OTTAWA GE³LS SERIES...

where Genomics, Public policy, and Society meet

G = **G**enomics *and its*

E^{3} = **E**thical, **E**nvironmental, **E**conomic,

L = **L**egal,

S = **S**ocial *aspects*

GPS Series - Objectives

- Broker knowledge transfer between researchers & federal policy-makers
- Foster a dialogue that can inform evidence-based public policy
- Identify timely and socially-relevant research priorities

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Welcome

GE³LS at Genome Canada

Frequently Asked Questions

Newsletters

Research Projects

Policy Portal

- GPS Series
- Policy Directions Briefs
- Pod casts

Events

Resources

Contacts

GPS Series: Overview

In 2009, Genome Canada launched "**GPS**: Where **G**enomics, Public **P**olicy and **S**ociety Meet" an Ottawa-based GE³LS series intended to broker a dialogue between federal policy-makers and researchers on issues that arise at the interface of genomics and society. The GPS events help foster evidence-based public policy and identify timely and socially-relevant research priorities.

2011 Series: Translational Genomics

Beyond pursuit of leading edge research across the life sciences, Genome Canada also endeavours to facilitate the translation of research into socio-economic benefits for Canadians, through activities that help "move genomics out of the laboratory and into the market, the clinic, or society at large." Embedded in this working definition, developed by Dr. Janet Atkinson-Grosjean and her Translational Genomics Research Group, are the many hurdles that stand in the way of translating research findings into practical applications that contribute to the welfare of Canadians. In 2011, GPS will devote its attention to some of these hurdles, seeking to advance the policy dialogue, enhance translational practices, and highlight their importance to prosperity and the public interest.

Genomics Research and Intellectual Property
April 28, 2011

Genomic Entrepreneurialism
Upcoming event

Regulatory Science
Upcoming event

2009-2010 Series: Genetic Information

http://www.genomecanada.ca/en/ge3ls/policy-portal/

http://www.genomecanada.ca/fr/ge3ls/portail-options-strategiques/

Theme for 2011 GPS Series

Translational Genomics… "to help move genomics out of the laboratory and into the market, the clinic, or society at large"*

Topics

- **Genomics Research and Intellectual Property**
- **Optimizing the Impact of Genomics Research, Beyond Commercialization**
- **Genomics and Regulatory Science**

*** Janet Atkinson-Grosjean,** Translational Genomics Research Group

Theme for 2012-2013 GPS Series

The Innovation Continuum…

Topics

- **Moving Promising Technologies off the Shelf (2012 Canadian Science Policy Conference)**
- **Receptor Capacity for Biotechnology Innovation in Canada (September 2013)**
- **Personalised Medicine and Health Care Policy: From Evidence to Value (2013 Canadian Science Policy Conference)**

POLICY BRIEF…charge given to the author

- Present a concise document, targeted at a policy-makers
- Frame / synthesize the policy issues in the current Canadian context
- Present a well-balanced spectrum of options; practical considerations
- Identify possible future research questions - the “evidence gap” (to be completed after the event).

Policy Brief is **NOT**

- intended to reflect a “Genome Canada” view
- intended to advocate a single recommendation
- intended to reflect a consensus

Objective: To leave open the policy positions that policy-makers and stakeholders may choose, informed by considerations contained in the brief.

Personalised Medicine and Health Care: From Science to Value.

Christopher McCabe, BA MSc, PhD mccabe1@ualberta.ca

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(1) Senior Associate, Institute of Health Economics, Edmonton, Alberta

(2) Adjunct Professor, Department of Epidemiology and Community Medicine, University of Ottawa

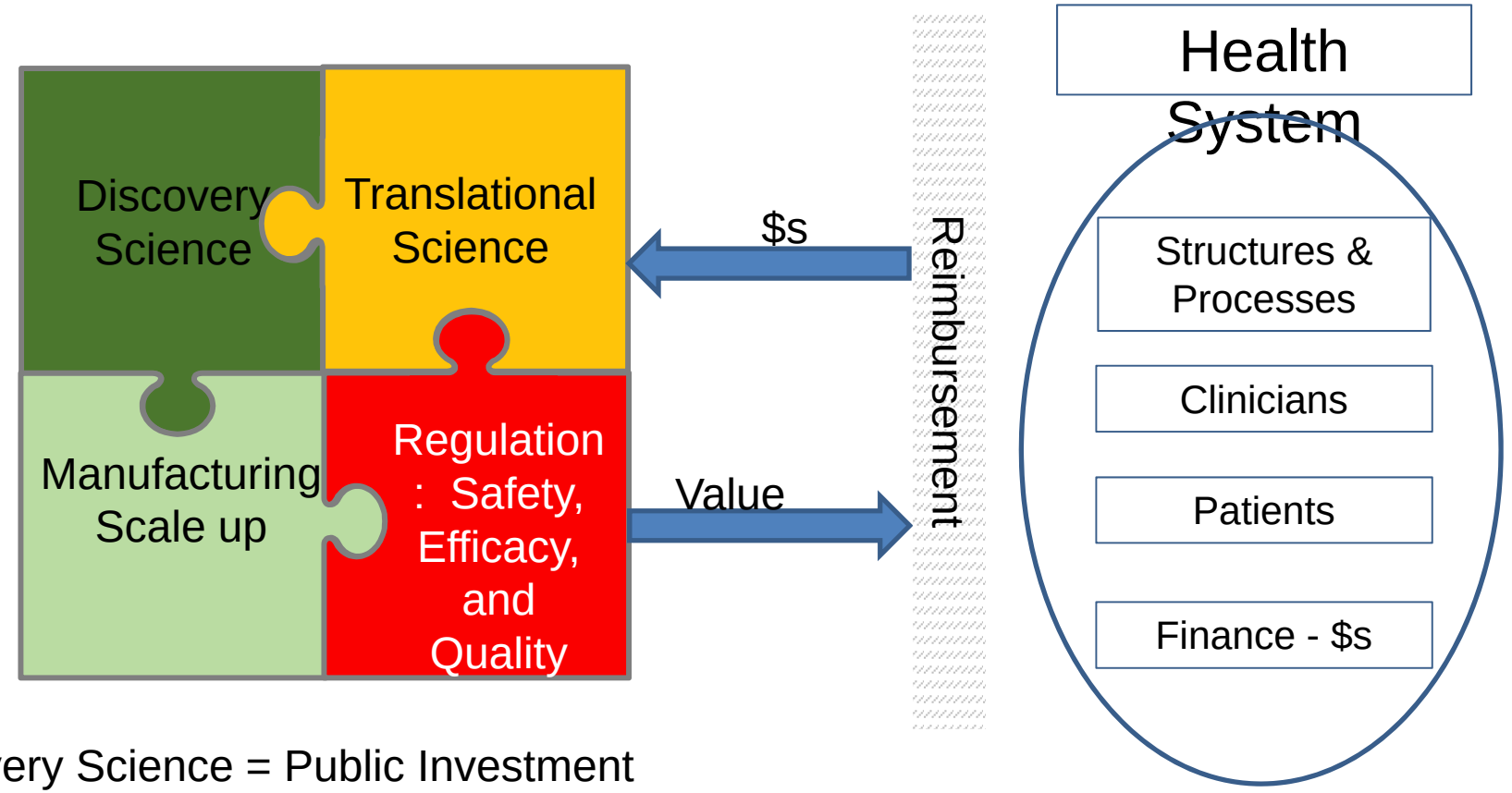
(3) Senior Scientist, Institute for Public Health, Medical Decision Making and Health Technology Assessment UMIT - Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik GmbH

