Long ICU stay >4 days	1.30 (1.2-1.41)	<0.001

RWE in TAVR

- Limited impact on regulatory and reimbursement process
- Substantial insights into implementation and dissemination

RWE in TAVR – missed opportunities

SPECIAL ACCESS
- Earlier initiation
- Define evidentiary needs
- ?Adaptive pathway

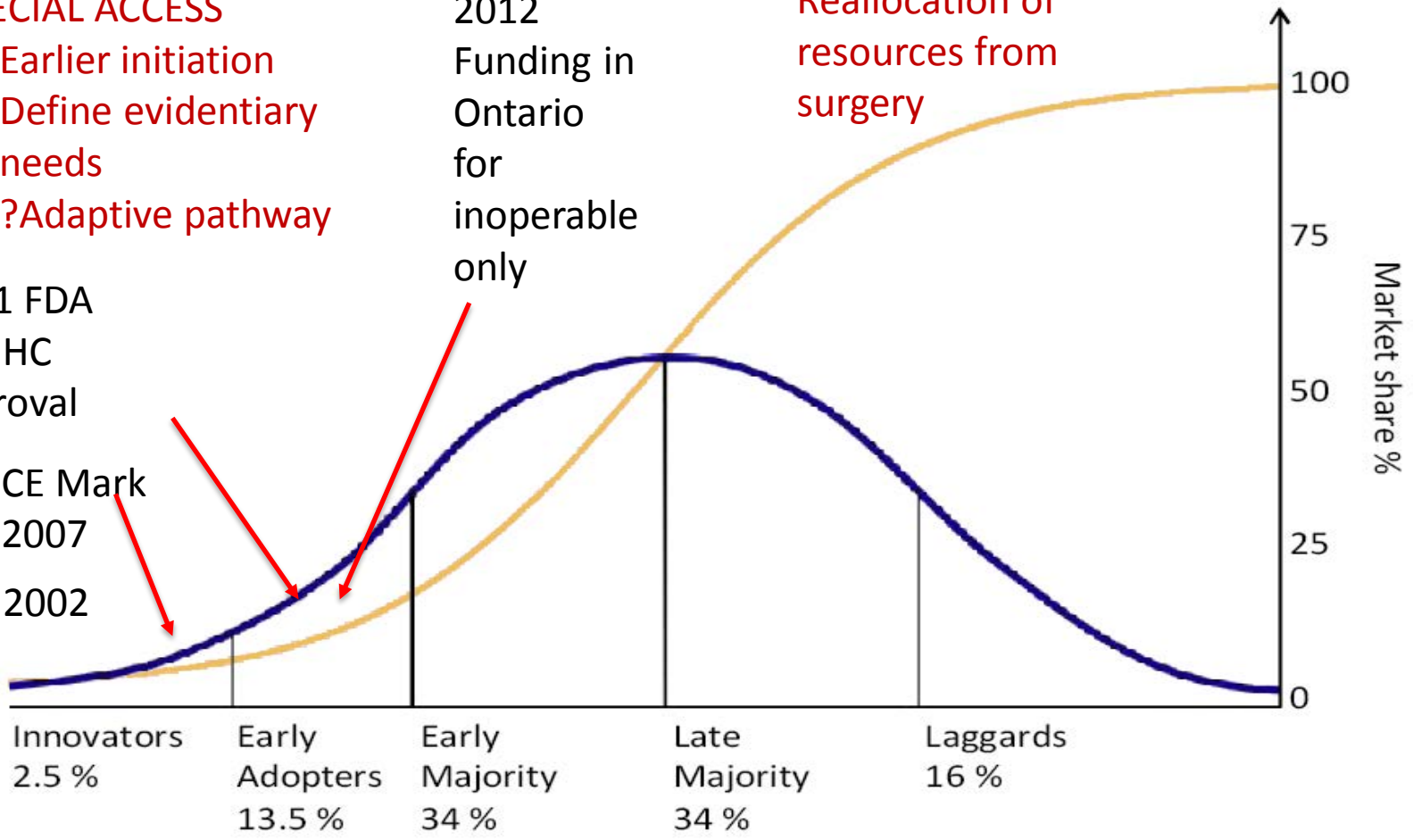
2012 Funding in Ontario for inoperable only

Dis-investment? Reallocation of resources from surgery

2011 FDA and HC approval

CE Mark 2007

2002



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Conclusions

- In rapidly changing landscape, early engagement to define the objectives of RWE collection is critical

- RWE is resource intensive
  - Prone to poor quality if front line health care providers are not convinced as to its utility

- Iterative re-evaluations of regulatory and reimbursement decisions, informed by RWE will potentially facilitate **earlier**, and **more efficient** dissemination and greater access

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