PCORI Methodology Workshop for Prioritizing Specific Research Topics

December 5, 2012

TWITTER: #PCORI EMAIL: getinvolved@pcori.org

Patient-Centered Outcomes Research Institute

Welcome and Introduction

Paul Wallace, MD

TWITTER: #PCORI EMAIL: getinvolved@pcori.org

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Setting the Stage: PCORI's Research Prioritization Process

Joe Selby, MD, MPH, Executive Director, PCORI

Research Prioritization Methods Workshop
December 5, 2012

Patient-Centered Outcomes Research Institute

PCORI Goals and Values

Who are we and what are we striving to accomplish?

PCORI's Mission and Vision

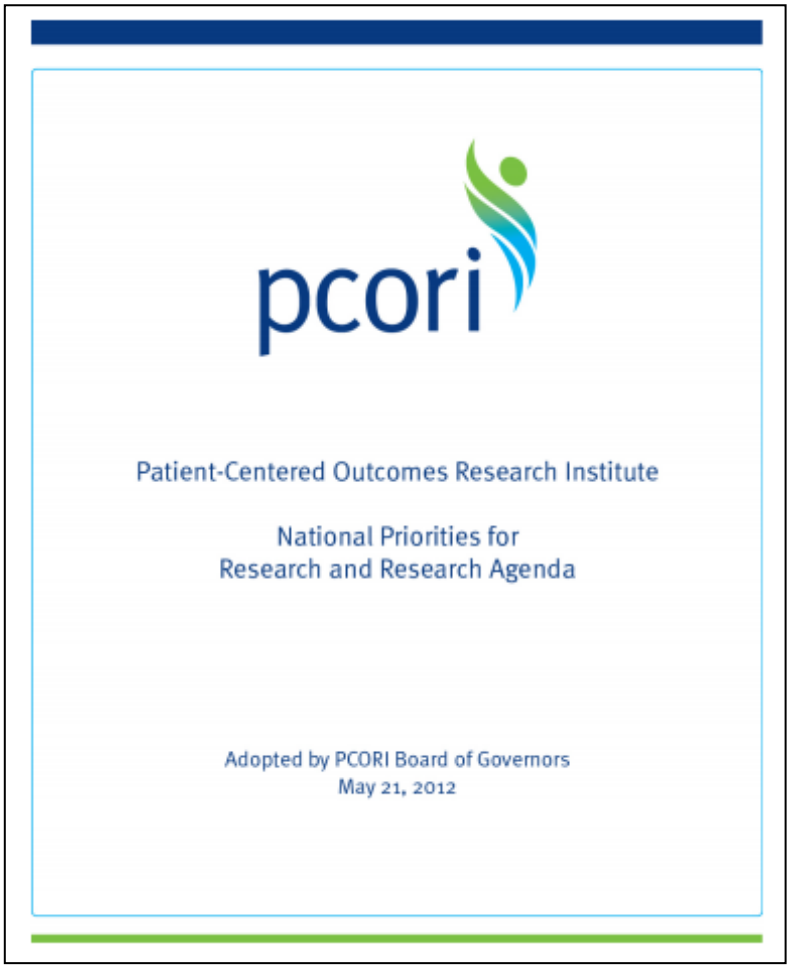
Mission

The Patient-Centered Outcomes Research Institute helps people make informed health care decisions, and improves health care delivery and outcomes by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community.

Vision

Patients and the public have information they can use to make decisions that reflect their desired health outcomes.

PCORI's National Priorities for Research*



- Assessment of Prevention, Diagnosis, and Treatment Options
- Improving Healthcare Systems
- Communication and Dissemination Research
- Addressing Disparities
- Accelerating Patient-Centered Outcomes Research and Methodological Research: Methods and Infrastructure

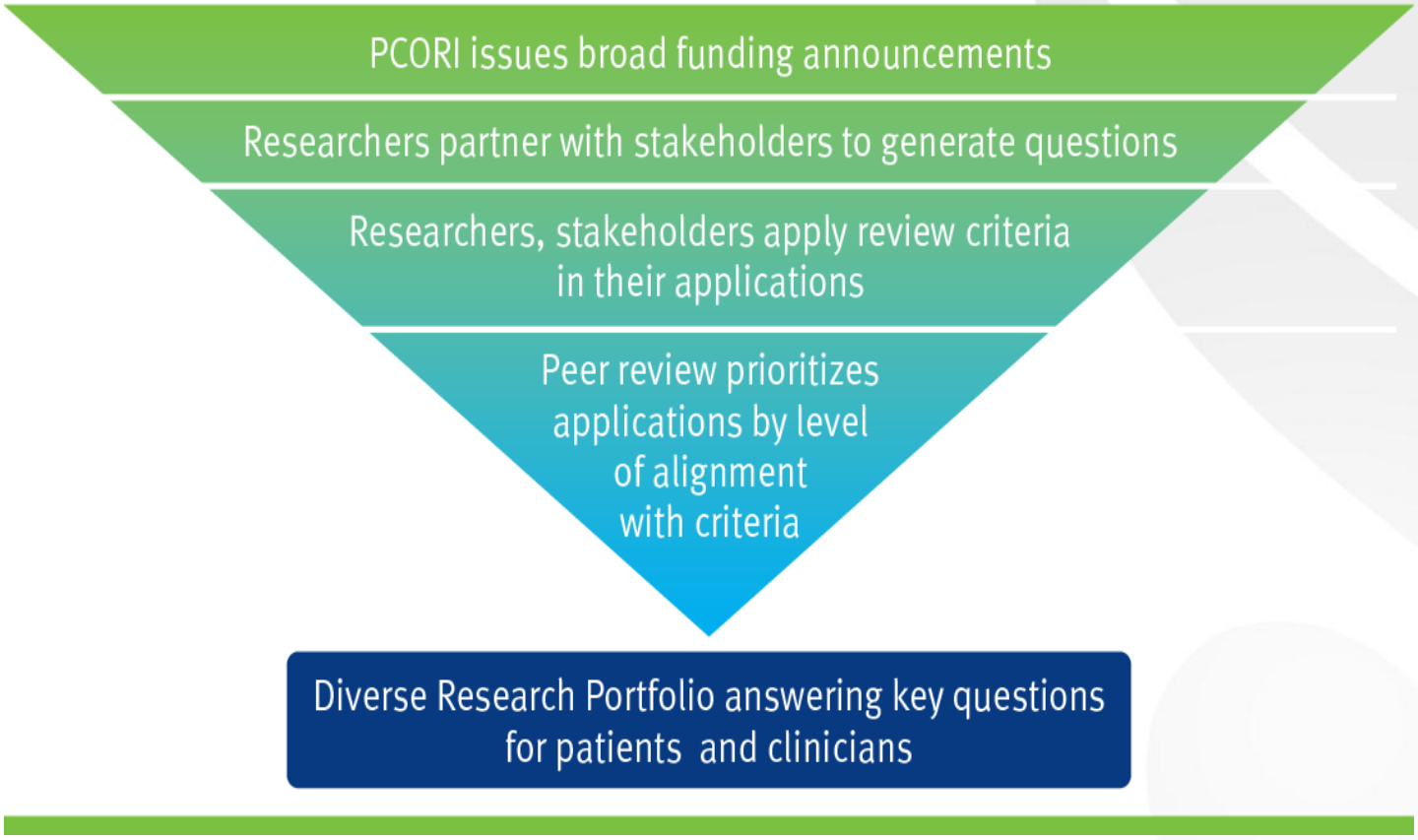
**PCORI also has a focus on rare diseases that may be underrepresented in previous research*

Getting to Specificity

How does PCORI fulfill this mission?

Engaging the Wider Community (1 of 2)

1. Investigator-Generated Research



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Engaging the Wider Community (2 of 2)

2. Patient/Stakeholder-Led Approach

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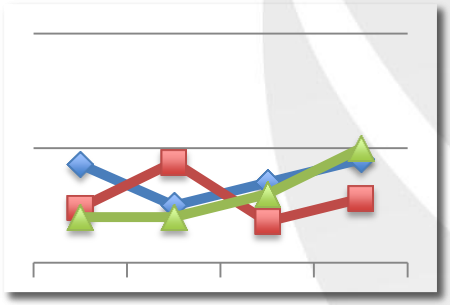
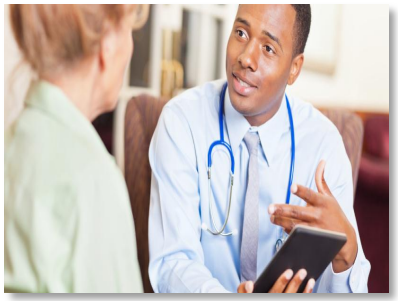
PCORI Prioritization Criteria

Patient-Centeredness



Impact on Population and Individual Health

Differences in Benefits and Harms & Reduction in Uncertainty



Implementation in Practice

Duration of Information

Developing a Multi-Stakeholder Process

Patients, Stakeholders Propose Research Topics and Questions

?????

?????

Topics and Questions Prioritized by Multi-Stakeholder Panels

Panels Advise PCORI Board on Selecting Research for Funding

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Characteristics of the Research Prioritization Process

PCORI will continuously adapt the process as it learns from experience, but key characteristics will be constant…

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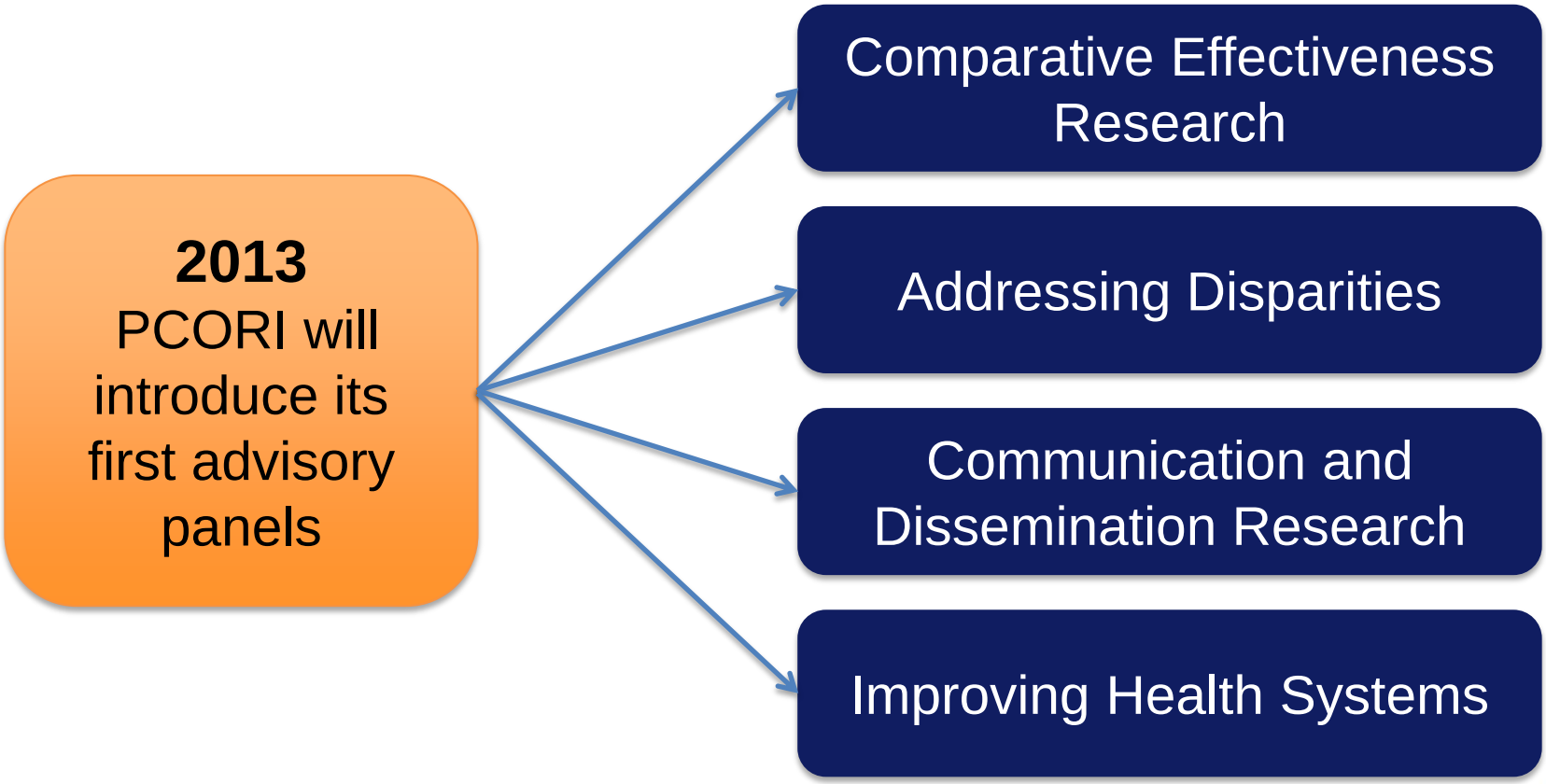
Launch of First Multi-Stakeholder Advisory Panels



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Today: Gathering Diverse Perspectives on PCORI's Prioritization Process

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Thank you

Getting to Specificity: Identifying and Prioritizing Patient-Centered Research Questions

Rachael Fleurence, PhD, PCORI Senior Scientist

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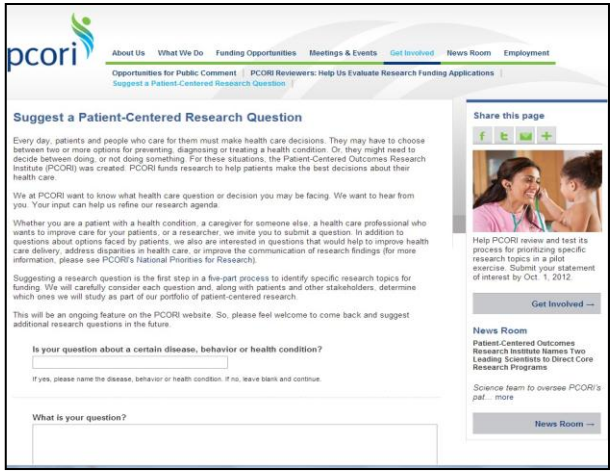
Getting to Specificity: Identifying Questions

Topic Generation

Getting to Specificity: Identifying Questions



AHRQ

Guideline Developers

Institute of Medicine 100

PCORI National Priorities for Research

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Workshops

NATIONAL INSTITUTES OF HEALTH

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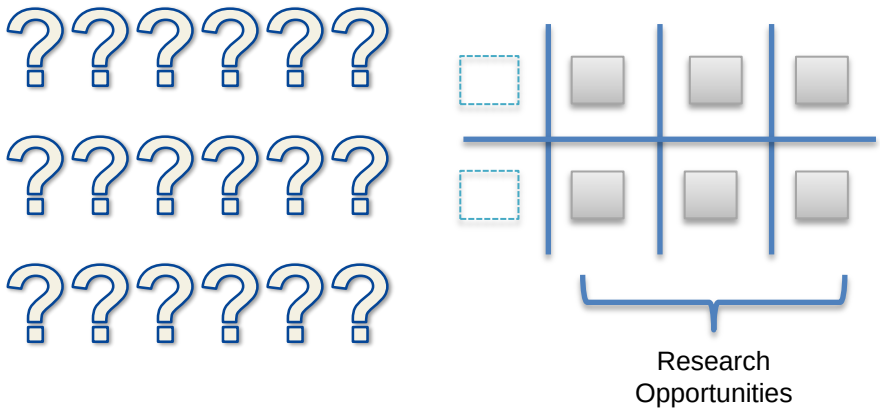
Getting to Specificity: Confirming Research Gaps