Presentation to Canadian Science Policy Conference– Toronto, Thursday, November 21, 2013

Outline of Session

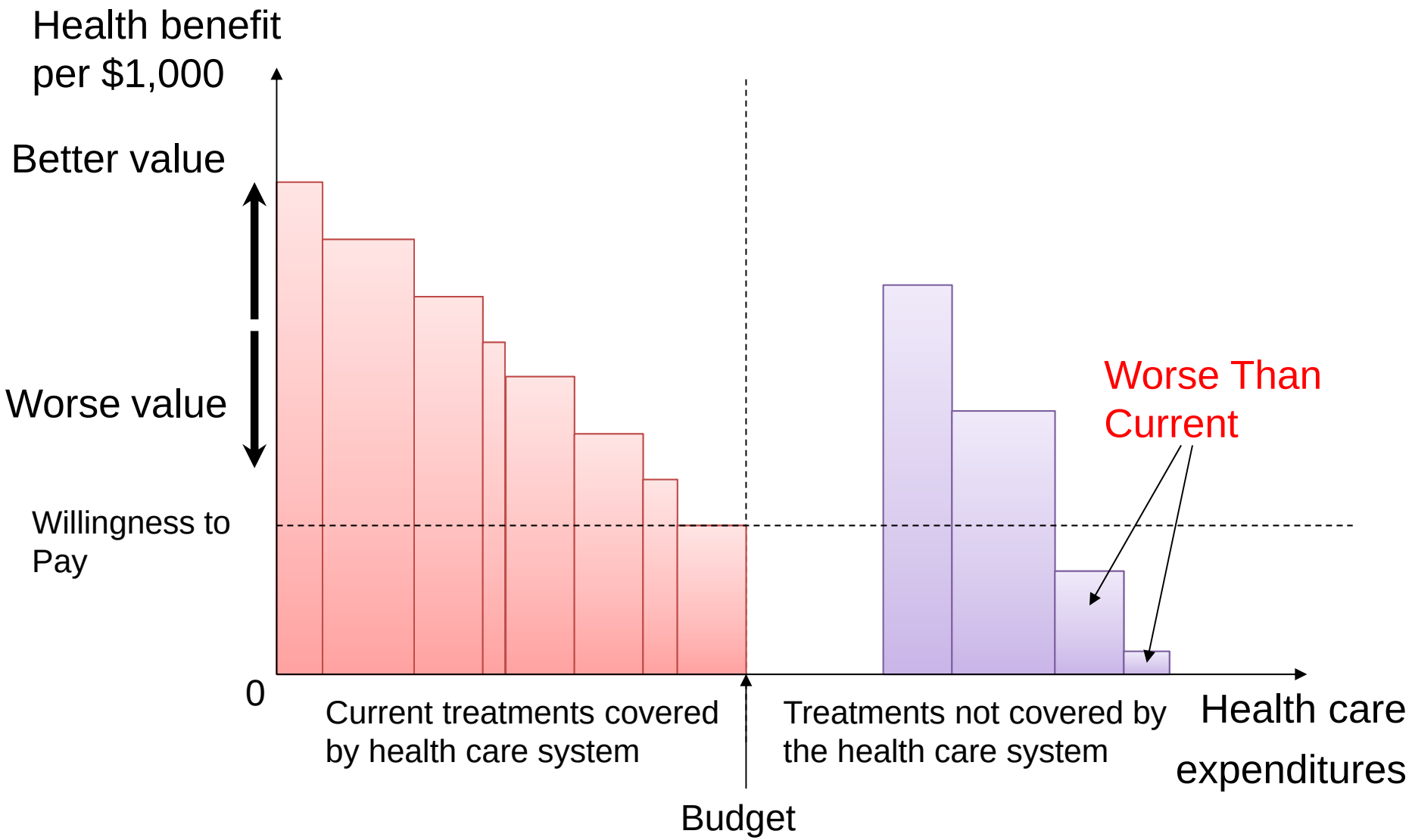
- Context
- What is Value?
  - Value and opportunity costs
  - What influences value?
- Issues with translational research and personalized medicine
  - Evidentiary Challenges
  - Analytic Challenges
  - Process Challenges
- Policy options

