

Improving Evidence for Clinical and Health Policy Decision Making

Doing the Right Thing – Edmonton, Alberta



Sean Tunis, MD, MSc | 22 February 2018

CENTER FOR MEDICAL TECHNOLOGY POLICY

Overview

- Overview of CMTP
- Affordability, Evidence, Uncertainty
- Intro to “Reimbursement Science”
- Core Outcomes
- The coreHEM project

CMTP Basics

Provides a multi-stakeholder platform:

- To support projects intended to improve the quality, relevance, and efficiency of clinical research
- With a focus on “post-regulatory decision makers”
- Mindful of growing attention to value and affordability
- Recognizing the need to sustain investment and innovation in life sciences



Better Evidence.



Better Decisions.

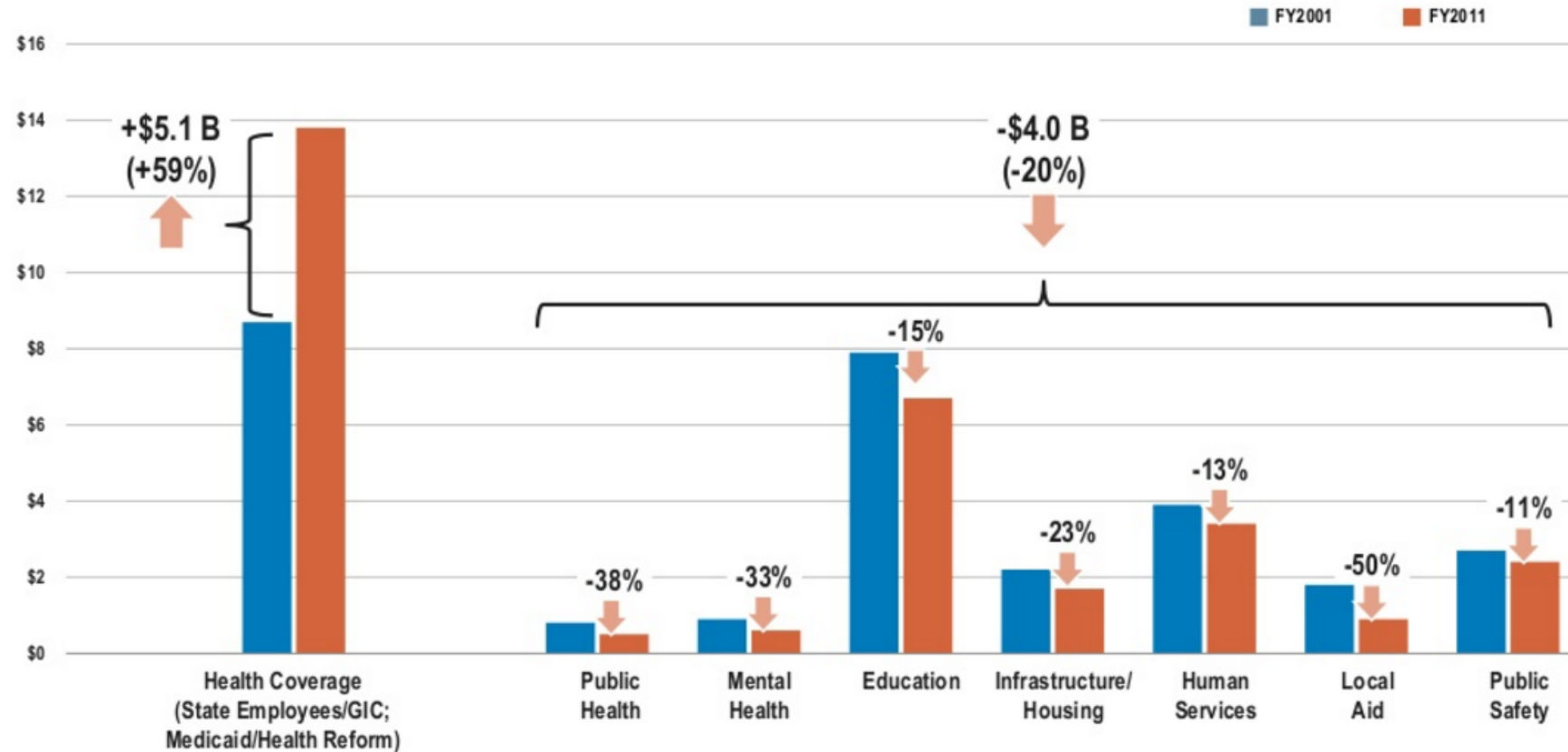


Better Health.

Affordability, Evidence and Uncertainty

Cost Concerns – Even at 18% GDP

STATE BUDGET, FY2001 VS. FY2011 (BILLIONS OF DOLLARS)



NOTE Dollar figures are inflation adjusted using a measure specific to government spending as developed by the U.S. Bureau of Labor and Statistics.