Topic Generation → **Gap Confirmation**



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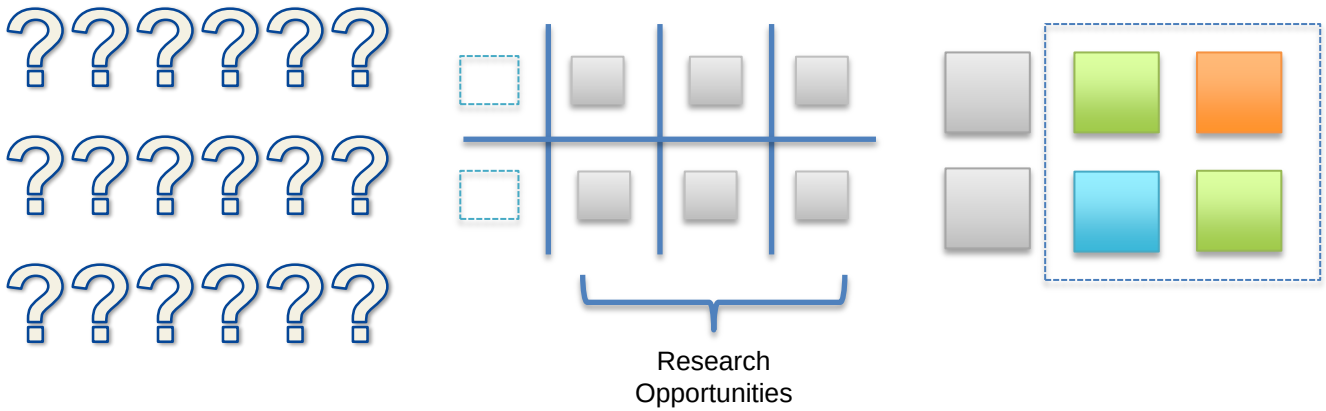
Getting to Specificity: Prioritizing Research Questions

Topic Generation → Gap Confirmation → Research Prioritization



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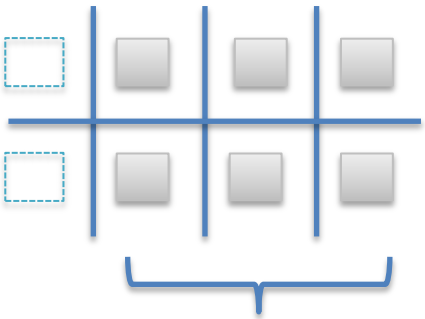
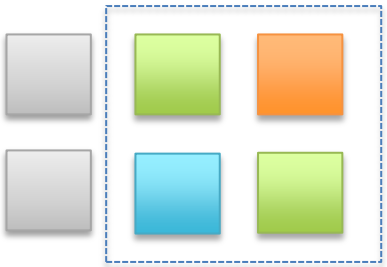
Getting to Specificity: Creating Funding Announcements

Topic Generation → Gap Confirmation → Research Prioritization → Final Selection for Specific PFAs



Research Opportunities



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Principles to Guide Us: Patients ask for Transparency, Efficiency, Collaboration

Transforming Patient-Centered Research: Building Partnerships and Promising Models

Washington DC,
October 27-28, 2012

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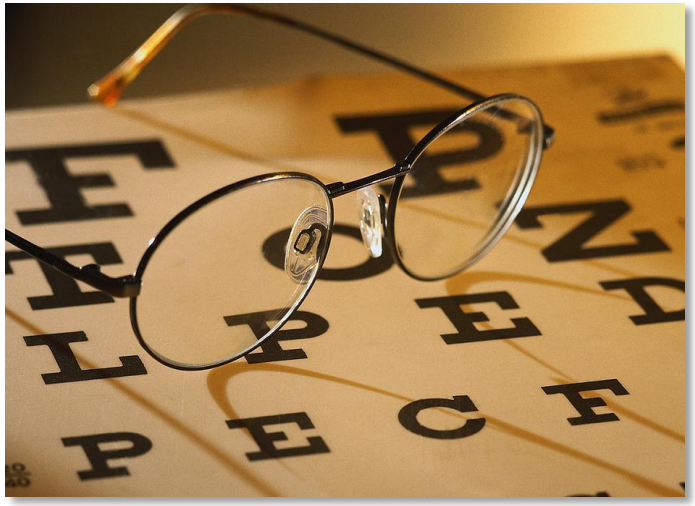
Getting to Specificity: PCORI's Progress and Plan for 2013

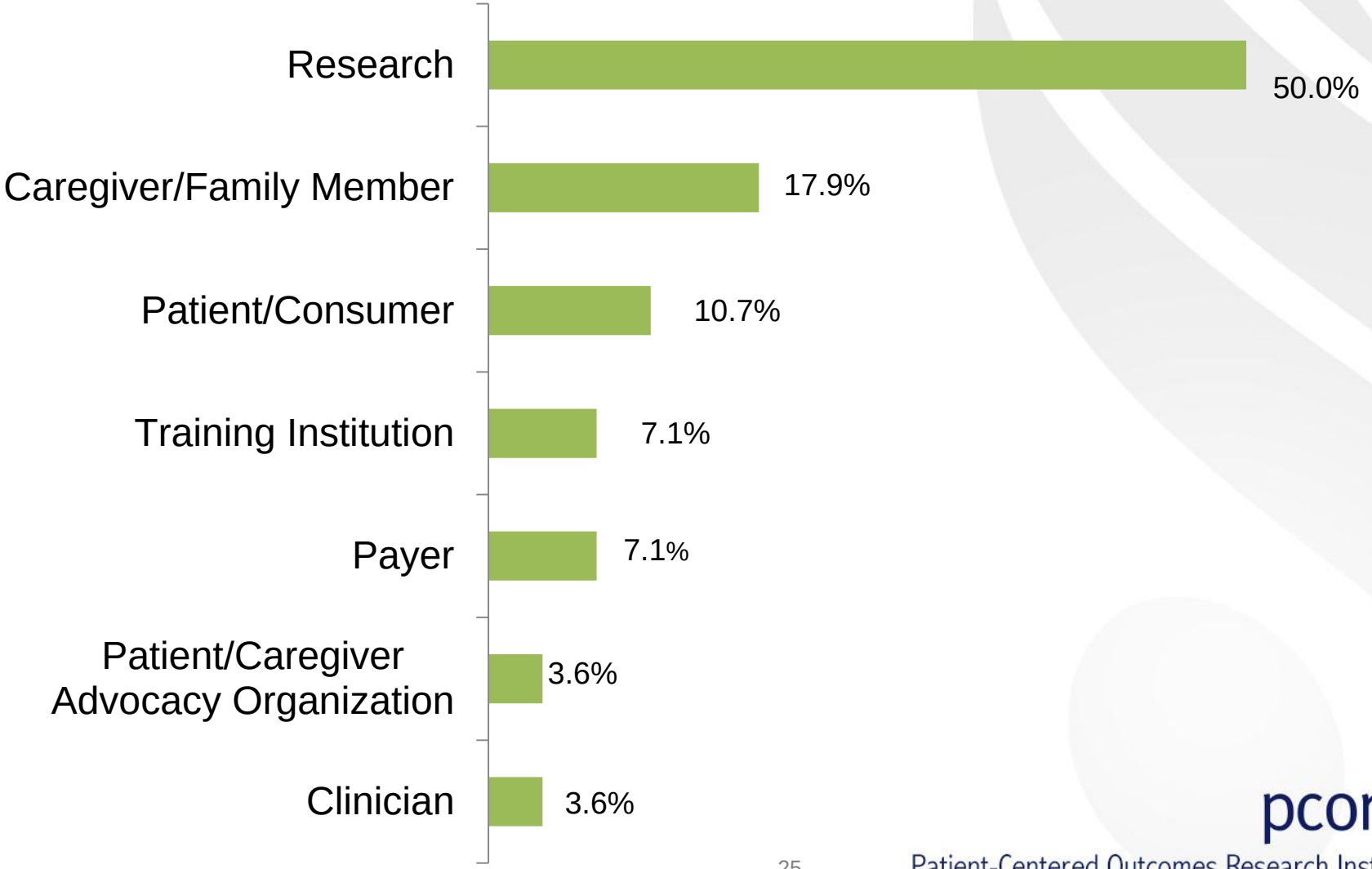
	Aug 2012	Sep	Oct	Nov	Dec	Jan 2013	Feb	Mar 2013
Initial process developed								
Technical Working Group feedback								
Pilot								
Methods Workshop								
Advisory Panel training on Research Prioritization Methods								
Advisory Panels implement and submit results to Board								

Piloting the Process

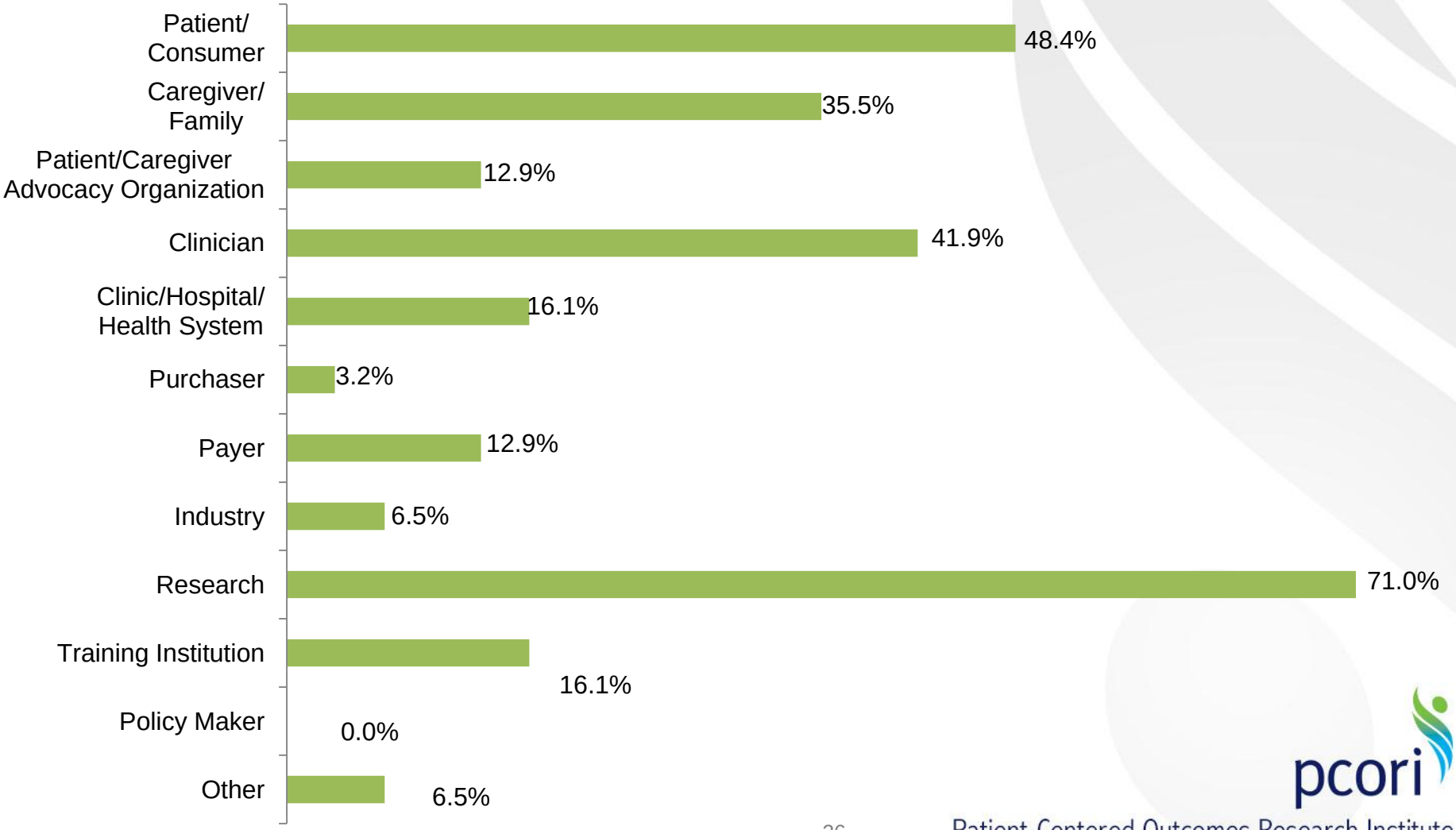


- Piloted from August to November 2012
- 35 Pilot participants
- 8 criteria to prioritize 10 topics
- Results
- Feedback

Composition of the Pilot Group: Primary Identity

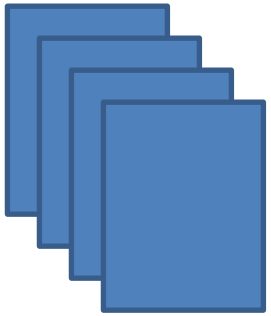


…But Pilot Participants Wear Many Different Hats

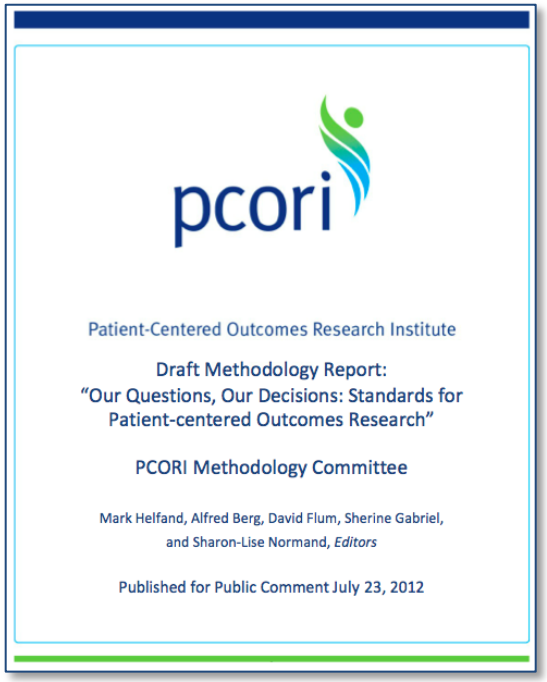


Building on the Existing Evidence Base and Prior Experience

Existing Scientific Work and Literature



Methodology Committee and Methodology Report



Experience of Other Agencies

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National Institutes of Health