Context: from science to value…

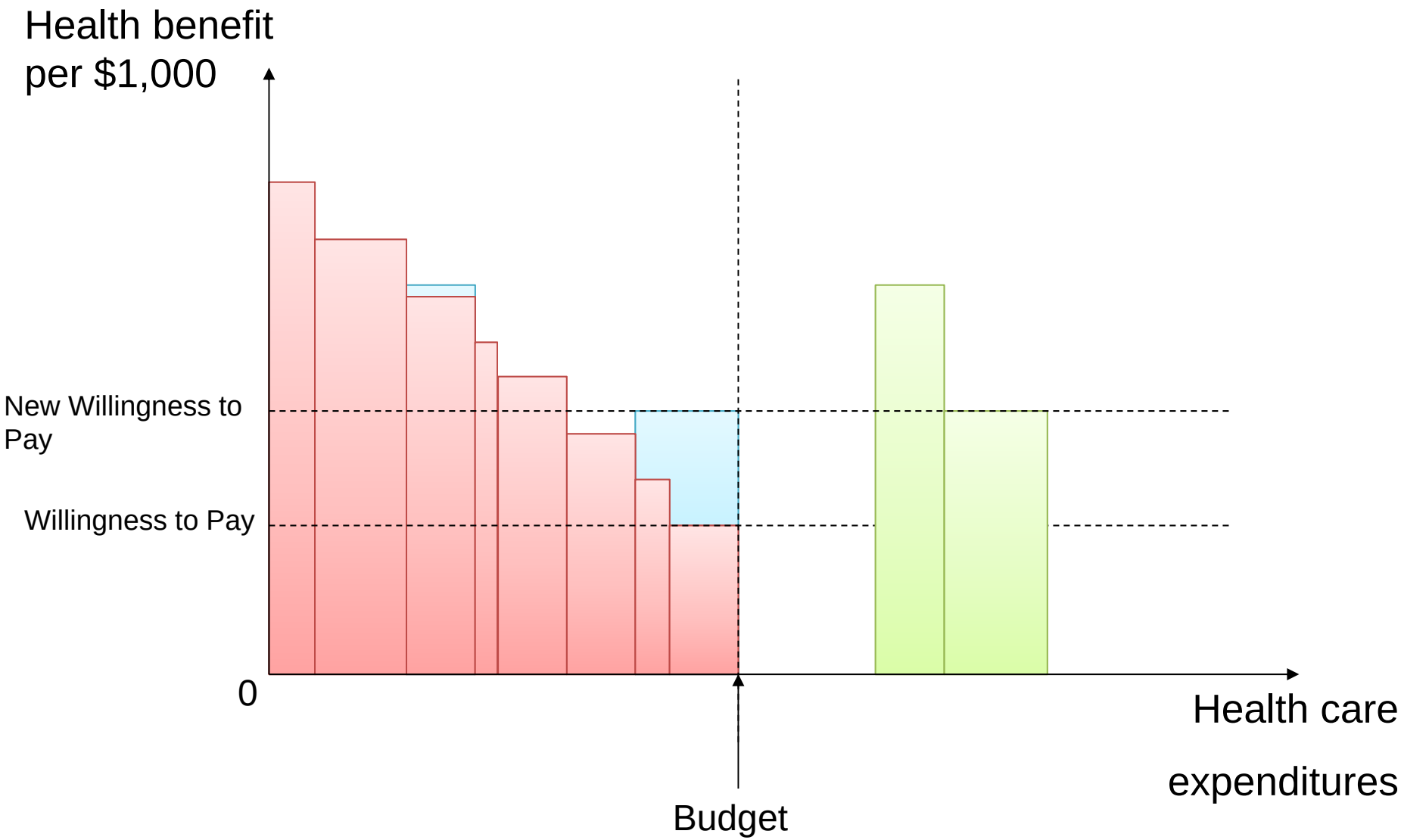


1. Discovery Science = Public Investment
2. Translational Science = Public and Private Investment
3. Manufacturing Scale Up = Private Investment
4. Regulation = Public and Private Investment

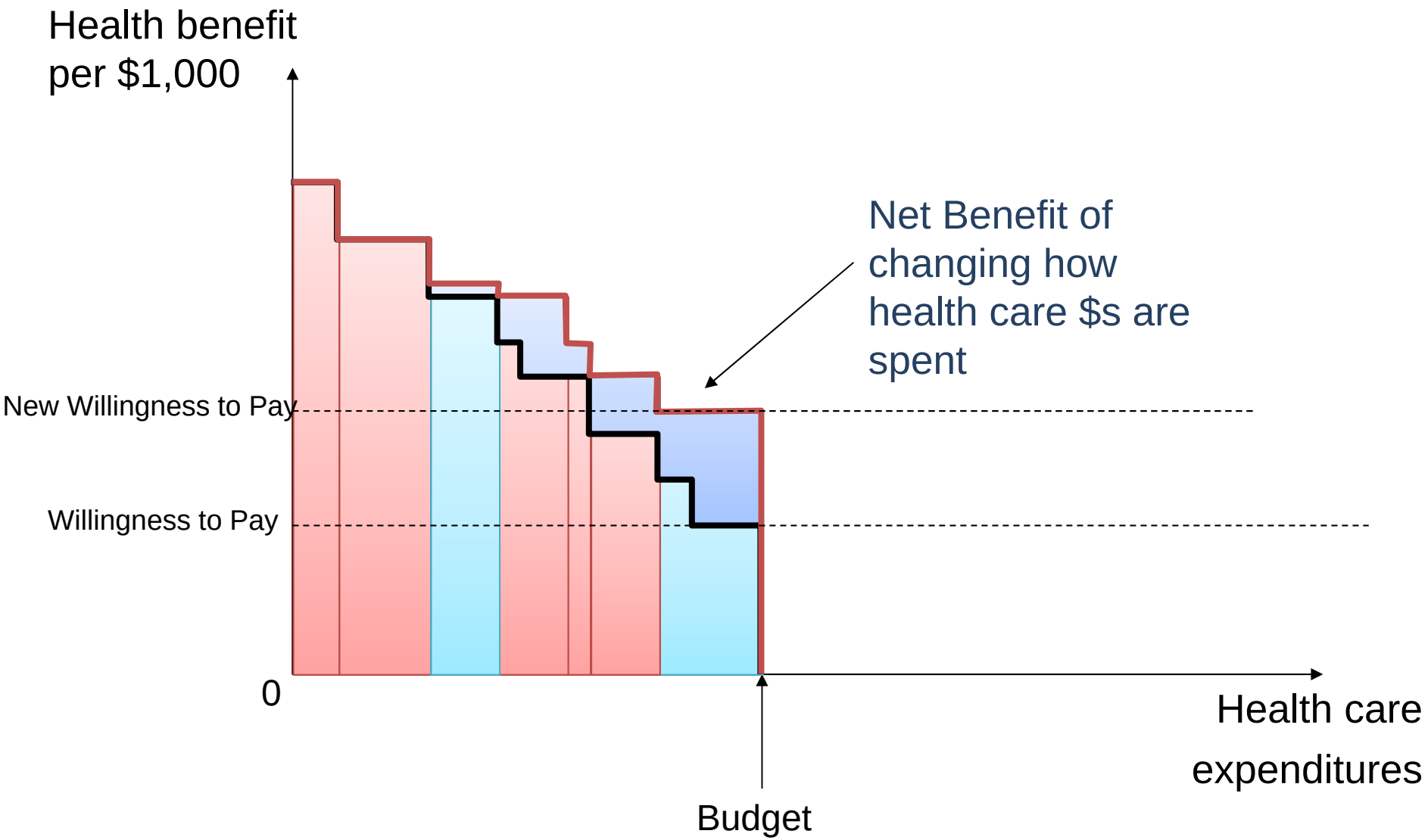
Health care reimbursement & value



Health care reimbursement & value



Health care reimbursement & value



Whose value(s)?: elements of value

- **Health outcomes (population and individual health outcomes)**
  - Increased effectiveness
  - Increased safety