World Health Assembly resolution on Health Intervention and Technology Assessment in Support of UHC

“Every pound can only be spent once. If we spend it unwisely... then we risk harming other people whose care will be adversely affected...

It is vital that priority setting is an **evidence-informed, procedurally fair process** that defines what will be covered through universal health coverage.”

Prof David Haslam, Chair of NICE, addressing the 25th World Health Assembly, Geneva, 2014



World Health
Organization

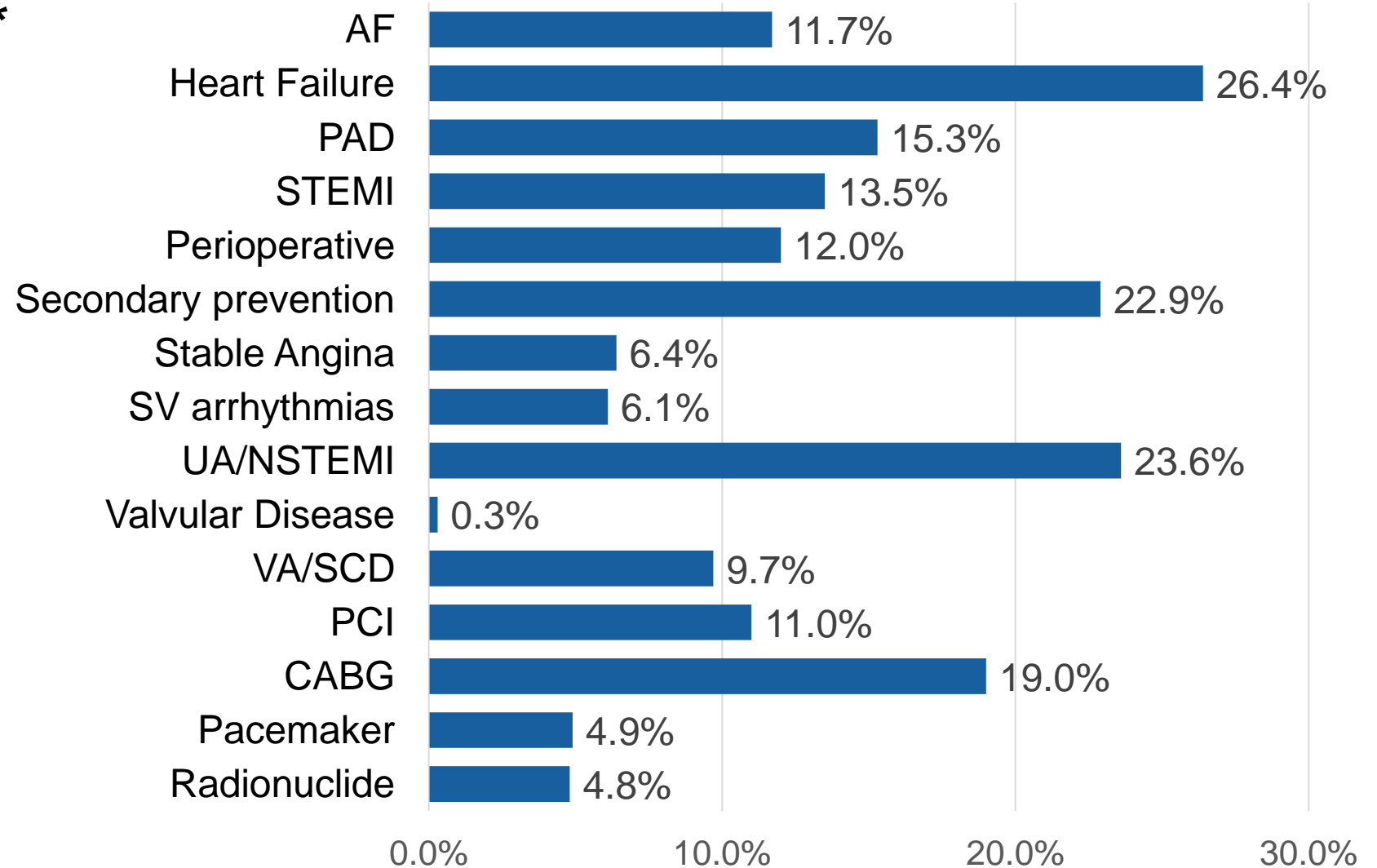
SIXTY-SEVENTH WORLD HEALTH ASSEMBLY
Provisional agenda item 15.7

A67/33
14 March 2014

**Health intervention and technology assessment in
support of universal health coverage**

Level of Evidence A

Current Guidelines*



**Guidelines expressing
Level of Evidence*

The Problem – Simply Stated

“Because of the paucity of high quality evidence, the data available – though voluminous – may have little meaning or value for informing clinical practice”