Federal Coordinating Council for Comparative Effectiveness Research

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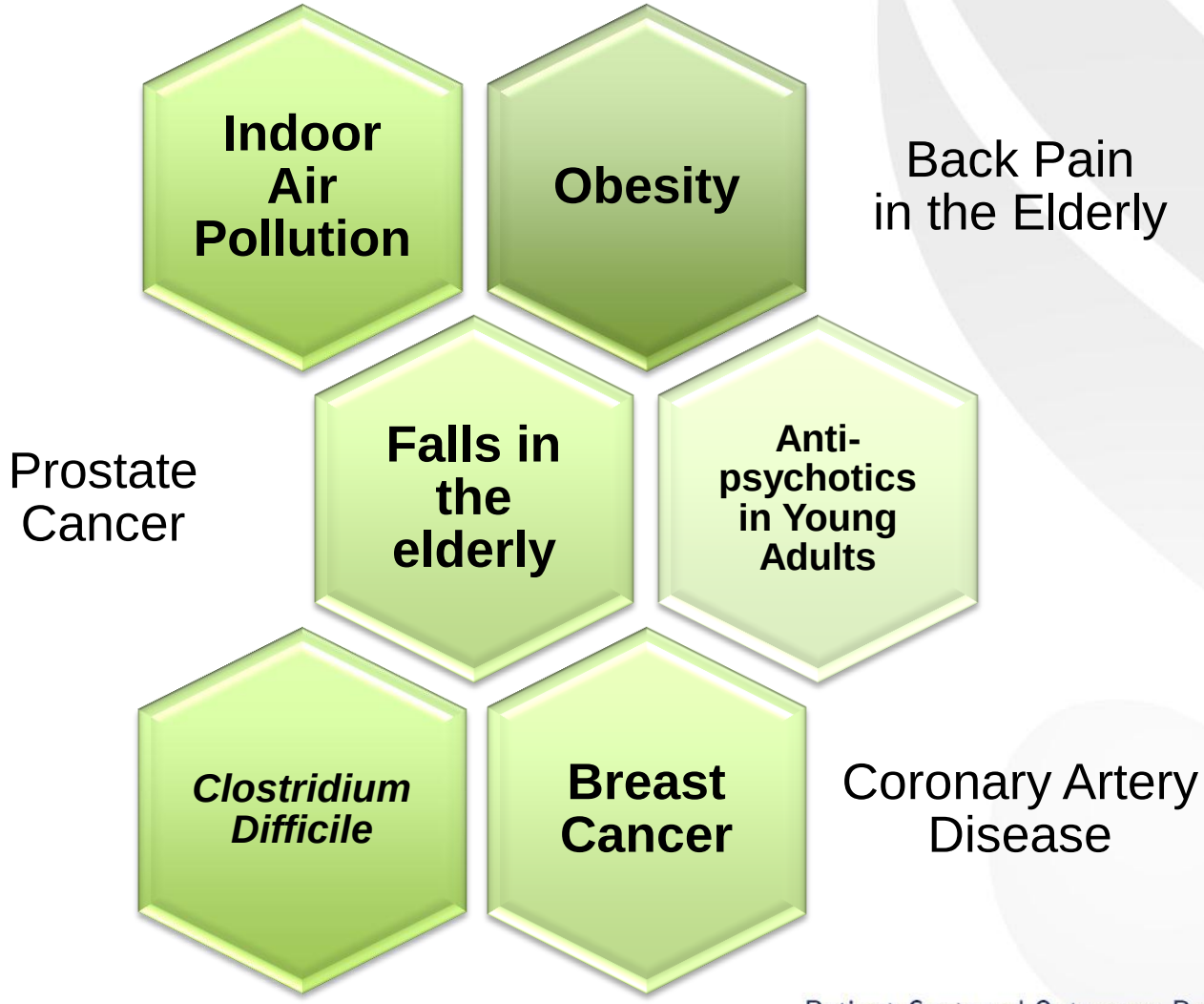
Original PCORI Criteria for Research Prioritization Process

Questions to Pilot from a Diverse Range of Disease Areas



Pilot Groups used 2 Different Tools to Prioritize

surveygizmo

expertchoice®

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Survey Gizmo

Welcome to PCORI Research Prioritization Tool!

Page One

1. Please rate the following topics. You have 100 points to distribute across the ten research topics. Do not allocate more than 30 points to any one topic. *

- What is the comparative effectiveness of antipsychotics in treating adolescents and young adults, particularly among those with ADHD, bipolar disorder, or schizophrenia?
- What is the comparative effectiveness of management strategies of elderly patients with back pain to evaluate many clinically relevant patient-reported outcomes?
- What is the comparative effectiveness of genetic and biomarker testing to identify optimal candidates for breast cancer risk-reduction medications and interventions?
- What is the comparative effectiveness of percutaneous coronary interventions (PCI) including bare metal stents(BMS), drug eluting stents(DES) and coronary artery bypass graft (CABG) for treatment of coronary artery disease?
- What is the comparative effectiveness of new antibiotic interventions compared with standard therapy (metronidazole, vancomycin) for management of the hospital-acquired diarrheal infection Clostridium difficile?
- What is the comparative effectiveness of management strategies for ductal carcinoma in situ (DCIS) to improve long term patient centered outcomes?
- What is the comparative effectiveness of primary prevention methods, such as exercise and balance training, to prevent falls versus clinical treatments in older adults at varying degrees of risk, including those patients post hip fracture and repair?
- What is the comparative effectiveness of indoor air pollution interventions to improve respiratory and cardiovascular health outcomes among high-risk populations?
- What is the comparative effectiveness of coordinated treatment options for patients with multiple chronic conditions?
- What is the comparative effectiveness of mindfulness-based interventions and usual care for promoting health behaviors to reduce the risk of becoming obese and developing metabolic syndrome?

0 out of 100 Total

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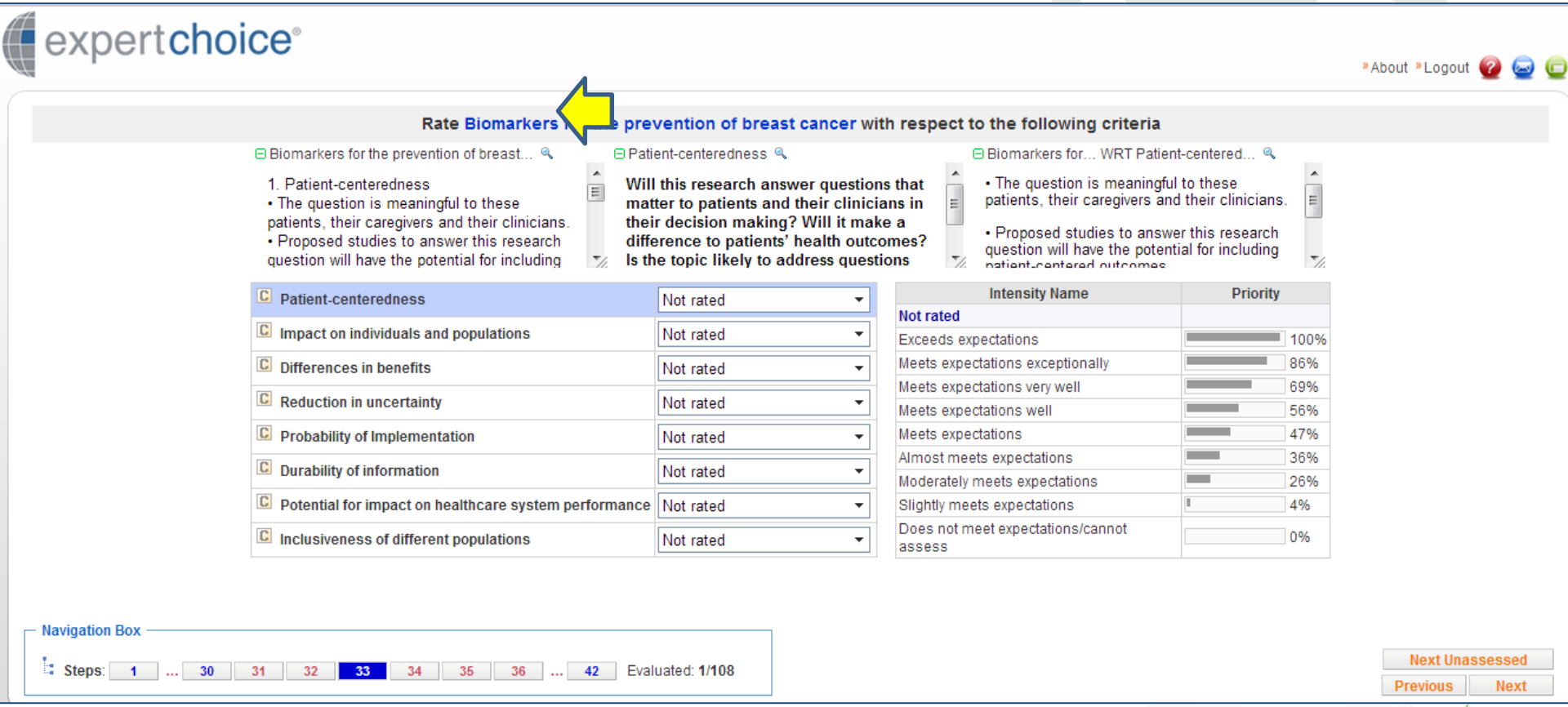
Expert Choice – Topic Ranking



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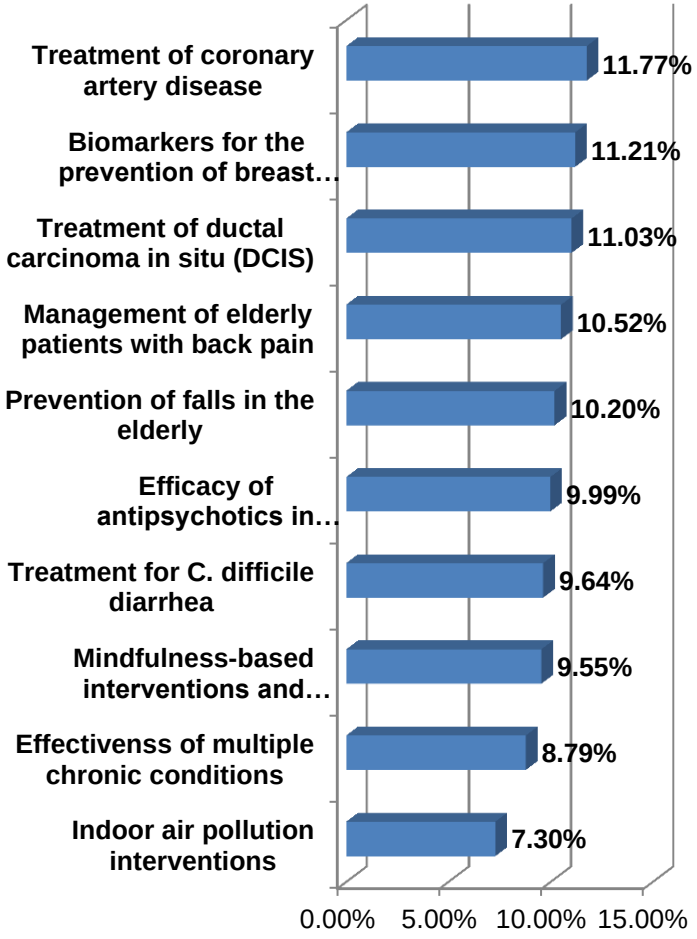
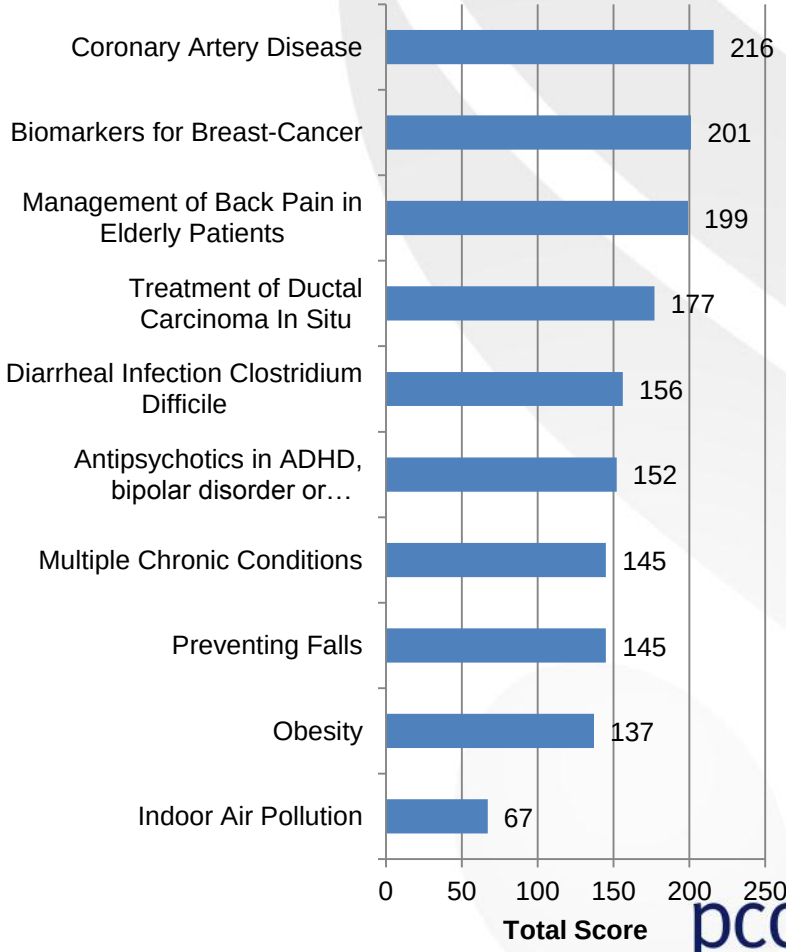
Group 1 Results Using Two Software Programs