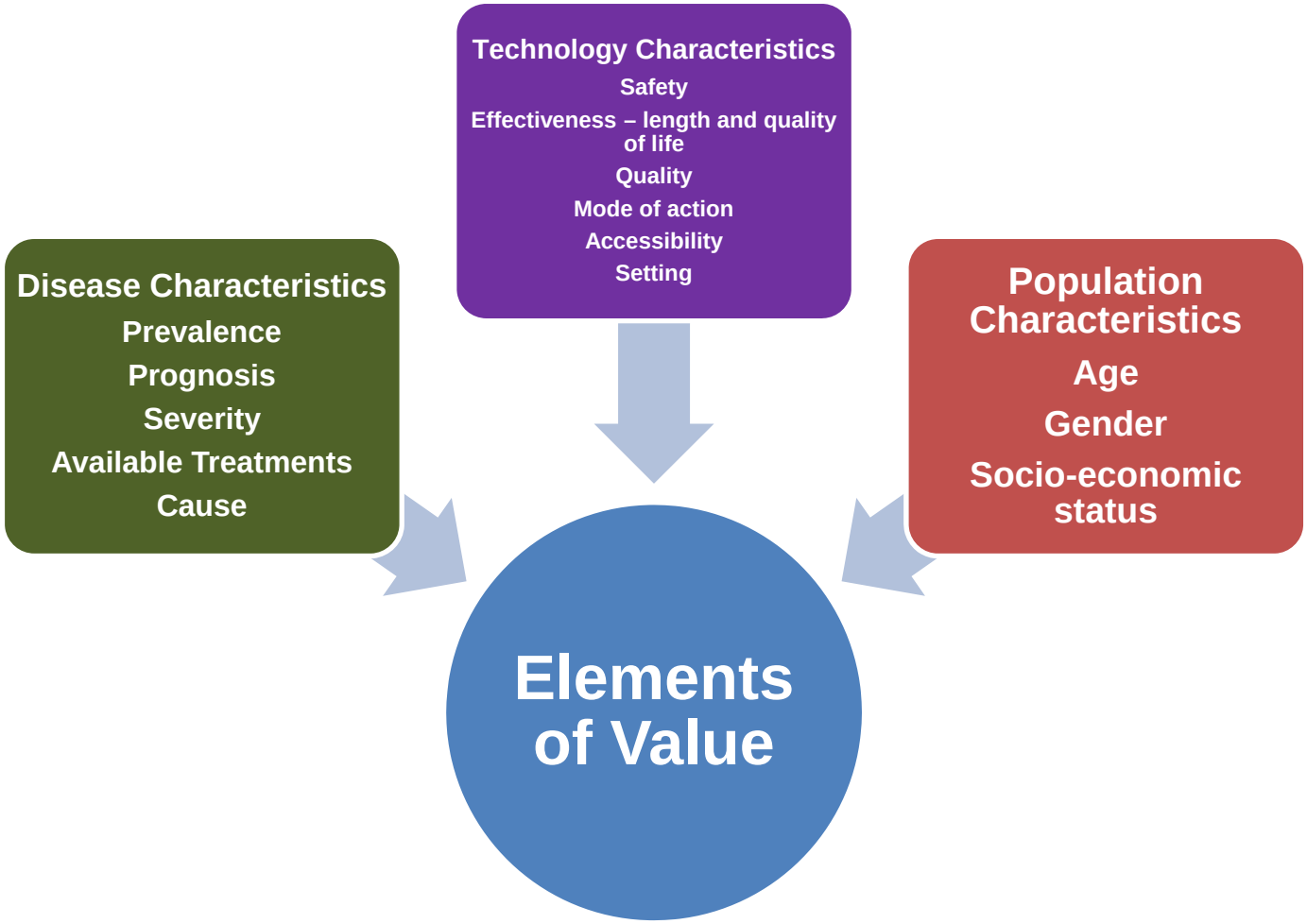
- **Other patient, caregiver and/or population health benefits**
  - Reduction of uncertainty (e.g., following diagnosis)
  - Reduced caregiver burden
  - Unmet needs
  - More treatment choice
  - Improved access to services
  - Greater equity

Whose value(s)?: elements of value

- **Health system benefits**
  - Greater ease of incorporating technology into current system (and ease of future disinvestment)
  - Solidarity
  - Improved administration/delivery/supply chain

- **Benefits beyond health system**
  - Costs to other areas of government (e.g., education, justice system)
  - Political acceptability
  - Social impact (e.g., environmentally friendly)
  - Infrastructure development

What influences value?



Evidentiary Challenges

- Technical information on test performance is different from evidence required to assess value
  - Value determined costs and outcomes that flow from all four alternative test results; and associated opportunity cost.

Evidentiary Challenges

- PM Tests are complex construct combing:
  - clinical material,
  - lab processes and
  - statistical models
- ‘The process is the product’ variation in process has implications for:
  - Validity,
  - Generalisability, and
  - Interpretation
  - Uncertainty in tests

– Will developers release all relevant data for value assessment?