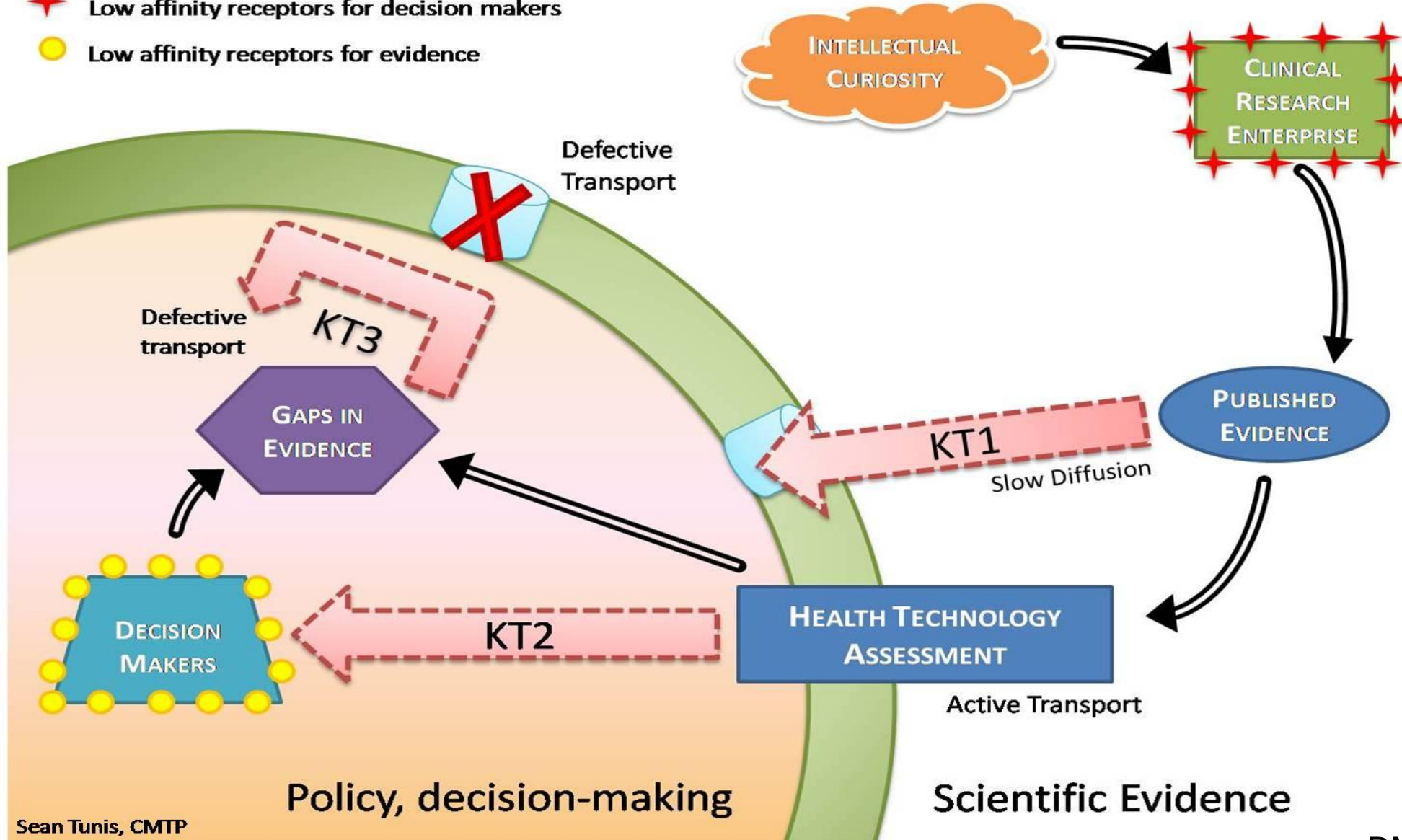
Abernethy AP, Coeytaux RR, Carson K, et al. Technology assessment report: report on the evidence regarding off-label indications for targeted therapies used in cancer treatment. Agency for Healthcare Research and Quality 2010

The Evidence Paradox

- 19,000+ RCTs published every year
- Tens of thousands of other clinical studies
- Systematic reviews intended to inform payers, guideline developers, patient education material routinely conclude that evidence is inadequate or poor quality

Molecular Basis of Uncertainty

- ★ Low affinity receptors for decision makers
- Low affinity receptors for evidence



Sean Tunis, CMTP

BMJ, 2013

Regulatory and Reimbursement Science

Regulatory Science

“Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.”

Regulatory Science

Why Regulatory Science is Important

- Clarity and consistency essential for regulated industries
- Several legitimate social objectives:
 - Ensure that marketed products are safe and effective
 - Promote rapid patient access to promising new products
 - Promote life sciences innovation
- These objectives create tension with respect to evidence standards
- Regulatory science provides an opportunity to develop a scientific framework that reflects multiple objectives
- FDA/EMA provide platforms to support this process
 - Largely funded through industry user fees

“Reimbursement Science”

“Reimbursement Science is the science of developing new tools, standards, and approaches to assess the comparative effectiveness and value of products covered by public and private payers.”