Expert Choice



Survey Gizmo



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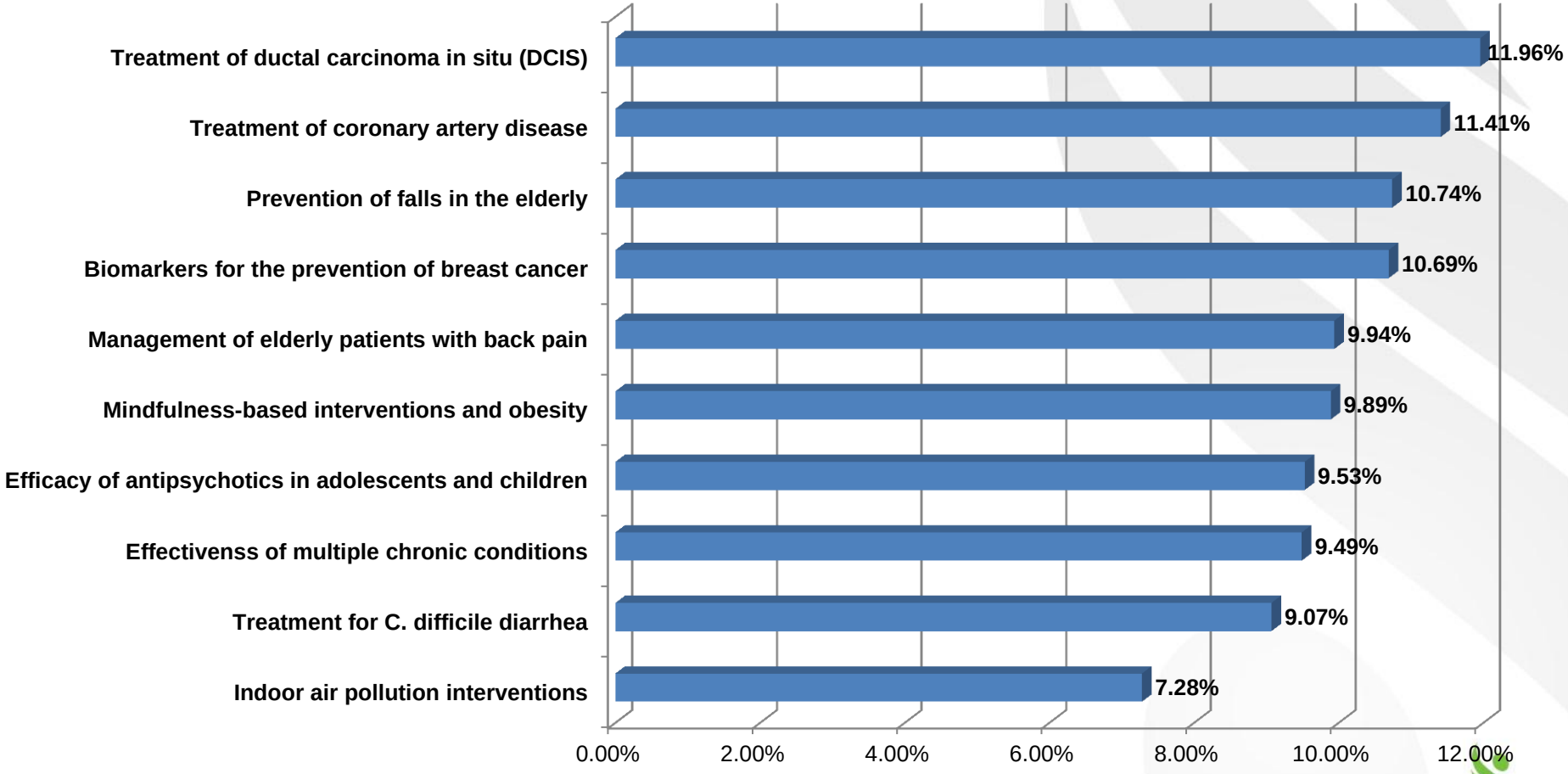
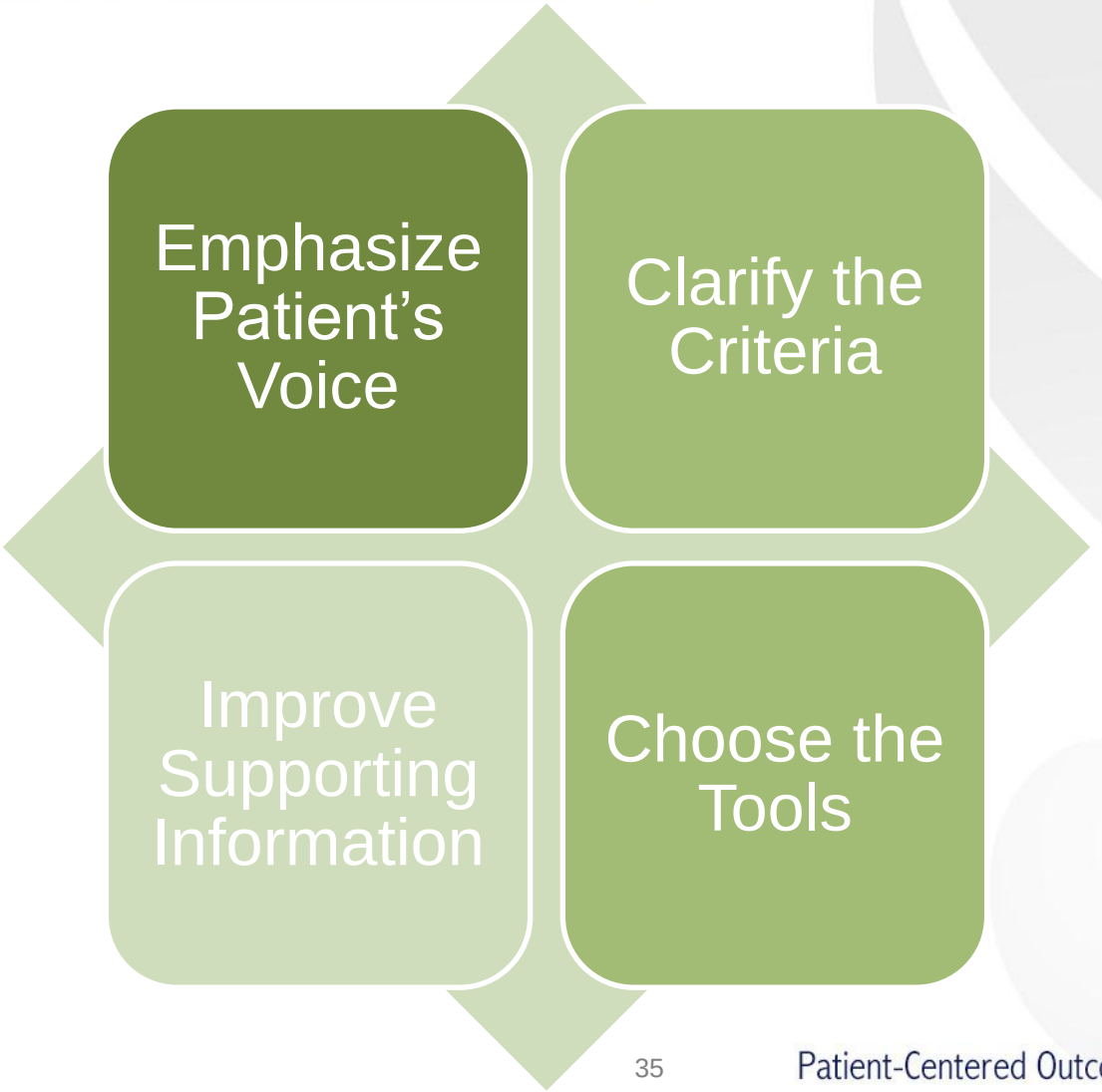
Group 2 Results



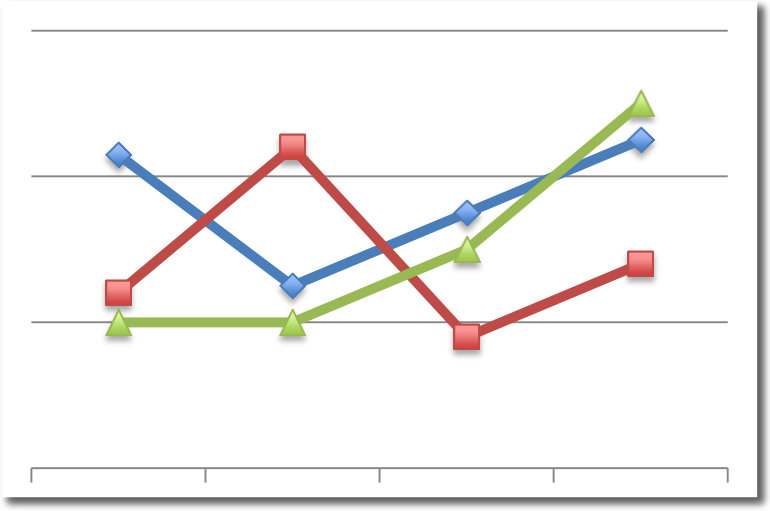
Participants Provided Valuable Insights to Improve the Process



1. Patient-Centeredness

- Are **patients and clinicians** asking for this research ?
- Will research findings make a **difference** to patients and their clinicians when making health care decisions ?

2. Impact on Population and Individual Health



- **Burden of disease** in terms of prevalence, mortality, morbidity, individual suffering, loss of productivity?
- **Rare disease**?

3. Differences in Benefits and Harms, And Reduction in Uncertainty

- Indications of differences in **benefits and harms** sufficient to warrant conducting new research?
- Does current evidence suggest **uncertainty** regarding treatment effectiveness and a need for additional evidence?

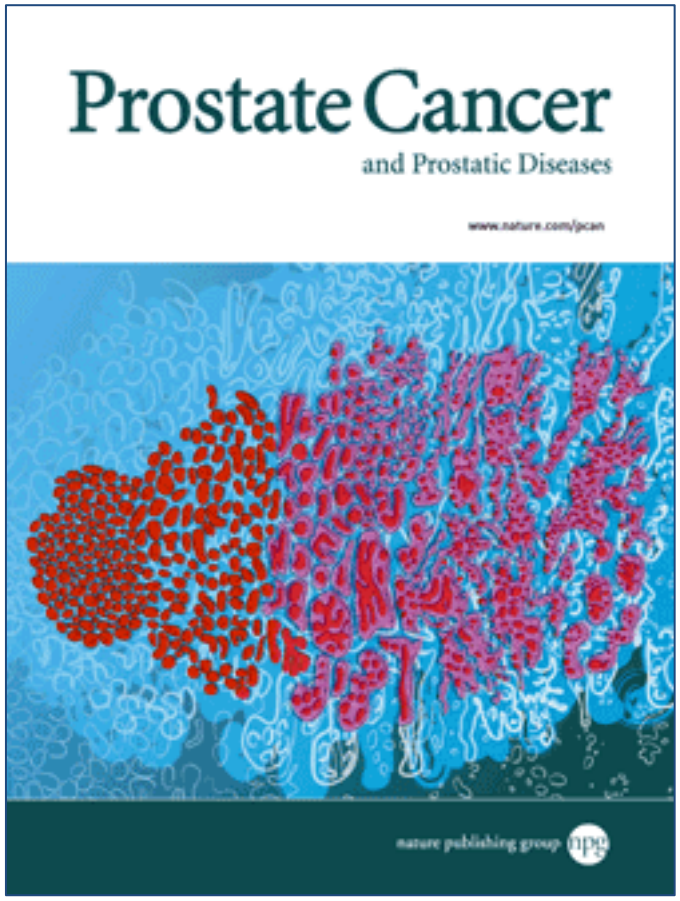
4. Implementation in Practice

How likely is it that the research findings will be implemented in practice?

5. Duration of Information

- Will research findings be valid by the time the study has concluded?

Radiation Therapy for Prostate Cancer



- Patient centeredness
- Impact on population and individual health
- Differences in benefits and harms and reduction in uncertainty
- Implementation in practice
- Duration of information

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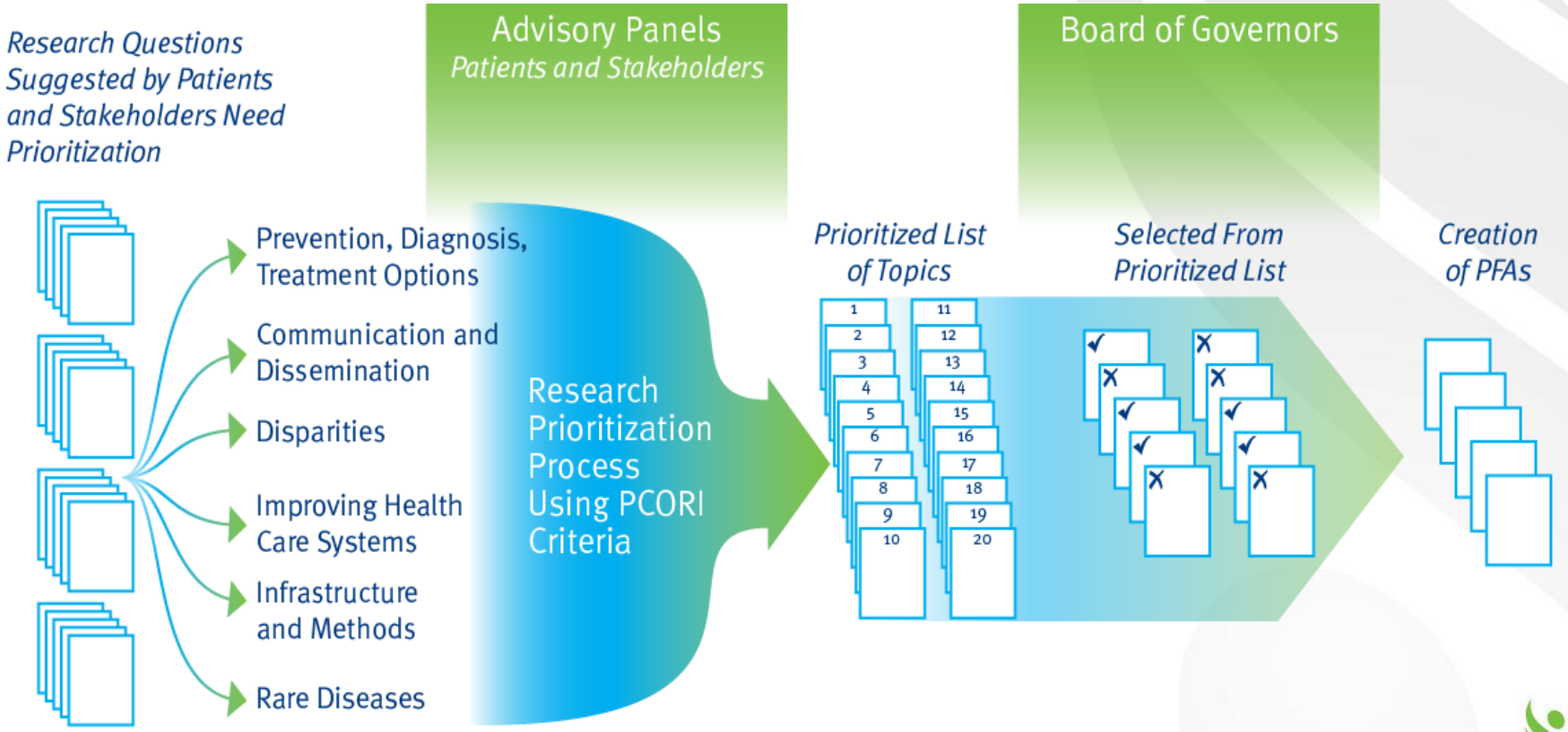
Next Steps