Statistical Evaluation of a Biomarker

Patrick Ray, M.D., Ph.D.,* Yannick Le Manach, M.D.,† Bruno Riou, M.D., Ph.D.,‡
Tim T. Houle, Ph.D.§

Different Populations

Diagnostic tests may substantially vary when measured in different patient populations, particularly when studied populations are defined by characteristics such as demographic features (age and sex) and spectrum of the disease (severity, acute *vs.* chronic illness, pathologic location of form).[61]

Role of Time

In most clinical situations, the issue of the time of biomarker measurement is of limited interest, mainly because the time of onset of the pathologic process and or disease is unknown. However, in other situations, the time of onset can be readily determined. This is the case for acute chest pain and for the appearance in the blood of a biomarker for myocardial infarction. In that example, although troponin is recognized as an ideal biomarker (both very sensitive and very specific), it needs more time to be detected than myoglobin, which is

Importance of the Biomarker Kinetics

A biomarker has its own kinetics implying metabolism and elimination. This important issue has been poorly recognized at least partly because the kinetics of biomarkers is often poorly investigated. Just as renal or liver insufficiency may influence the pharmacokinetics of drugs, they also could influence the kinetics of a biomarker and interfere with their diagnostic properties. For example, procalcitonin has been

Imperfect Reference Test

In a diagnostic study, the reference test should be a gold standard, but in many clinical situations this is not possible. A universally recognized standard may not exist (*e.g.*, cardiac failure), may not have been performed in many patients (*e.g.*, autopsy), or logistically could not be concurrently performed. For example, when evaluating BNP, echocardiography for heart failure is not always performed in the emergency department but is usually performed later during hospitalization.[34] Moreover, in many situations, biomarkers

Analytic challenges

- Clinical utilisation of test results highly uncertain
- PM will make ‘no treatment’ personal as well
  - Identified and unidentified beneficiaries of decisions at the centre of PM reimbursement decision.
  - Countervailing value propositions will become explicit and central to decisions
  - Incorporation of these considerations into analysis is problematic both methodologically and evidence-wise.

CURRENT OPINION

Pharmacoeconomics 2009; 27 (12): 983-989
1170-7690/09/0012-0983/$49.95/0

Weighting Must Wait

Incorporating Equity Concerns into Cost-Effectiveness Analysis May Take Longer than Expected

Allan Wailoo,[1] *Aki Tsuchiya*[1,2] and *Christopher McCabe*[3]

1 Health Economics and Decision Science, School of Health and Related Research, University of Sheffield, Sheffield, UK
2 Department of Economics, University of Sheffield, Sheffield, UK
3 Academic Unit of Health Economics, Institute of Health Sciences, University of Leeds, Leeds, UK

Abstract

Current practice in economic evaluation is to assign equal social value to a unit of health improvement ('a QALY is a QALY is a QALY'). Alternative equity positions are typically considered separately from efficiency. One proposal seeks to integrate these two sets of societal concerns by attaching equity weights to QALYs. To date, research in pursuit of this goal has focussed on candidate equity criteria and methods for estimating such weights. It has implicitly been assumed that should legitimate, valid and reliable equity weights become available, it would be a straightforward task to incorporate them as a separate simple calculation after estimating cost per un-weighted QALY. This article suggests that, in many situations, these simple approaches to incorporating equity weights will not appropriately reflect the preferences on which the weights are based and that the appropriate incorporation of equity weights in cost-effectiveness analyses will be technically challenging. In addition to the technical challenges, there are a number of issues that arise in the movement from implicit to explicit consideration of equity. Whilst equity weights can, conceptually, be incorporated in economic evaluation, there are a number of challenges to be addressed before the results of such analyses can be considered robust and a fit basis for resource allocation decisions.

Process Challenges

- Mind the gap
  - There is always a gap between the evidence and the decision
  - HTA decisions = Deliberative process to bridge the gap
    - More complex evidence base requires greater pool of expertise feeding into the process

Policy Option 1: Defining values

"…policymakers in a liberal democracy are making decisions on behalf of society who elected them to represent their interests. …further work in this area …required …to support decisions leading to differential access to PM and conventional technologies."

Policy Option 2: Align regulation and HTA

"…increasing recognition of … overlapping roles in regulation and HTA. This has led to numerous documented interactions between HTA bodies and regulators ranging from enhanced communication and information sharing to proposals for aligning evidentiary requirements and processes of assessment.."

Policy Option 3:
Separate basic and applied science goals

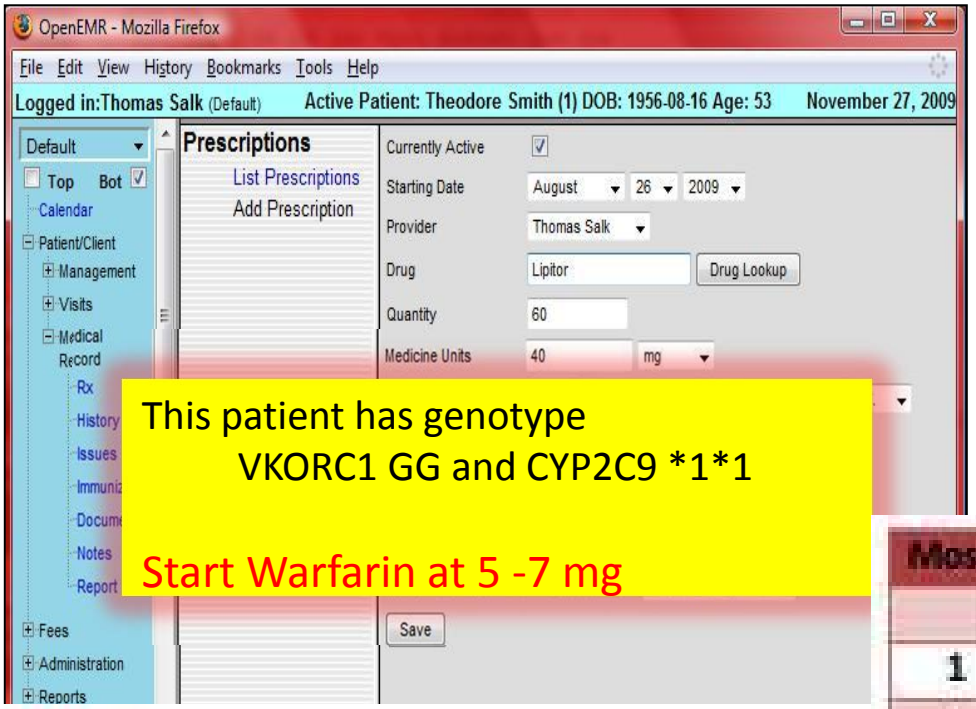
"…we would suggest… freeing basic science researchers from the pursuit of barely attainable and largely inappropriate deliverables of showing value. Good funding strategies require …. how to understand, measure and realize social value.