Defining Core Outcomes: An Experiment in Reimbursement Science

Value – A matter of perspective



*Patients have a unique perspective and will consider issues differently than regulators, manufacturers, scientists, clinicians, and payers.**



Slide from Mark Skinner

Value: Basic Definition










Health outcomes achieved
per dollar spent

IOM 2006





































Health outcomes are
inherently condition specific
and multi-dimensional

Michael Porter, NEJM, 210

Ratings and Test Results

Brand & Model		Overall Score	Speed	Power	Run Time	Charge	Handling	Noise at	Weight (lbs)	Volts
✓	Hitachi DS18DMR  Tougher job drill/drivers	85	●	●	●	●	○	○	8	18
✓	Makita LXT BDF451  Tougher job drill/drivers	82	●	●	●	●	●	○	4.9	18
✓	Milwaukee 0824-24  Tougher job drill/drivers	81	●	●	●	●	○	○	6.2	18
✓	Panasonic EY6432GQKW  General use drill/drivers	80	●	○	●	●	●	○	4.8	15.6
✓	Bosch 33618-2G  Tougher job drill/drivers	80	●	●	●	●	○	○	5.9	18
✓	Makita 6347DWDE  Tougher job drill/drivers	79	●	●	●	●	○	○	5.4	18
✓	Ryobi P813  General use drill/drivers	77	●	○	●	●	○	○	4.8	18
✓	Makita 6980FDWDE  Cordless impact drivers	75	●	●	●	●	●	●	3.6	12
✓	Ryobi P230C  Cordless impact drivers	74	●	●	○	●	●	●	4.6	18

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A recent Cochrane systematic review

Non-steroidal anti-inflammatory drugs versus corticosteroids for controlling inflammation after uncomplicated cataract surgery (Review)

Juthani VV, Clearfield E, Chuck RS

Mean

- Primary outcome – “~~proportion of patients with~~
intraocular inflammation ~~at 1 week of follow-up~~
after surgery”
by 1 month
- 48 included trials
 - 0 trials!
 - 7 trials
 - 11 trials

Core Outcome Sets

“An agreed standardised set of outcomes that should be measured and reported, as a minimum, in all clinical research in specific areas of health or health care”

Definition from the COMET Initiative

coreHEM

A Core Outcome Set for Gene Therapy in Hemophilia

coreHEM



Green Park Collaborative

A partnership for innovation and effectiveness



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders



coreHEM: The Journey



From the HAAB, Amsterdam, Jan 16, 2017



To Baltimore, Maryland, Nov 15, 2017

coreHEM: Goals & Rationale

- Establish a “core set” of outcomes to measure the effectiveness and value of gene therapy in hemophilia
- Outcomes associated with a “cure” may be different than for existing treatments
- Outcomes should focus on perspective of patients, care givers, and clinicians
- The same core outcomes should be measured in all GT trials, to allow informed comparisons and decisions

coreHEM: Core Organizations



Alfonso Iorio



Primary mission is to disseminate high-quality, high impact research
Member and contributor of GRADE working group and the Cochrane Collaboration



Mark Skinner



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders



Sean Tunis



Green Park Collaborative
A partnership for innovation and effectiveness

GPC is a multi-stakeholder forum that seeks consensus on evidence needs for regulatory approval and market access.