- Revisions
- Implementation
- Learning from ARRA

Launching PCORI's Research Prioritization Process

From Research Questions to Research Studies



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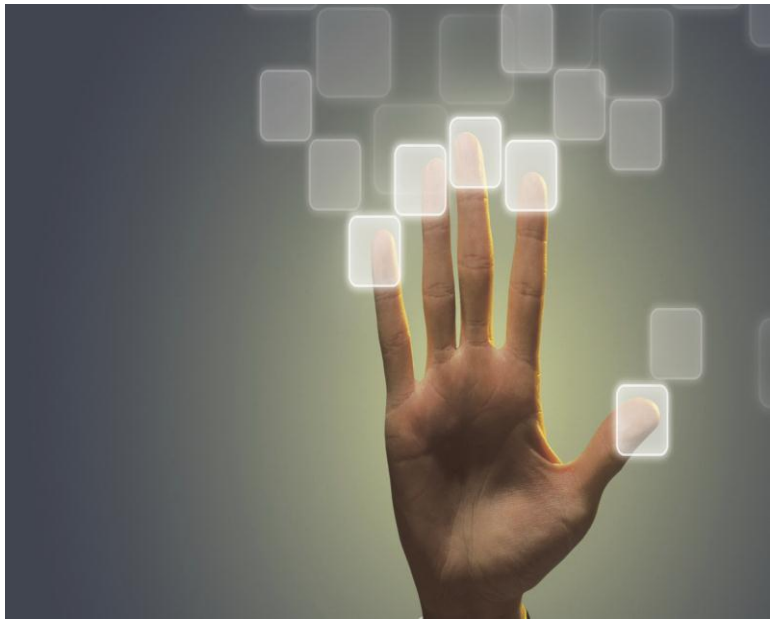

- 35 Pilot Group Members
- Technical Working Group
- PCORI staff, Board Members and MC Members
- NORC at University of Chicago

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Gail Wilensky, PhD

Economist, Senior Fellow, Project HOPE

TWITTER: #PCORI

EMAIL: getinvolved@pcori.org

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Improving Research Prioritization Methods

David Meltzer MD, PhD
PCORI Methodology Committee
Research Prioritization Methods Workshop
December 5, 2012

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Pragmatic Approaches to Value of Information Analysis: A Whitepaper for PCORI

David Meltzer MD, PhD
Ties Hoomans, PhD
Anirban Basu, PhD

The University of Chicago
Erasmus University
The University of Washington

The Role of Methods in Mission: Example of the U.S. Centers for Disease Control (CDC)

- CDC Mission
  - Collaborate to create the expertise, information, and tools that people and communities need to protect their health – through health promotion, prevention of disease, injury and disability, and preparedness for new health threats
  - Extremely limited resources relative to need, NIH
- Decision-Making
  - Legislative mandates
  - Administrative action
  - Peer review (administrative decision making)
- Tools for Population Health Analysis
  - Economic Cost of Illness
    - Dorothy Rice, Director, National Center for Health Statistics, 1976-82
    - "Estimating the Economic Cost of Illness", 1966
  - Cost-Effectiveness Analysis
    - Jeff Koplan, Director, Centers for Disease Control and Prevention, 1998-2002
    - "Pertussis Vaccine: An Analysis of Benefits, Risks, and Costs", 1979

Patient-Centered Outcomes Research Defined

Patient-Centered Outcomes Research (PCOR) helps people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options. This research answers patient-centered questions such as:

- "Given my personal characteristics, conditions and preferences, what should I expect will happen to me?"
- "What are my options and what are the potential benefits and harms of those options?"
- "What can I do to improve the outcomes that are most important to me?"
- "How can clinicians and the care delivery systems they work in help me make the best decisions about my health and healthcare?"

Criteria for Research **Outlined by Law**

- Impact on Health of Individuals and Populations
- Addresses Current Gaps in Knowledge/ Variation in Care
- Patient-Centeredness
- Improvability through Research
- Impact on Health Care System Performance
- Rigorous Research Methods
- Inclusiveness of Different Populations
- Potential to Influence Decision-Making
- Efficient Use of Research Resources

PCORI Research Prioritization Criteria

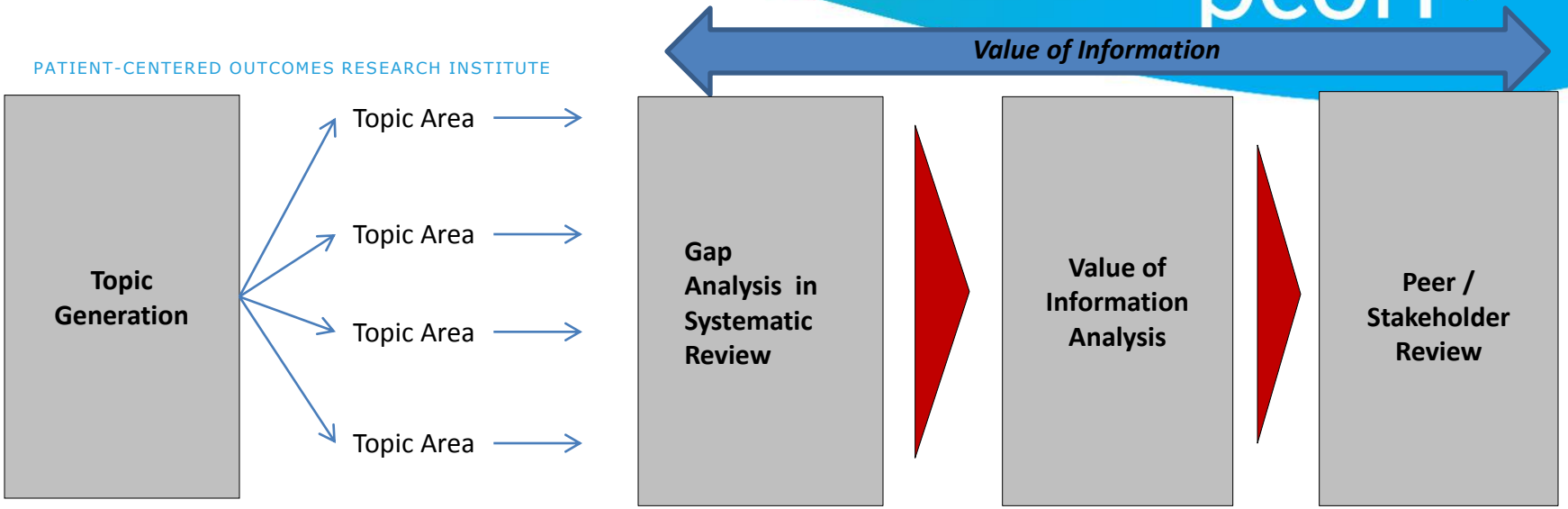
- Impact of the condition on the health of individuals and populations (including measures of prevalence, incidence, and other measures of burden of disease)
- Innovation and potential for improvement (including measures to define difference in benefits, reduction in uncertainty, probability of implementation, durability of information)
- Potential impact on health care performance
- Potential for patient-centeredness
- Potential for inclusiveness of different populations.

DRAFT

Methods for Establishing Research Priorities

Draft Chapter Framework

PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE



- Need to consider topic if are going to prioritize it
- PCOR perspective creates large number of new questions
- How do you involve patients and other stakeholders?

- How should systematic reviews be performed?
- How used to generate research topics?
- How to incorporate patient perspective?

- Provide Board and/or grant applicants with tools to quantify expected benefits of research
- When is VOI worth it? Is it a $$ amount? Can costs of VOI be reduced?
- How to incorporate patient perspective?

- Design of review process?
- Balance between directive and investigator-initiated research?
- Feedback for grant recipients and format for feedback?

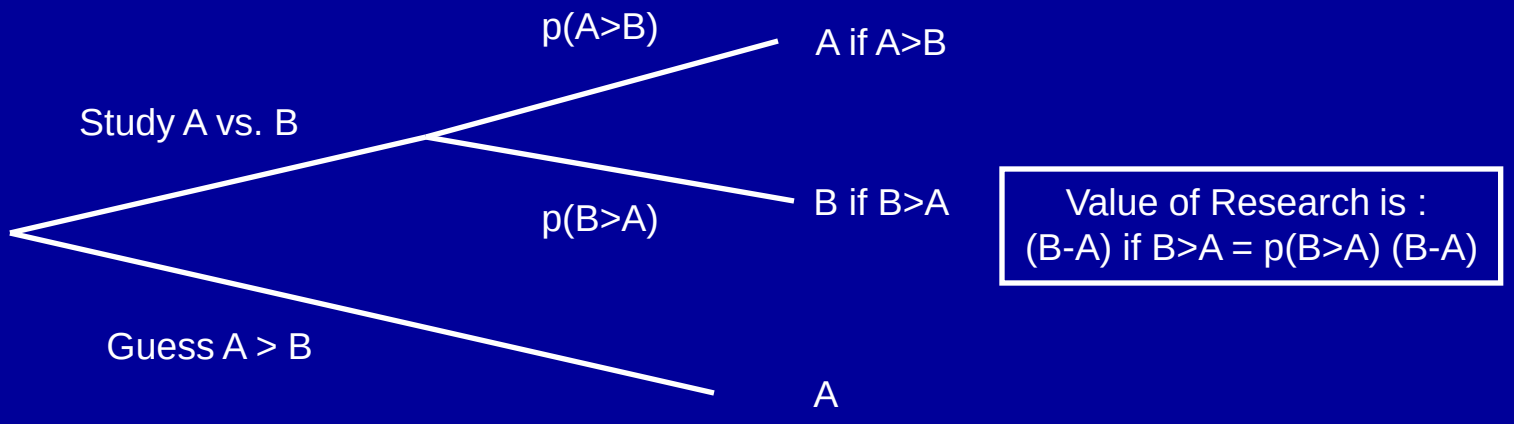
Two broad tasks:

Prioritize specific research studies

Prioritize research areas

Value of Information Approach to Prioritizing Research

- Systematic approach to valuing benefits of research
  - Change in expected value of outcome given decision with research compared to without research
  - Developed by Raiffa & Schleifer 1950s, Claxton 1999, Meltzer 2001
  - Used in UK by National Institute of Health and Clinical Excellence
  - Growing use in US



Value of Information Approach to Value of Research

- Without information
  - Make best compromise choice not knowing true (T) state of the world (e.g. don't know if intervention is good, bad)
    - With probability p: get V(Compromise|G)
    - With probability 1-p: get V(Compromise|B)
- With information
  - Make best decision knowing true state
    - With probability p: get V(Best choice|G)
    - With probability 1-p: get V(Best choice|B)
- Value of information

  = E(outcome) with information - E(outcome) w/o information

  = [p*V(Best choice|G) + (1-p)*V(Best choice|B)] -

  [p*V(Compromise|G) + (1-p)*V(Compromise|B)]

  = Value of Research

  = P(research changes decision) * [V(Best choice|T) –V(Compromise|T)]

Information Requirements for Value of Information Calculations (Meltzer. J Health Econ 2003)

	Conceptual Basis	Information Required			Missing Elements
		Burden of Illness	Priors for Subject of Research	Posteriors for Subject of Research	
Expected Value of Information	Expected Gain in Welfare from Research	Yes	Yes	Yes	Serendipity
Expected Value of Perfect Information	Expected Gain from Perfectly Informative Specific Experiment	Yes	Yes		Serendipity, Likelihood Potential Gains
Maximum Value of Information	Maximum Possible Gain from Specific Experiment	Yes	Minimal Bounds		Serendipity, Likelihood Potential Gains
Maximum Value of (Disease-Specific) Research	Maximum Possible Gain for Target Disease	Yes			Serendipity, Likelihood Potential Gains

A Simple Example of Perfect and Imperfect Information

Payouts and best choices if know those payouts

	B=1	B=4
A =0	B (1)	B (4)
A=3	A (3)	B(4)

Possible Strategies

Choose A: EV = 0*½ + 3*½ = 1.5

Choose B: EV = 1*½ + 4*½ = 2.5

Max Value Research = Max–Min = 4-0 = 4

EVPI = ¼ (1+3+4+4) = 3

EVI test (A=0,B=1) (p =1/4)

if Y, choose B(1), if N, choose B since 4+4+1>0+3+3. Always choose B so EV = 2.5

EVI test (A=3, B=1) (p=1/4)

if Y, choose A(3), if N choose B since 1+4+4>0+0+3 (EV = 1/3*((1+4+4)= 3 so EV = 3

EVI test (A=3) (p=1/2)

if Y, choose A since 3+3>4+1 EV= 3

if N, choose B since 1+4>0+0 EV=(1+4)/2=2.5

EV = ½*3 + ½*2.5 = 2.75

Fit of PCORI Research Criteria with VOI

Criterion	Fit wit VOI
Impact of condition on health of individuals and populations	Yes (Populations), Potentially (individuals)
Innovation and potential for improvement (Δ benefits, reduced uncertainty, p(implementation), durability)	Yes
Potential impact on health care performance	Yes
Potential for patient-centeredness	Yes, potential
Potential for inclusiveness of different populations	Yes, potential

Practical Applications of Value of Information

- VOI requires modeling population value of information

$$VOI = \sum_t \beta^t \times D(t) \times I(t) \times N_t \times IVOI$$

where

β^t *is time preference discount factor*

$D(t)$ *is depeciation of knowledge over time*

$I(t)$ *is extent of implementation*

N_t *is number of eligible individuals* in *each cohort*

IVOI is individual VOI

- VOI based on decision models
  - IVOI modeled with decision model
  - UK (NICE): Alzheimer's Disease Tx, wisdom teeth removal
- Minimal modeling approaches to VOI
  - IVOI comes (nearly) directly from clinical trial
  - US (NIH): CATIE Trial of atypical antipsychotics
- Bound with more limited data (conceptual VOI, burden of illness)

Full and Minimal Modeling Approaches to VOI

(Meltzer, et al. Medical Decision Making, AHRQ EPC Report, 2011)

Approaches	Definitions*	VOI Calculations	Data Requirements	Clinical Application(s)		Advantages (+) and Disadvantages (-)
Full Modeling	Full characterization of the disease/ treatment using a decision model or other simulation model of relevant health state	Simulation/ bootstrapping, parametric and/or nonparametric	Data on all model parameters	Chronic conditions, complex diseases	-	Complex and time-consuming modeling exercises
		Equation-based computation, parametric			+	Detailed uncertainty analysis and VOI estimates, including calculation of EVPPI
Limited Modeling	Any modeling necessary (e.g., modeling of patient survival, mapping of treatment effect to utilities or aggregate approximation of costs) without using a decision model or other simulation model of relevant health states	Simulation/ bootstrapping, parametric and/or nonparametric	Intermediate measures for health outcomes or QALYs, costs and/or NBs; Survival data	Acute conditions, end of life treatments	+	Reduced need for complex and time-consuming modeling
		Equation-based computation, parametric			+	Complementary to adaptive clinical trial design
					-	Requires clinical trial that can requires only modeling of survival or other limited modeling to generate comprehensive measure of net benefit
					-	No comprehensive uncertainty analysis and VOI estimates (EVPPI)
No Modeling	Direct replication or direct calculation of (incremental) effects on comprehensive health outcomes (e.g. QALYs, and/or net benefits)	Simulation/ bootstrapping, parametric and/or nonparametric	Distributions of comprehensive health outcomes or, QALYs and/or net benefits	Acute conditions, end of life treatments Direct measurement of final health outcomes	+	No need for complex and time-consuming modeling
		Equation-based computation, parametric			+	Complementary to adaptive clinical trial design
					-	Requires clinical trial that can provide comprehensive measure of net benefit
					-	No comprehensive uncertainty analysis and VOI estimates (EVPPI)

* All approaches seek to address specific treatment or coverage decisions, to characterize decision uncertainty and to establish VOI estimates
EVPPI: expected value of partial perfect information

Practical Applications of Value of Information

- VOI requires modeling population value of information

$$VOI = \sum_{t} \beta^{t} \times D(t) \times I(t) \times N_{t} \times IVOI$$

where

β^{t} *is time preference discount factor*

$D(t)$ *is depeciation of knowledge over time*

$I(t)$ *is extent of implementation*

N_{t} *is number of eligible individuals* in *each cohort*

IVOI is individual VOI

- VOI based on decision models
  - IVOI modeled with decision model
  - UK (NICE): Alzheimer's Disease Tx, wisdom teeth removal
- Minimal modeling approaches to VOI
  - IVOI comes (nearly) directly from clinical trial
  - US (NIH): CATIE Trial of atypical antipsychotics
- Bound with more limited data (conceptual VOI, burden of illness)

“Bayesian Value of information analysis: An application to a policy model of Alzheimer's disease.”