….This model would emphasize the need and alignment of experts in HTA, decision-making and economic evaluation in all translational and applied health research activities."

Thank you.

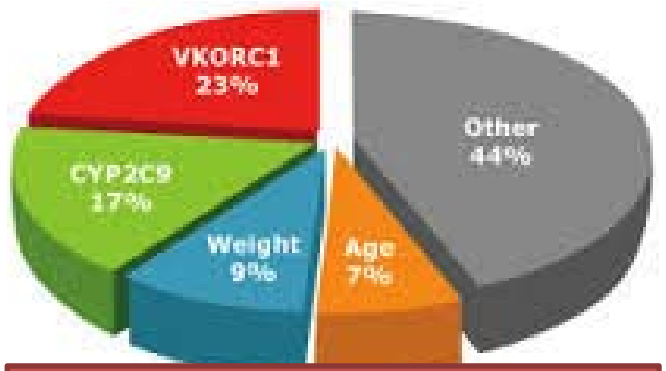
Science Policy-Personalized Medicine

Robyn **T**amblyn
Scientific **D**irector
Institute of **H**ealth **S**ervices and **P**olicy **R**esearch
Canadian **I**nstitutes of **H**ealth **R**esearch



This patient has genotype
VKORC1 GG and CYP2C9 *1*1

Start Warfarin at 5 -7 mg



Adverse Drug Events

Most Commonly Implicated Medications

	Drug	% of Total
1	Warfarin	33.3%
2	Insulins	13.9%
3	Oral antiplatelet agents	13.3%
4	Oral Hypoglycemic agents	10.7%
5	Opioids	4.8%
6	Antibiotics	4.2%
7	Digoxin	3.5%
8	Antineoplastic agents	3.3%
9	Antiadrenergic agents	2.9%
10	Renin-angiotensin inhibitors	2.9%
11	Sedative-hypnotics	2.5%
12	Anticonvulsants	1.7%
13	Diuretics	1.1%

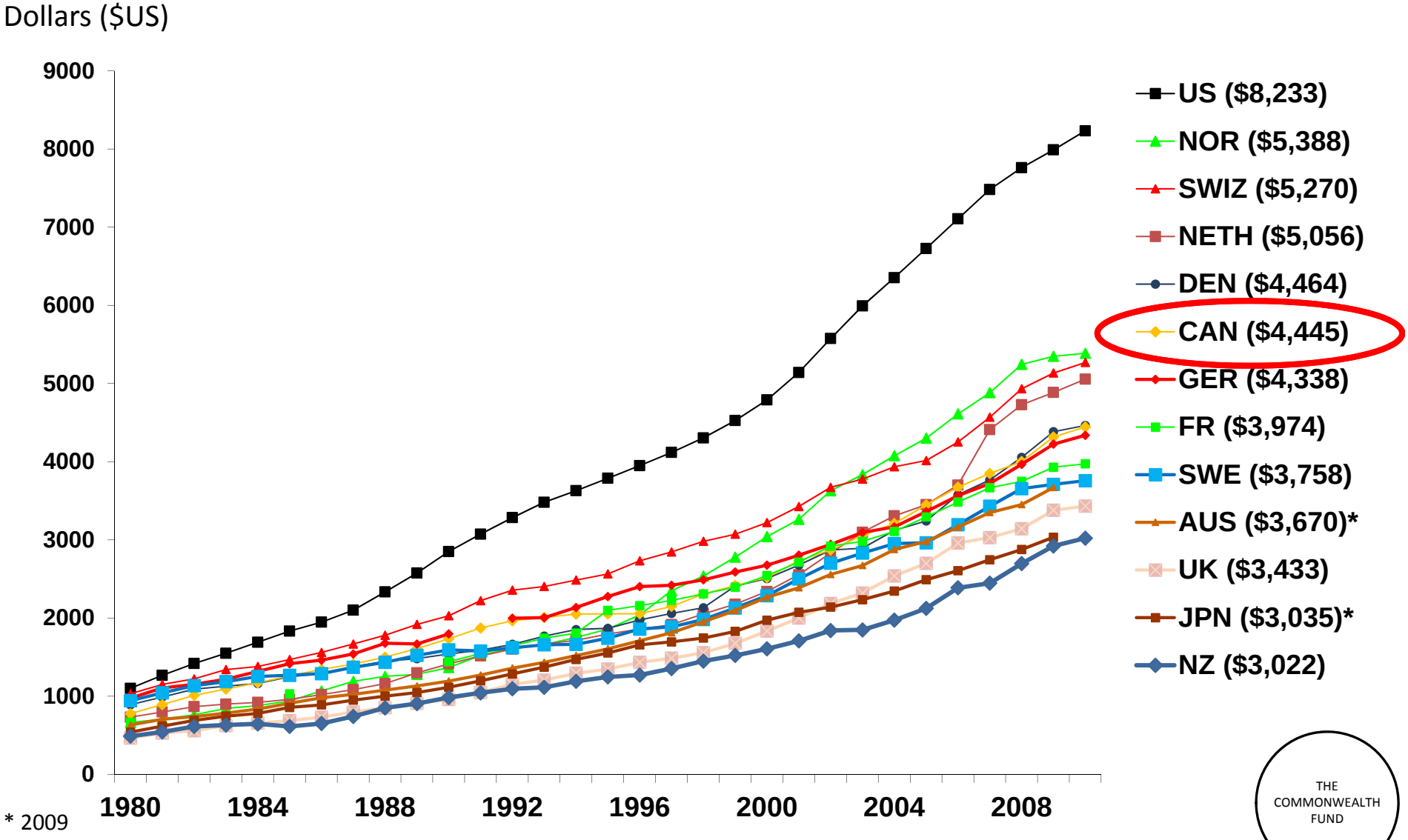
ARTICLES

Integration of Genetic, Clinical, and INR Data to Refine Warfarin Dosing

P Lenzini[1], M Wadelius[2], S Kimmel[3,4], JL Anderson[5], AL Jorgensen[6], M Pirmohamed[7], MD N Limdi[8,10], JK Burmester[11], MB Dowd[12], P Angchaisuksiri[13], AR Bass[14], J Chen[3,4], N Eriks A Rane[16], JD Lindh[16], JF Carlquist[5], BD Horne[5], G Grice[17], PE Milligan[1], C Eby[1,18], J Shin[19] D Kurnik[20], CM Stein[20], G McMillin[21], RC Pendleton[21], RL Berg[22], P Deloukas[23] and BF Ga