coreHEM Sponsors / Partners



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders



B:OMARIN®



Shire



St. Jude Children's
Research Hospital

uniQure

OBSERVERS



Green Park Collaborative

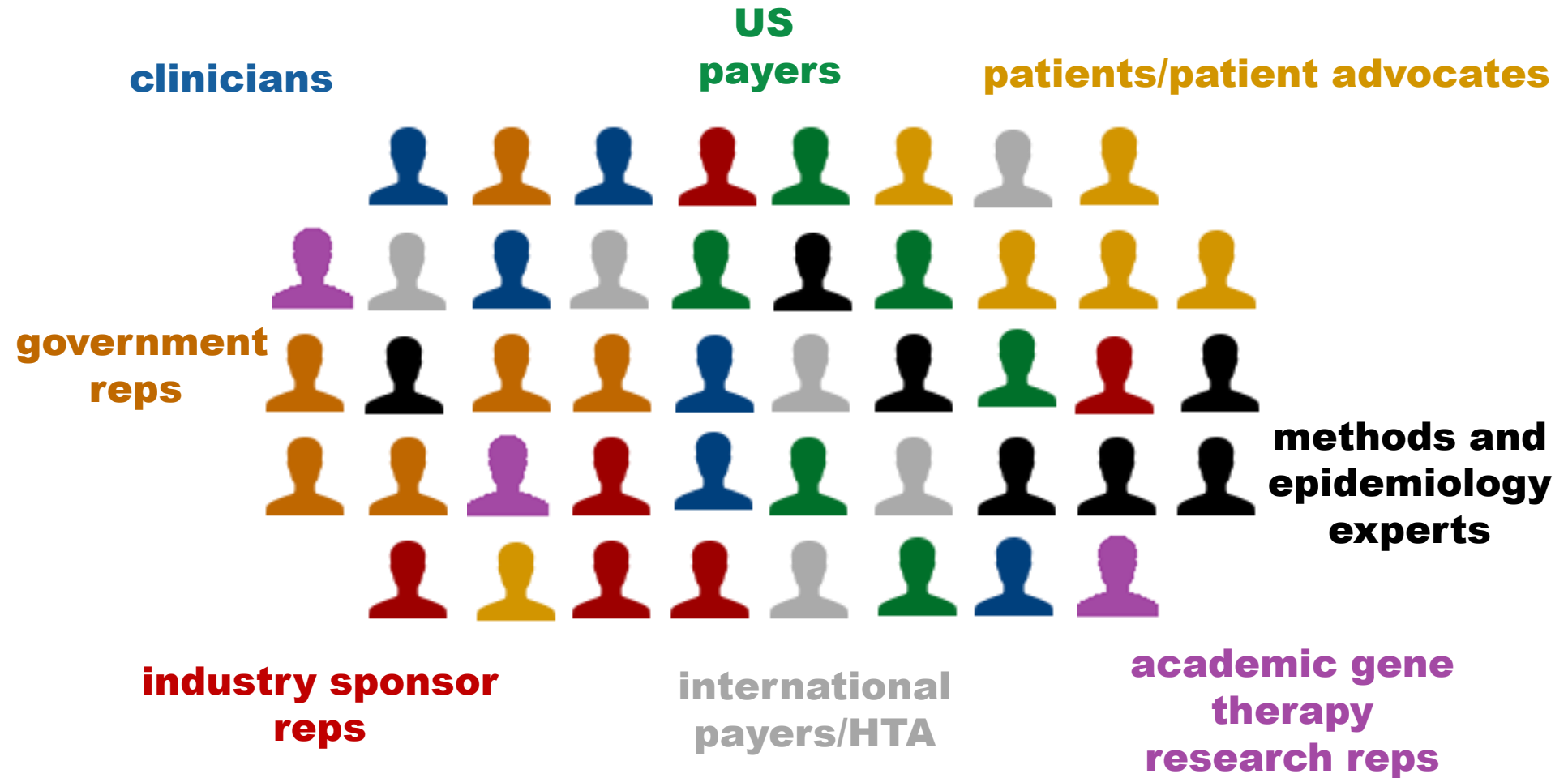
- A multi-stakeholder forum to clarify the evidence expectations of public and private payers
 - Informed by input from patients, clinicians, and regulators,
 - Focus on comparative effectiveness and value
- Other Key Stakeholders
 - CMS, numerous private payers engaged
 - FDA, NIH, PCORI, AHRQ, VA, etc.
 - Ongoing involvement of life sciences
- Output / Activities
 - Develop “effectiveness guidance documents”
 - Condition and technology specific workshops