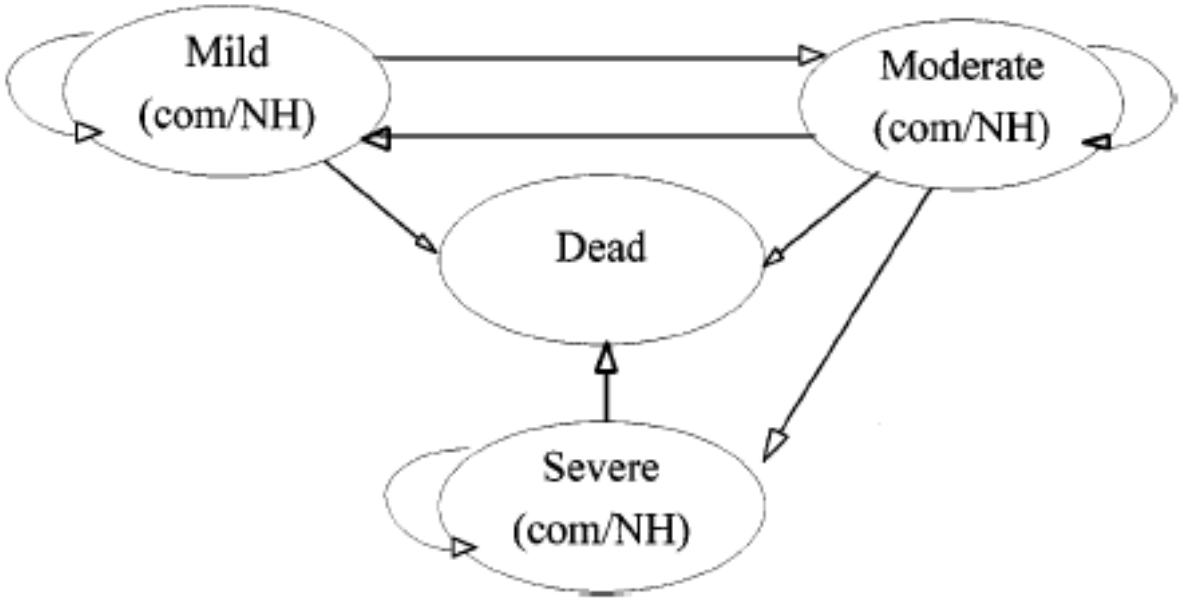


Figure 1. A Markov model of disease progression.

Uncertainty in Incremental Net Benefits

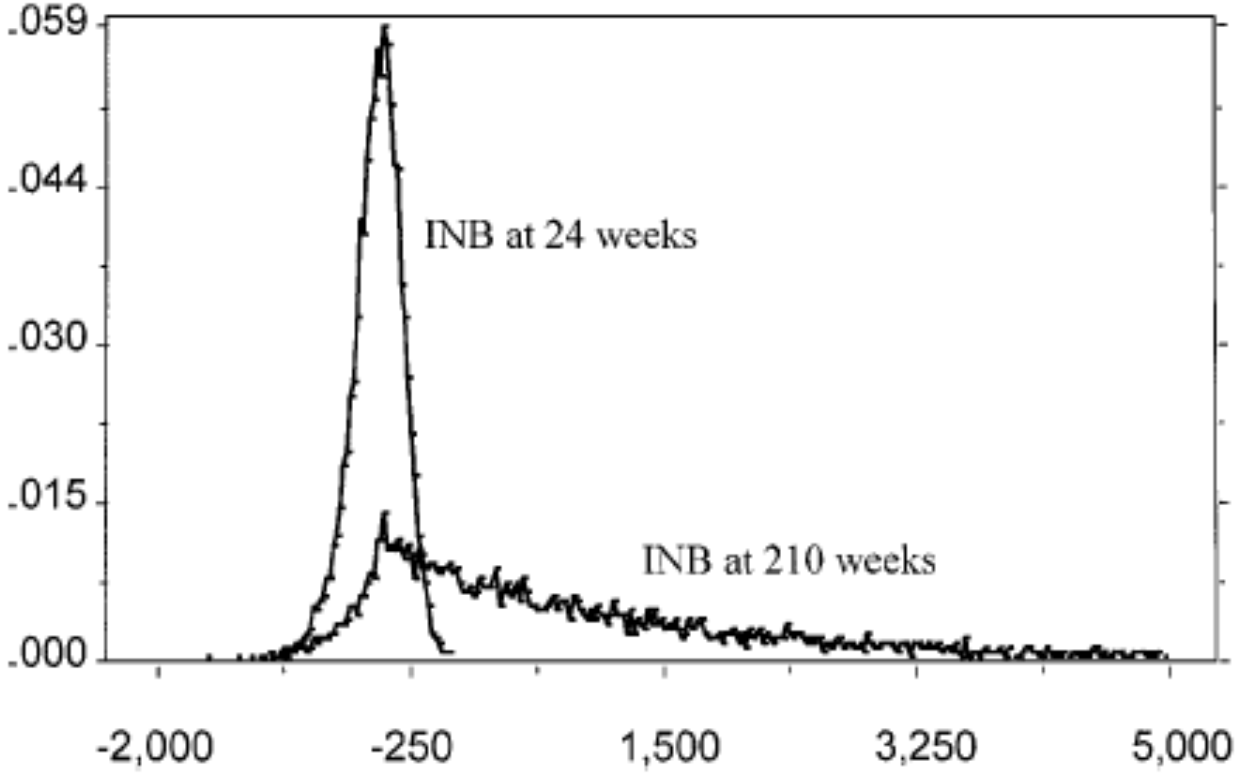


Figure 2A. Prior distribution of incremental net benefit.

Contributors to Value of Research

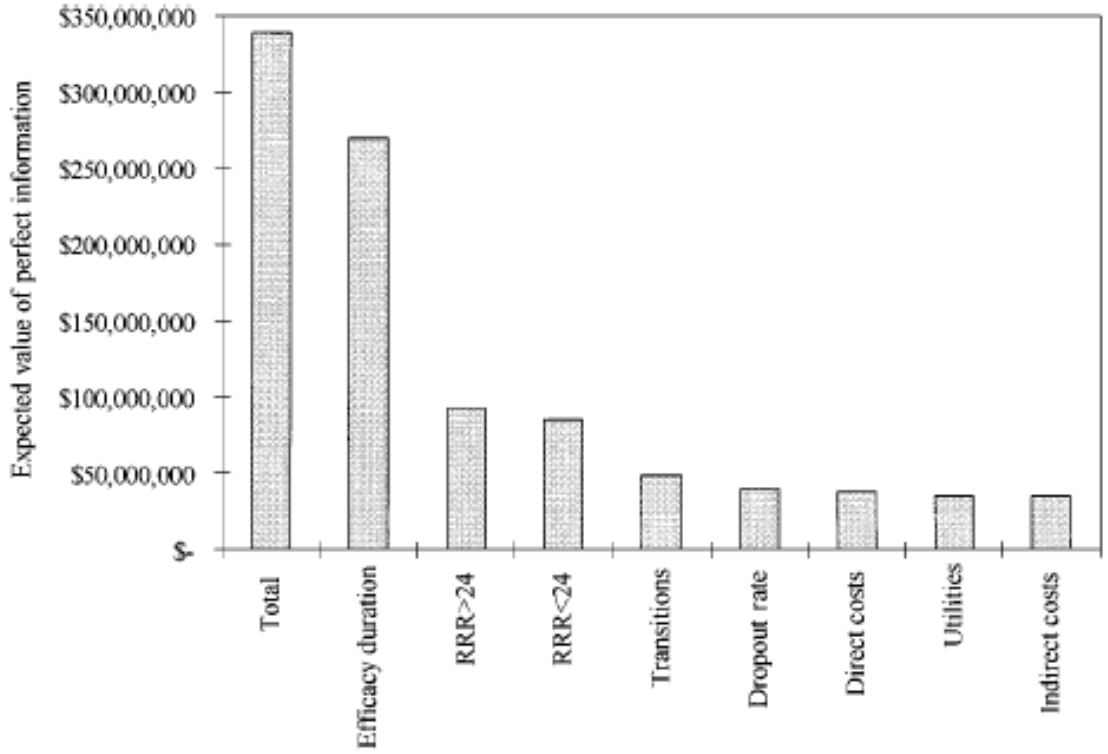


Figure 4. EVPI for model inputs (210 weeks).

Practical Applications of Value of Information

- VOI requires modeling population value of information

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- Bound with more limited data (conceptual VOI, burden of illness)

Limited Modeling Approach: Value of Research on the Comparative Cost-Effectiveness of Antipsychotics Drugs

(Meltzer, Basu and Meltzer, Health Affairs, 2009)

- Clinical Antipsychotic Trials in Intervention Effectiveness (CATIE) Trial
  - $42.6 million, NIMH-funded randomized trial of atypical antipsychotic drugs vs. a neuroleptic (Perphenazine) in established schizophrenia
- Major findings
  - Discontinuation rates similar with A-APDs and Perphenazine
  - Perphenazine cost-effective first-line treatment
- Limitations
  - Discontinuation as major endpoint
  - Limited precision in estimates of effectiveness and costs
  - Limited precision worrisome given prevalence/impact of schizophrenia
- Impact
  - Frequently discussed in coverage decisions
  - Some have argued results should be considered definitive

CATIE Cost-Effectiveness Results

	Monthly Costs Mean (sd) ($)	QALY Mean (sd)	ICER ($/QALY)
Perphenazine	**817 (728)**	**0.722 (0.0064)**	**-**
Olanzapine	**1619 (1442)**	**0.723 (0.0063)**	**9,624,000**
Risperidone	**1635 (1457)**	**0.706 (0.0066)**	**Dominated**
Quetiapine	**1680 (1497)**	**0.721 (0.0065)**	**Dominated**

(Ref: Rosenheck et al , 2006; Private Communications with Dr. Rosenheck)

Only statistically significant difference:

$QALY_{Perphenazine} > QALY_{Risperidone}$ (p-value < 0.001)

Aims of VOI Analysis

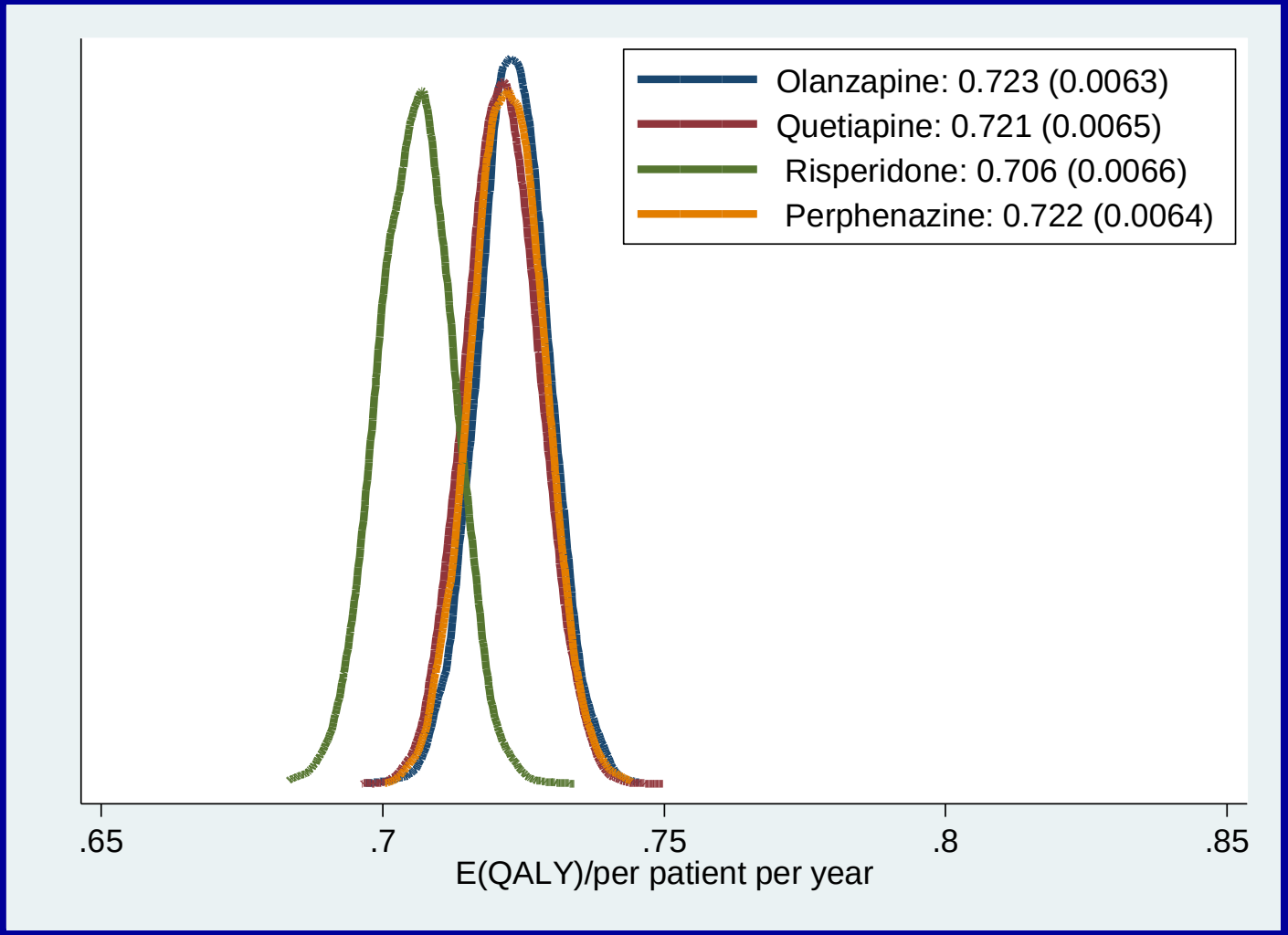
1) To determine the expected value of more precise determination of effects of AAPDs and Perphenazine on costs and QALYs.