Well-characterized genes that affect warfarin metabolism (cytochrome P450 (CYP) 2C9) and sensitivity (vit epoxide reductase complex 1 (*VKORC1*)) explain one-third of the variability in therapeutic dose before the normalized ratio (INR) is measured. To determine genotypic relevance after INR becomes available, we der and pharmacogenetic refinement algorithms on the basis of INR values (on day 4 or 5 of therapy), clinical f genotype. After adjusting for INR, *CYP2C9* and *VKORC1* genotypes remained significant predictors ($P < 0.0$ dose. The clinical algorithm had an R^2 of 48% (median absolute error (MAE): 7.0 mg/week) and the pharma algorithm had an R^2 of 63% (MAE: 5.5 mg/week) in the derivation set ($N = 969$). In independent validation

Average Health Care Spending per Capita, 1980–2010
Adjusted for Differences in Cost of Living



* 2009

Source: OECD Health Data 2012.

THE COMMONWEALTH FUND

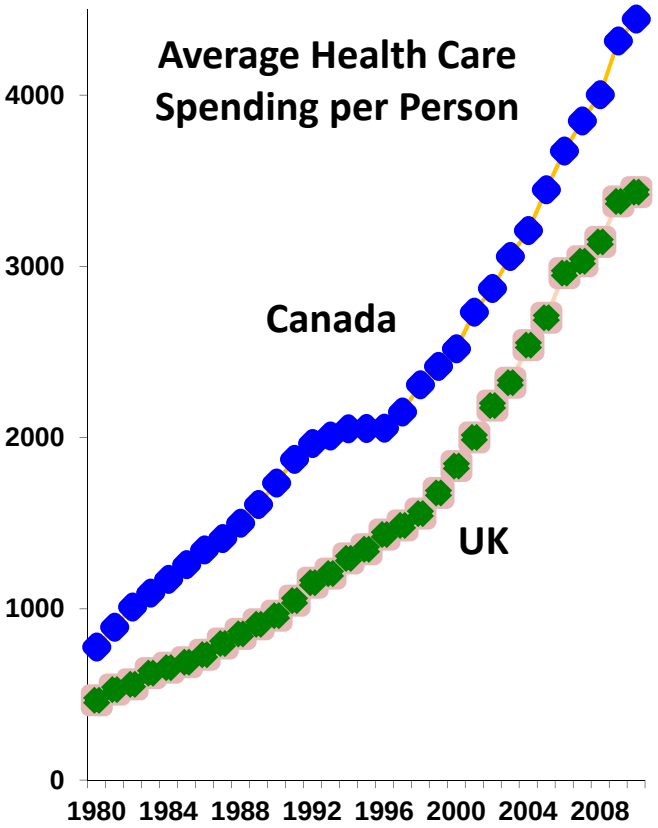
Is Canada getting value for money?
How we compare:

Country Rankings	
	1.00–2.66
	2.67–4.33
	4.34–6.00

	Australia	Canada	Germany	New Zealand	United Kingdom	United States
Overall Ranking (2007)	3.5	5	2	3.5	1	6
Quality Care	4	6	2.5	2.5	1	5
Right Care	5	6	3	4	2	1
Safe Care	4	5	1	3	2	6
Coordinated Care	3	6	4	2	1	5
Patient-Centered Care	3	6	2	1	4	5
Access	3	5	1	2	4	6
Efficiency	4	5	3	2	1	6
Equity	2	5	4	3	1	6
Healthy Lives	1	3	2	4.5	4.5	6
Health Expenditures per Capita, 2004	$2,876*	$3,165	$3,005*	$2,083	$2,546	$6,102

Source: Calculated by the Commonwealth Fund based on the Commonwealth Fund 2004 and 2005 International Health Policy Surveys, the 2006 Commonwealth Fund International Survey of Primary Care Physicians, and the Commonwealth Fund Commission on a High Performance Health System National Scorecard.

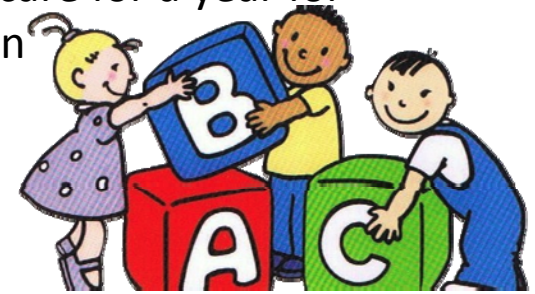
What could we gain with a more cost-effective health system?



Cumulative Difference in Health Spending between Canada and the UK 1980-2010
$659 billion