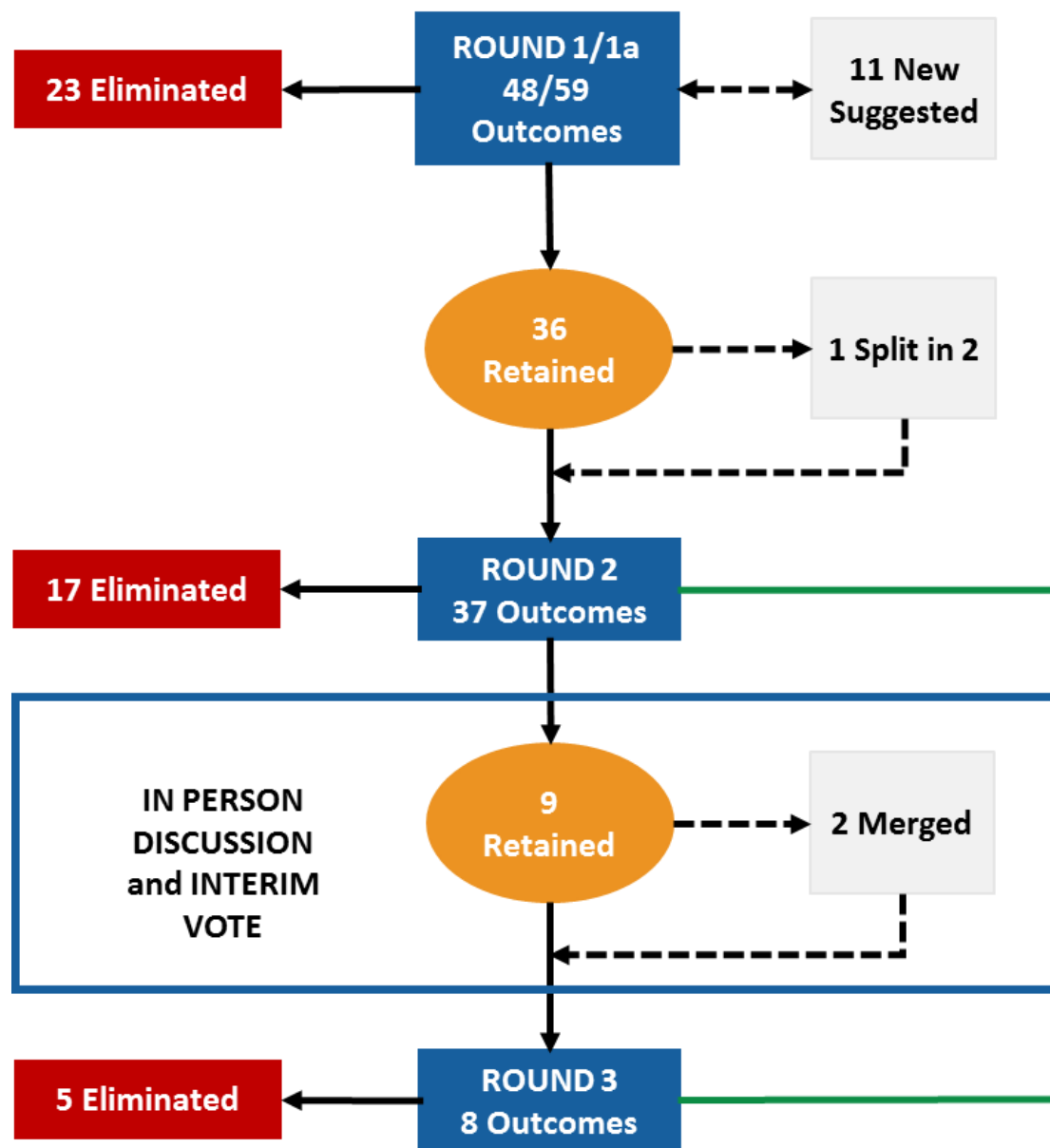


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coreHEM Stakeholders





coreHEM FINAL CORE SET

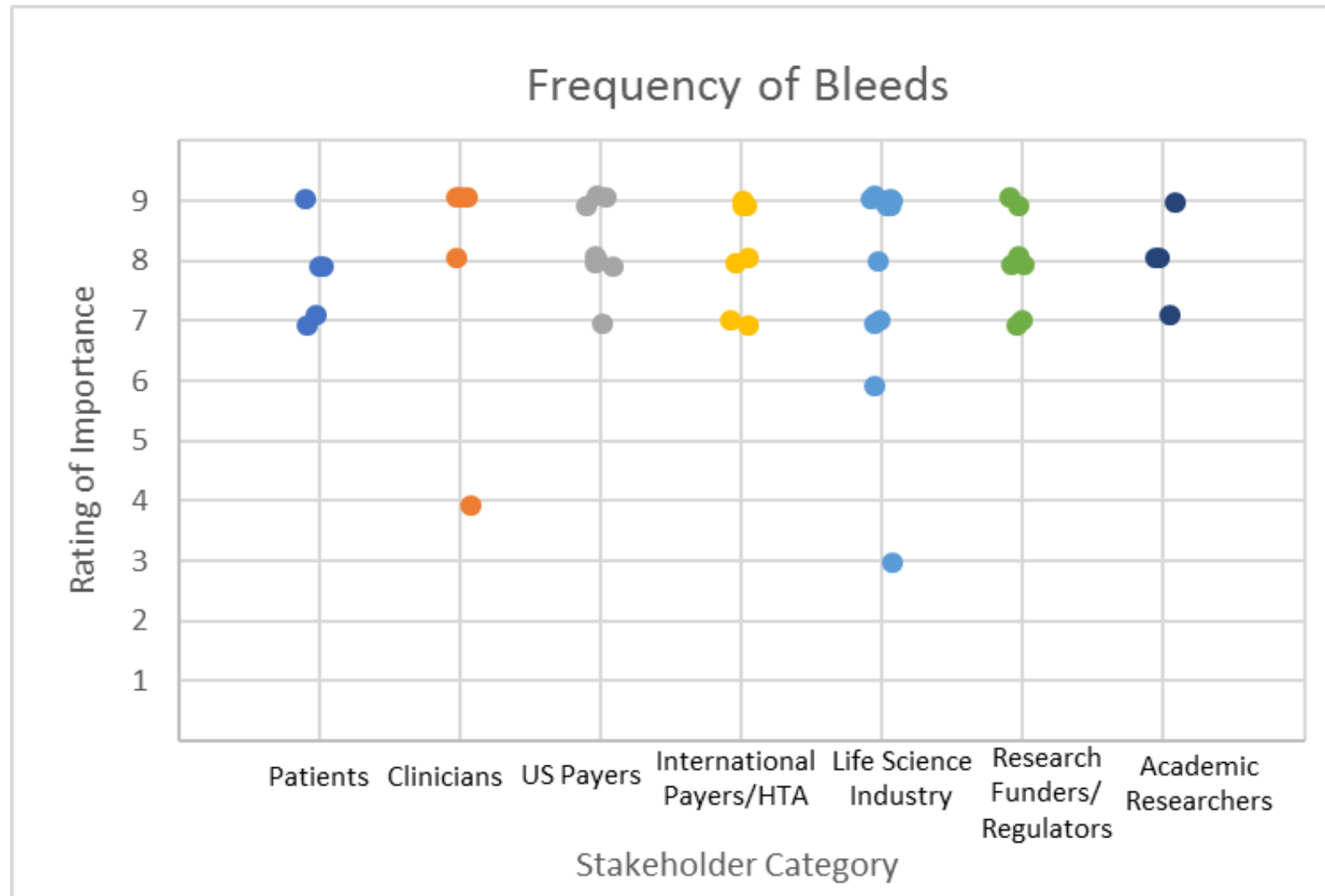
Consensus to Select	≥70% of all voters rated the outcome with a score of 7-9 (critical importance).
Consensus to Select (Patient-Important)	<70% of all voters rated 7-9, but the stakeholders in the patient group gave the outcome an average rating of ≥7.