2) To determine the optimal sample size for a future trial of the effects of AAPDs and Perphenazine on costs and QALYs

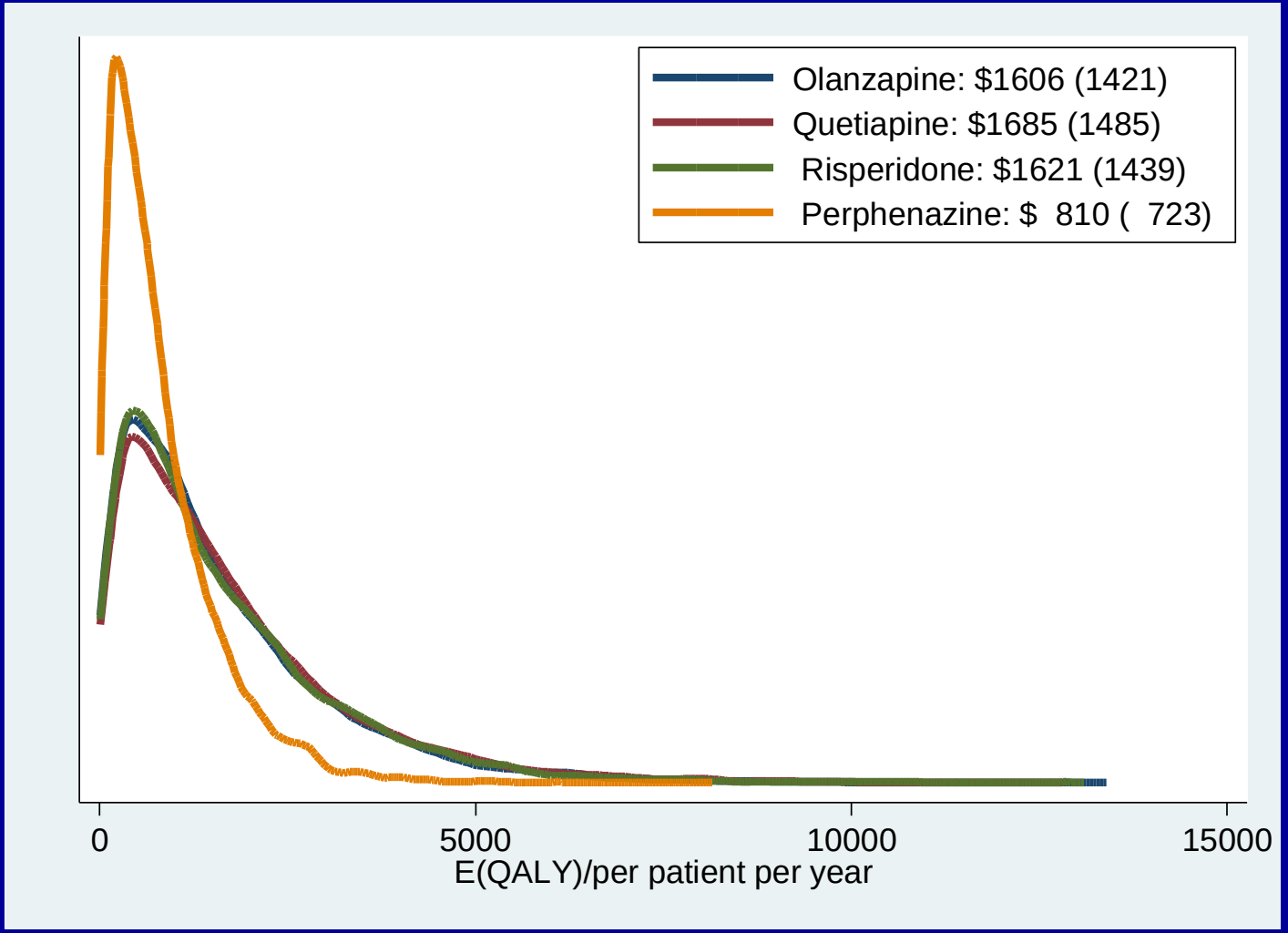
Methods

- Limited modeling approach
  - Used CATIE estimates of effects of alternative treatments on annual quality of life, costs
  - Calculated (modeled) population value of information based on benefits to the prevalent cohort over their lifetimes and the welfare of next 20 incident cohorts over their lifetimes
  - Discounted future years at 3% per year

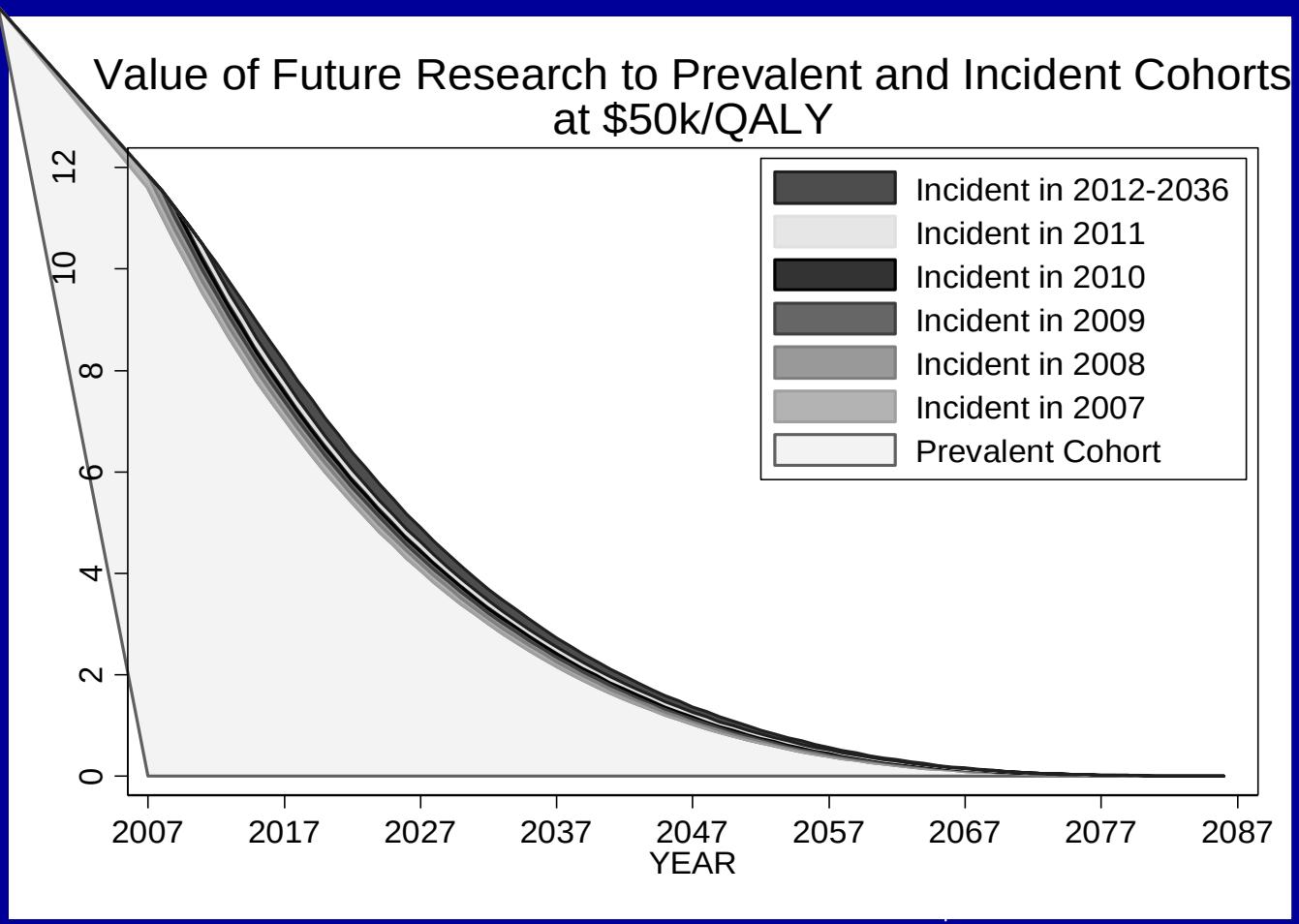
Simulated Distribution of Mean QALYS
(Based on uncertainty around CATIE results)



Simulated Distribution of Mean Costs
(Based on uncertainty around CATIE results)



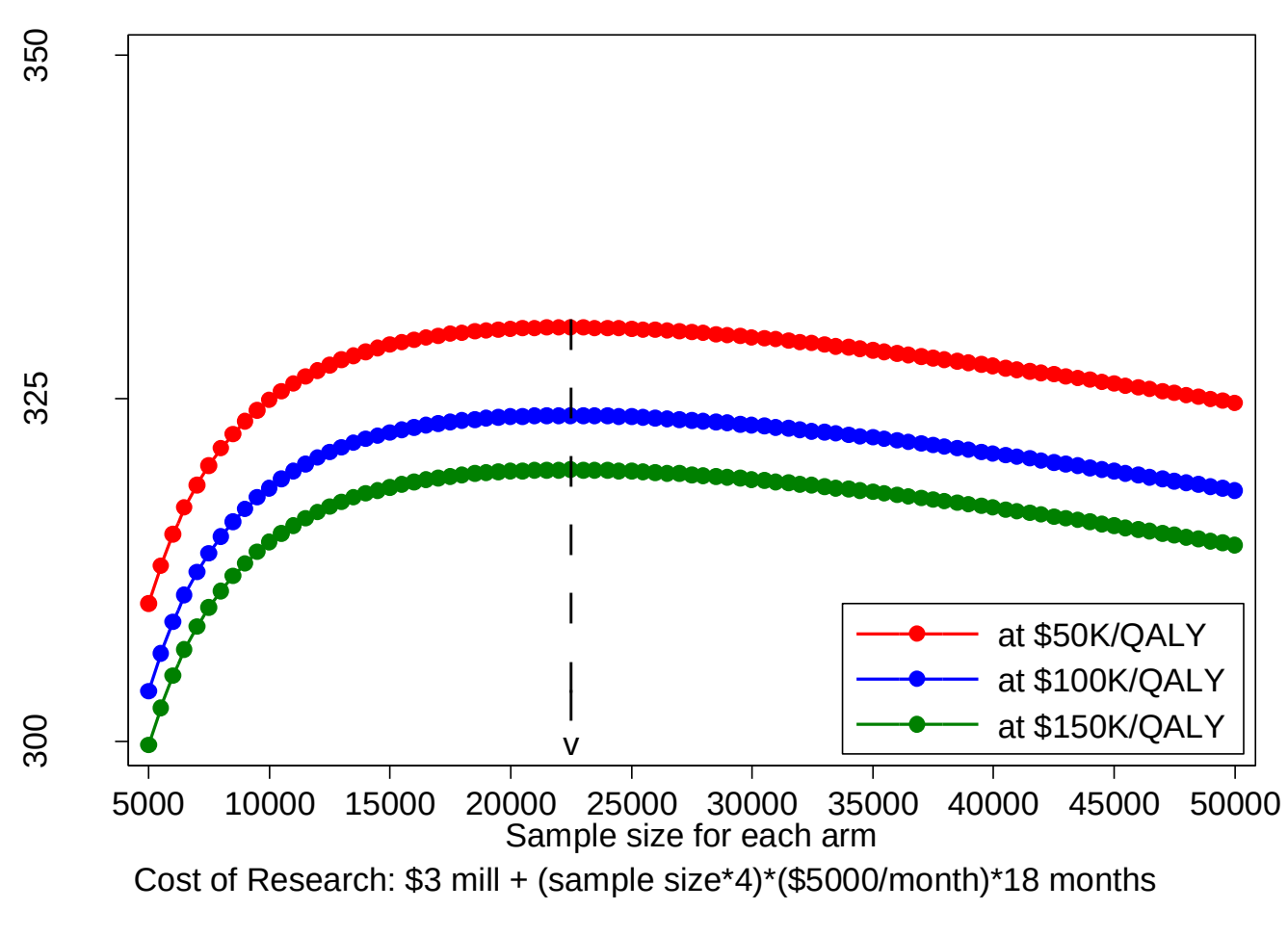
Realizations of Value of Research Over Time



Total Value to Each Incident Cohort: $6.6 billion

Total Value to Prevalent & Next 20 Incident Cohorts: **$342 billion**

Net Expected Value of Sample Information (at $50K, $100K and $150K/QALY)



Optimal sample size for each arm = 22,500

No Modeling Approach: Azithromycin vs. Augmentin in Acute Sinusitis

- Existing small RCT (Marple et al 2010)
  - Primary outcome resolution of symptoms within 5 days
    - 29.7% azithromycin vs. 18.9% amoxicillin/clavulanate
    - Difference: 10.8%; 95% confidence interval [CI]: 3.1–18.4%
  - By day 28, 11% in each.
  - Completion of trial to equal resolution is key
- Net Benefit = WTP – Costs $41.72 - $23.69 = $18.03 (cost-effective)
- Bootstrap from distribution of net benefit to estimate individual-level VOI
- Scale up to population level
- VOI effectiveness: $40 million
- VOI cost-effectiveness: $250 million

Conceptual Value of Information

- VOI requires modeling population value of information

$$VOI = \sum_{t} \beta^{t} \times D(t) \times I(t) \times N_{t} \times IVOI$$

where

β^{t} *is time preference discount factor*

$D(t)$ *is depeciation of knowledge over time*

$I(t)$ *is extent of implementation*

N_{t} *is number of eligible individuals* in *each cohort*

IVOI is individual VOI

- I VOI
  - p(change decision) * Expected value of change given change desirable
  - IVOI low if either of these gets small enough unless other is very large
- Other multiplicative items above
  - Population size, implementation, durability
- Mechanisms to represent these
  - Probability distributions, visual representaions, logic models

Quantitative VOI Estimates

Topic Area	VOI Estimate ($ Million)
MR in Knee Trauma	8
LVAD as Destination Therapy	8
Azithromycin vs. Augmentin in Sinusitis (ignoring costs)	40
Pegylated Liposomal Doxyrubicin in Ovarian CA	206
Azithromycin vs. Augmentin in Sinusitis (including costs)	250
Treatment of Intermittent Claudication	573
Cognitive Behavioral Therapy for Post-partum Depression	603
Typical/Atypical Antipsychotics in Schizophrenia	124,658