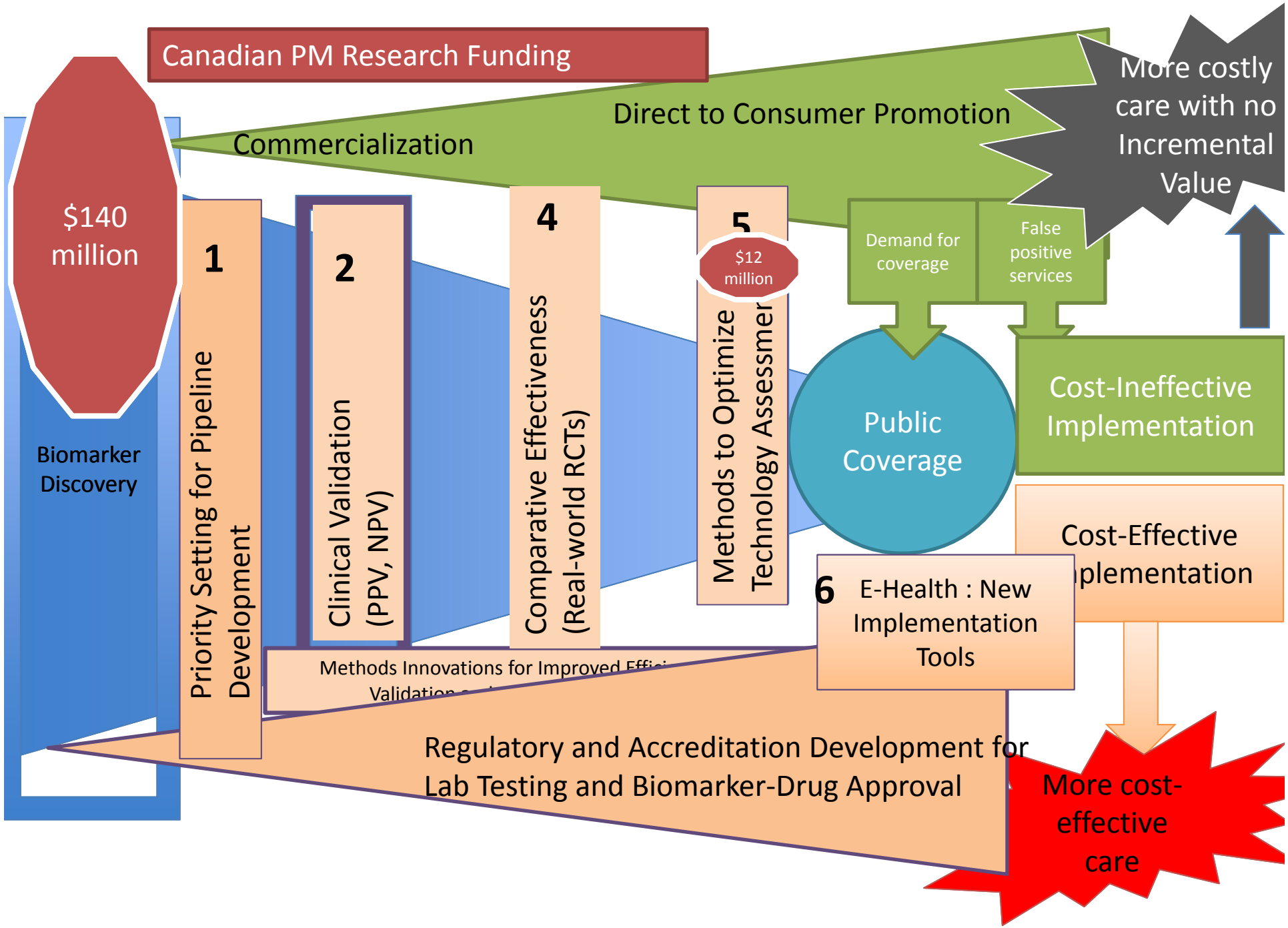
With $659 billion we could:

Provide $5/day daycare for a year for **14.6 million** children



Send **23.5 million** students to university for 4 years

Build **9,171 Trans-Canada highways**


Canadian PM Research Funding
$140 million
Biomarker Discovery
Commercialization
Direct to Consumer Promotion
More costly care with no Incremental Value
1
Priority Setting for Pipeline Development
2
Clinical Validation (PPV, NPV)
4
Comparative Effectiveness (Real-world RCTs)
5
$12 million
Methods to Optimize Technology Assessmer
Demand for coverage
False positive services
Public Coverage
Cost-Ineffective Implementation
Cost-Effective
6
E-Health : New Implementation Tools
Methods Innovations for Improved Effi
Validation
Regulatory and Accreditation Development for Lab Testing and Biomarker-Drug Approval
More cost-effective care

Policy Options

1. **Define a Value Target**
   - Equal or better outcomes at lower cost

1. **Align Regulatory and HTA Requirements**
   - Essential to raise the bar on required evidence of comparative effectiveness for market entry
   - To avoid undesirable demand on publically-funded system to address false positives from private sector testing

2. **Emphasize Distinctions between Discovery and Applied Research Activities**
   - Already differentiated in most countries with 80%-90% in investigator-driven discovery

Personalized medicine and health care policy: From Science to Value

FIONA A. MILLER, PHD

ASSOCIATE PROFESSOR OF HEALTH POLICY, IHPME

DIRECTOR, DIVISION OF HEALTH POLICY & ETHICS, THETA

Genome Canada, GPS Event
Canadian Science Policy Conference
Toronto, Ontario
November 21, 2013

Institute of Health Policy, Management & Evaluation
UNIVERSITY OF TORONTO

theta
Toronto Health Economics and Technology Assessment Collaborative

My perspective

- Program of research in health technology policy
  - Interest in non-drug technologies, especially diagnostics
  - Including genetic/ genomic technologies, used in diagnosis and screening
- Perspective:
  - Expanded role of HTA:
    - Approaches to integrating ethics and social values issues
    - 'Early' HTA to support innovation design, development and validation
    - Innovation adoption
  - Health innovation systems:
    - Sectoral systems responsive to users (patients, payers) through cross-sectoral connections and incentives

Does the brief identify relevant policy issues?

- Characterize a 'perfect storm' facing translation
  - Researchers/ funders
    - Concerned at poor return on major investments
    - Limited capacity for strategic approaches to research (including balance between basic and strategic)
    - Don't understand the user
  - Healthcare systems/ payers
    - Resistant to technologies of high cost & questionable value
    - Limited mechanisms to manage uncertainty
    - Don't signal need clearly or consistently
- Address as issue of "value" in health care
  - How value is defined
  - How value is assessed through HTA
  - Challenges arising for PM

Does the brief offer a well-balanced spectrum of policy options?

- 2 proposals related to HTA
  - Define a value target
    - Generic HTA issue. Relevant.
    - But “whose value”? Especially in Canadian context
  - Increase regulatory requirements for market access
    - Generic medical device issue. Relevant.
    - But how feasible? Especially for Canada
- What’s not here?
  - Other approaches to HTA given Short innovation cycle, Barriers to evidence generation, Practice based innovation
    - “Progressive health system decision making”? (Henshall and Sculler, 2013)
    - CED, Managed entry, early HTA?

Does the brief offer a well-balanced spectrum of policy options?

- 1 proposal related to research policy
  - Tackle the research machine: Reduce emphasis on inappropriate translation, Manage and govern translational research more effectively
    - Timely. Relevant.
- What's not here?
  - Reflection on the varied translational pathways of PM – problems of **under**- and **over**-adoption
    - Commercial: Blockbuster diagnostics (test scores from multiple assays) & Test-Treat combinations
    - Largely non-commercial: Hospital-based clinical research translation – WGS/WES