3 SELECTED

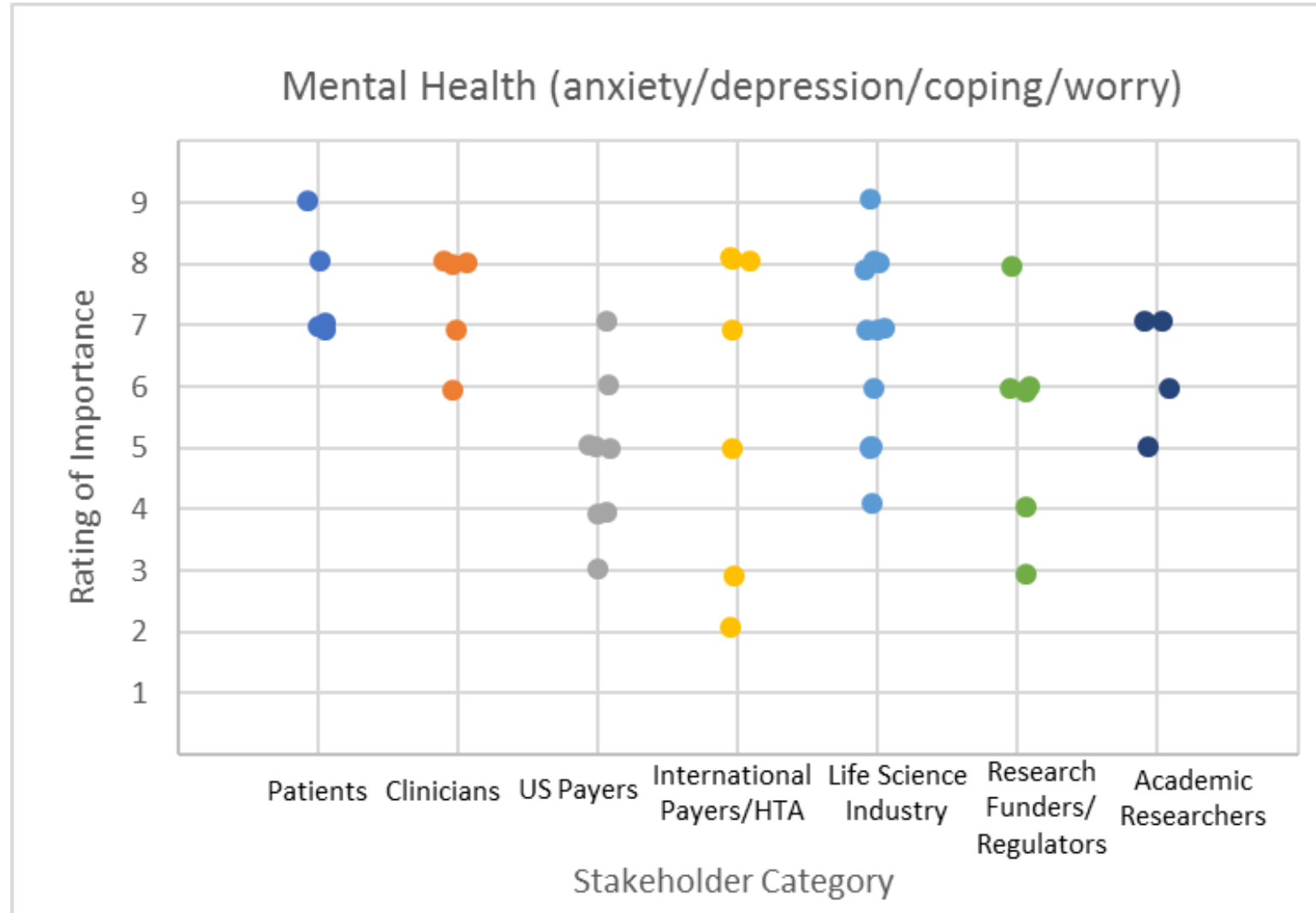
**8 ADVERSE
EVENTS
SELECTED**

3 SELECTED

EXAMPLE OF OUTCOME WITH HIGH CONSENSUS



EXAMPLE OF OUTCOME RETAINED DUE TO PATIENT IMPORTANCE



Core Outcomes: Effectiveness

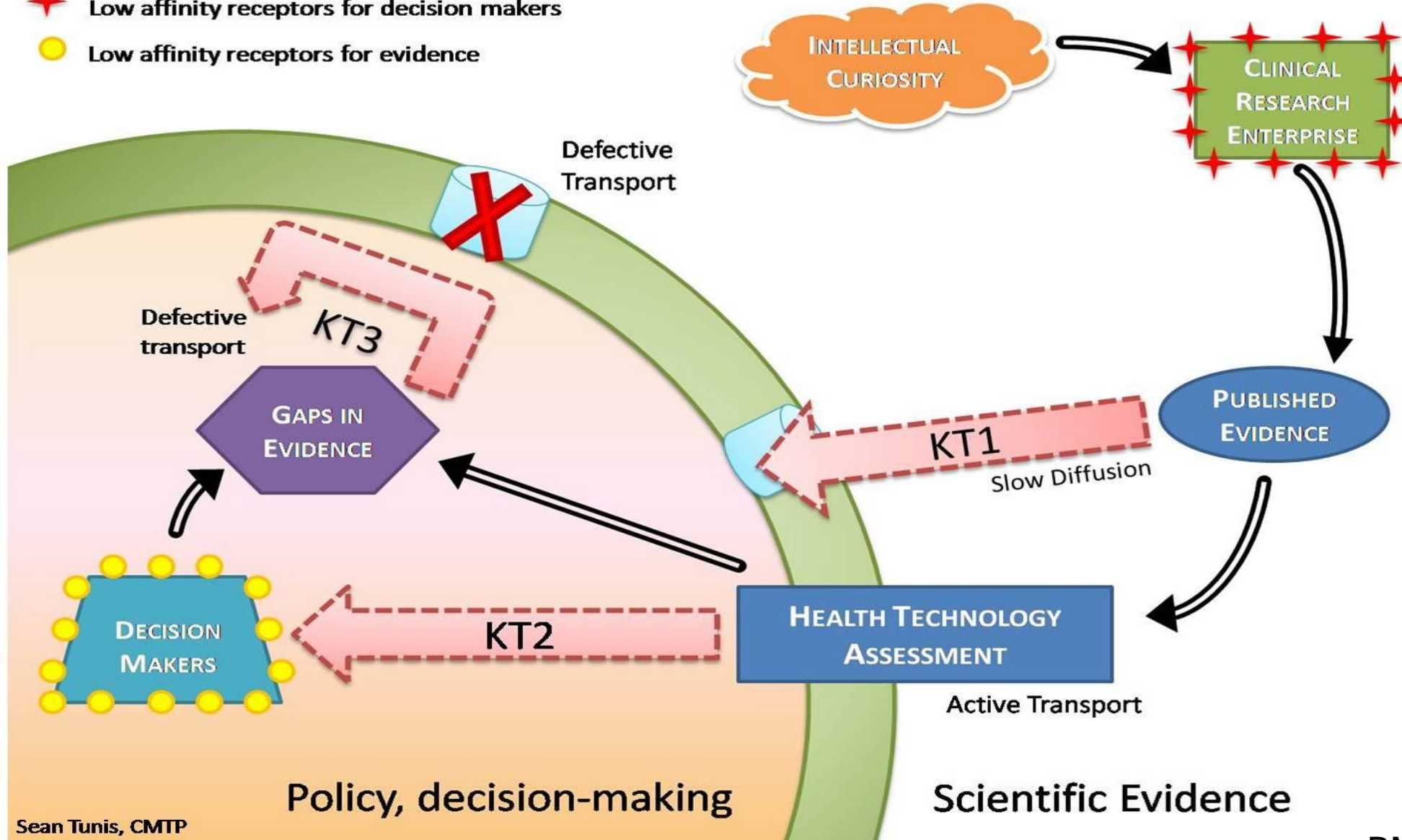
	Domain	Outcome
Core Outcome Set	Physiological/Clinical	Frequency of bleeds
		Factor activity level
		Duration of expression
	Pain/Discomfort	Chronic pain
	Resource Use	Healthcare Utilization (direct costs)
	Emotional Functioning	Mental health

Core Outcomes: Adverse Events

	Domain	Outcome
Important Adverse Events	Short-term Adverse Events	Liver Toxicity
		Short-term immune response to FVIII/FIX (inhibitor development)
		Immune response to gene therapy (cytotoxic)
		Thrombosis
	Long-term Adverse Events	Development of other disorders
		Vector integration into host genome
		Duration of vector-neutralizing response
	Mortality	Cause of death

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BMJ, 2013

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