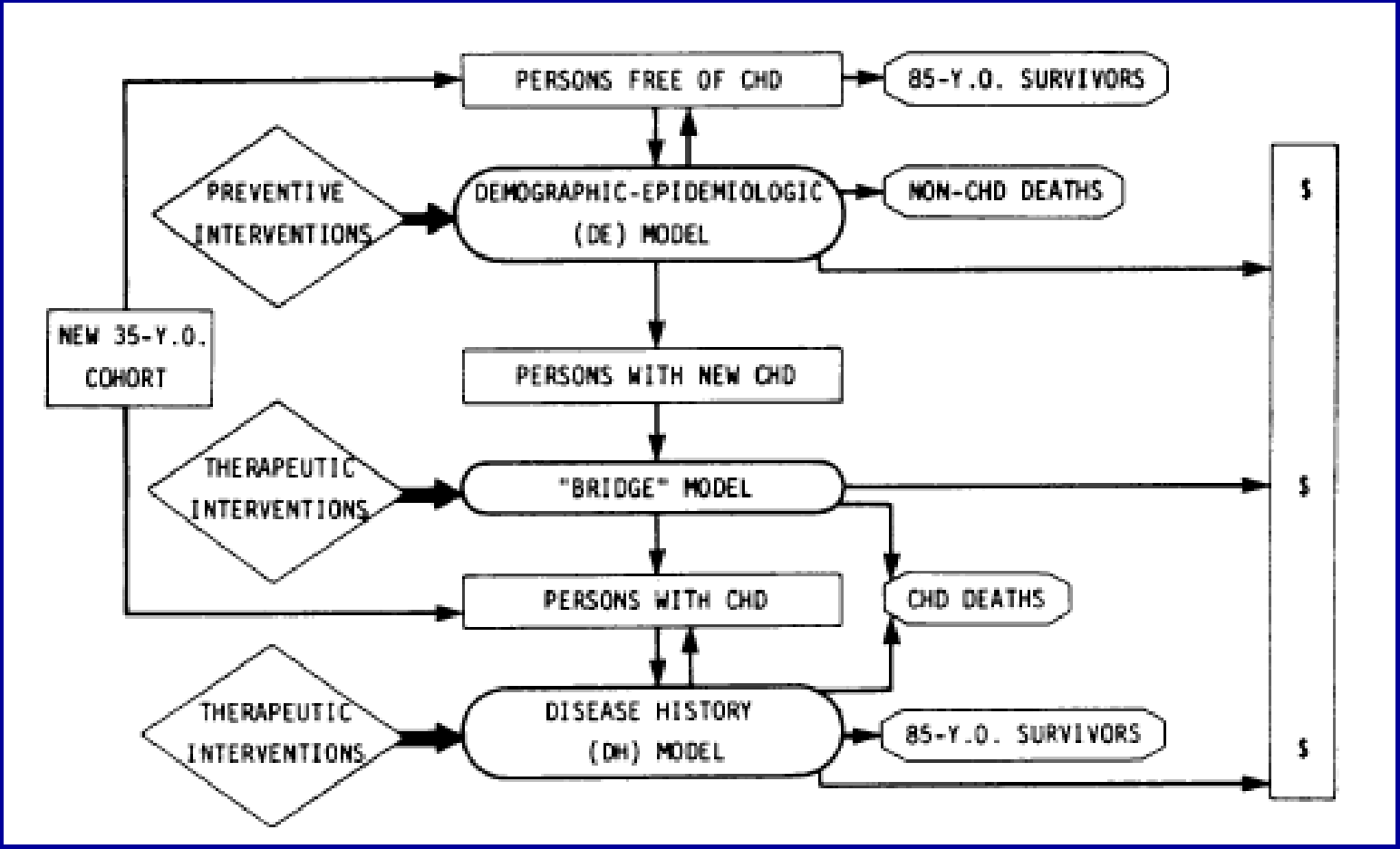
Algorithm: Approaches to Calculating VOI

	Definition	Requirements	Application
Conceptual VOI	**Bounding exercise using information on $E_\theta NB(j,\theta)$, Imp_j, Dur_j, Pop_j**	**Quantitative estimates of VOI elements (useful if $1+ \approx 0$)**	**Rare diseases, controversial treatment, active R&D**
Minimal Modeling	**Direct replication of data, or modeling that is limited to survival or quality of life**	**Comprehensive outcomes, e.g., QALYs, life expectancy, and/or costs**	**Acute conditions, end-of-life treatment**
Full Modeling	**Full characterization of disease and treatment, incl. health states**	**Structuring of model, data input for each parameter**	**EVPPI, (additional) primary data collection**
Maximal Modeling	**Comprehensive modeling organized around clusters of topics**	**Clustering of topics in clinical domain(s)**	**Chronic conditions, complex diseases, integrated care**

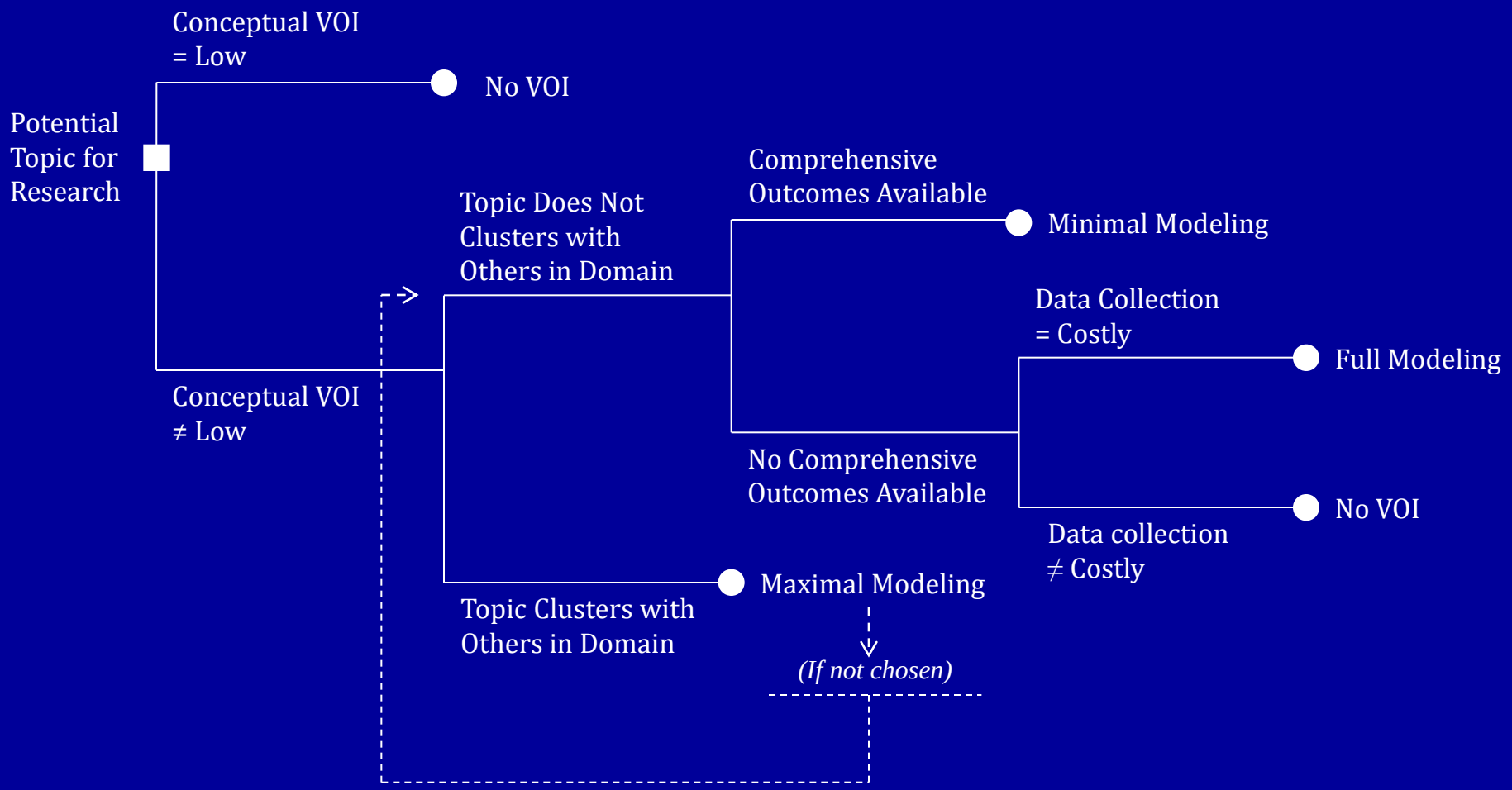
Least complex / costly

Most complex / costly

Maximal modeling VOI: Coronary Heart Disease Model [Weinstein et al., 1987]



Algorithm for selecting approach to VOI



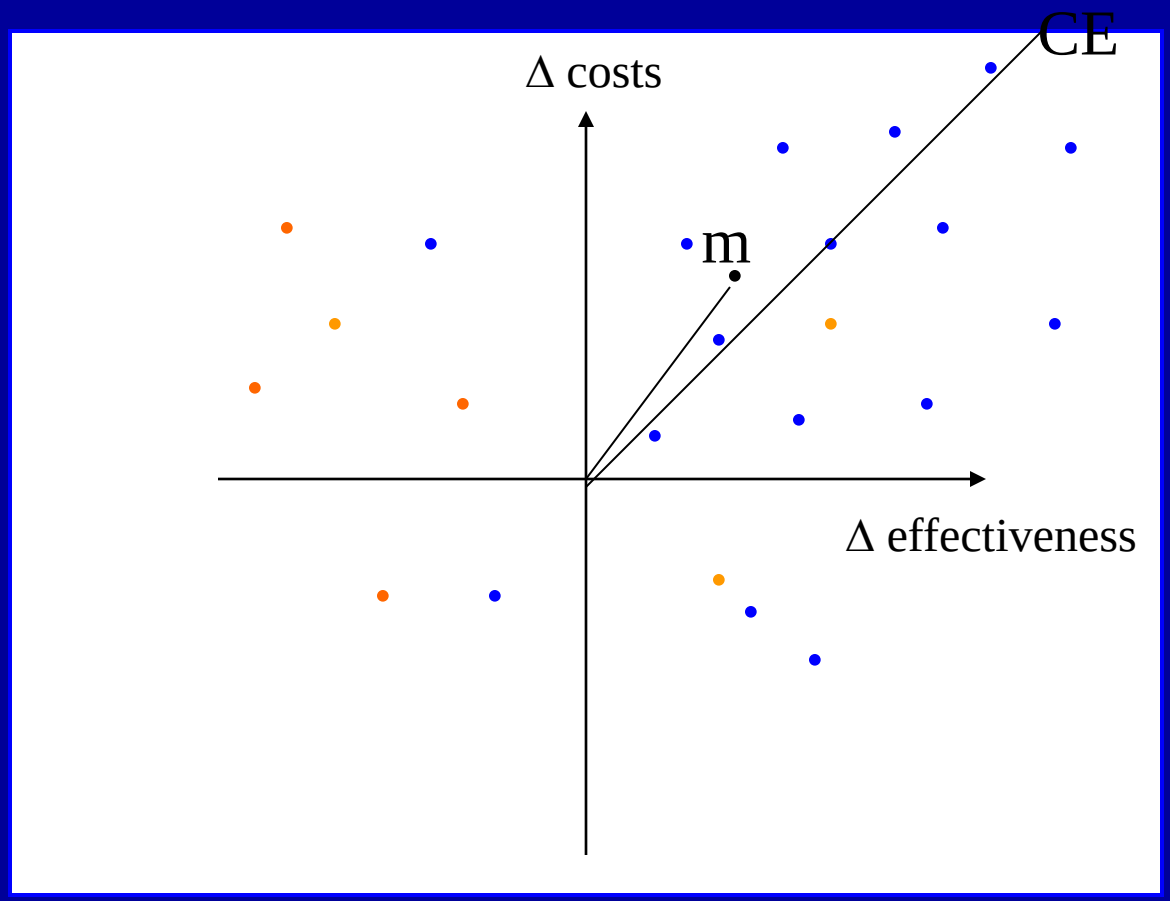
Fit of PCORI Research Criteria with VOI

Criterion	Fit wit VOI
Impact of condition on health of individuals and populations	Yes (Populations), Potentially (individuals)
Innovation and potential for improvement (Δ benefits, reduced uncertainty, p(implementation), durability)	Yes
Potential impact on health care performance	Yes
Potential for patient-centeredness	Yes, potential
Potential for inclusiveness of different populations	Yes, potential

Reflecting Individualization in VOI

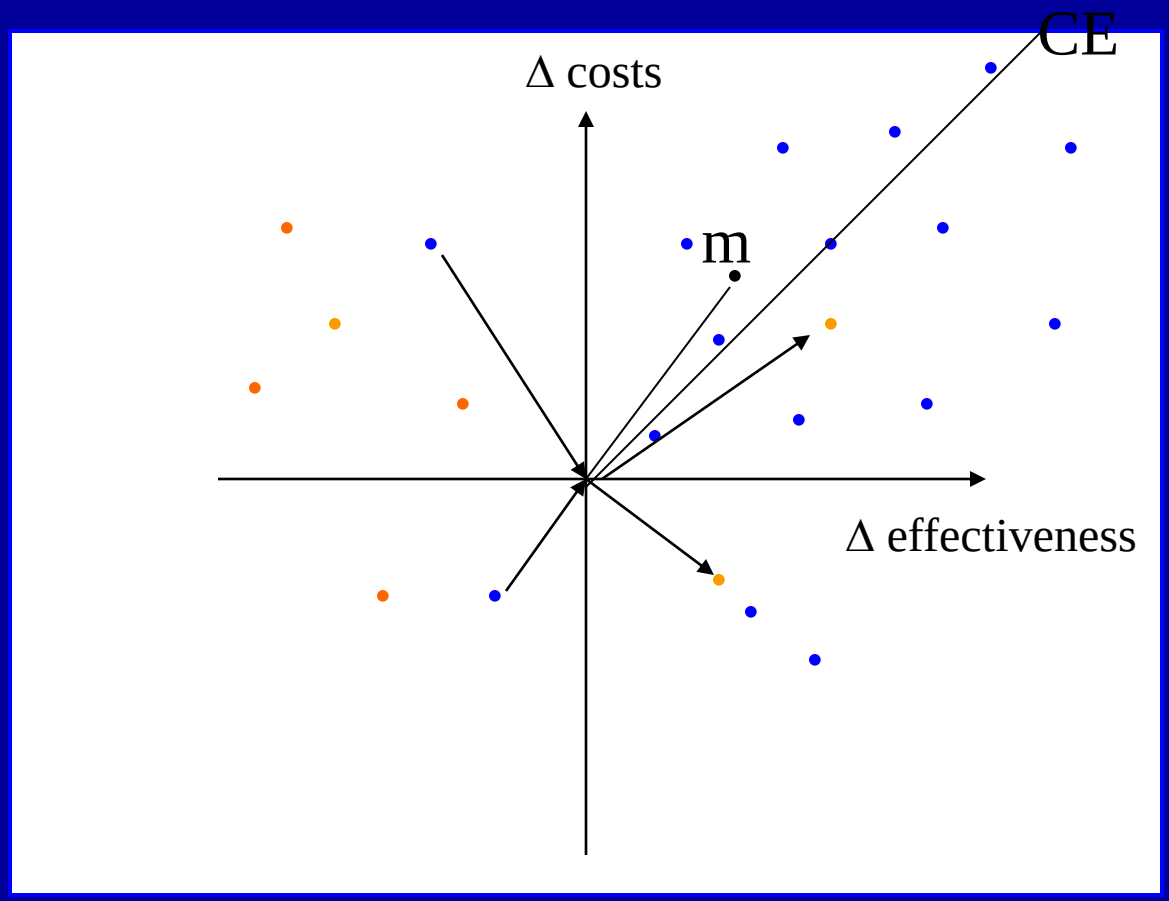
- Incorporate individual-level attributes into decision models
  - Traditional health-related covariates
  - Preferences
  - Choices

Value of Individualization
(Basu and Meltzer, Medical Decision Making, 2007)



Blue Dots=Pts getting Tx; Orange Dots=Pts not getting Tx

Value of Improved Individualization (e.g., Decision Aids)



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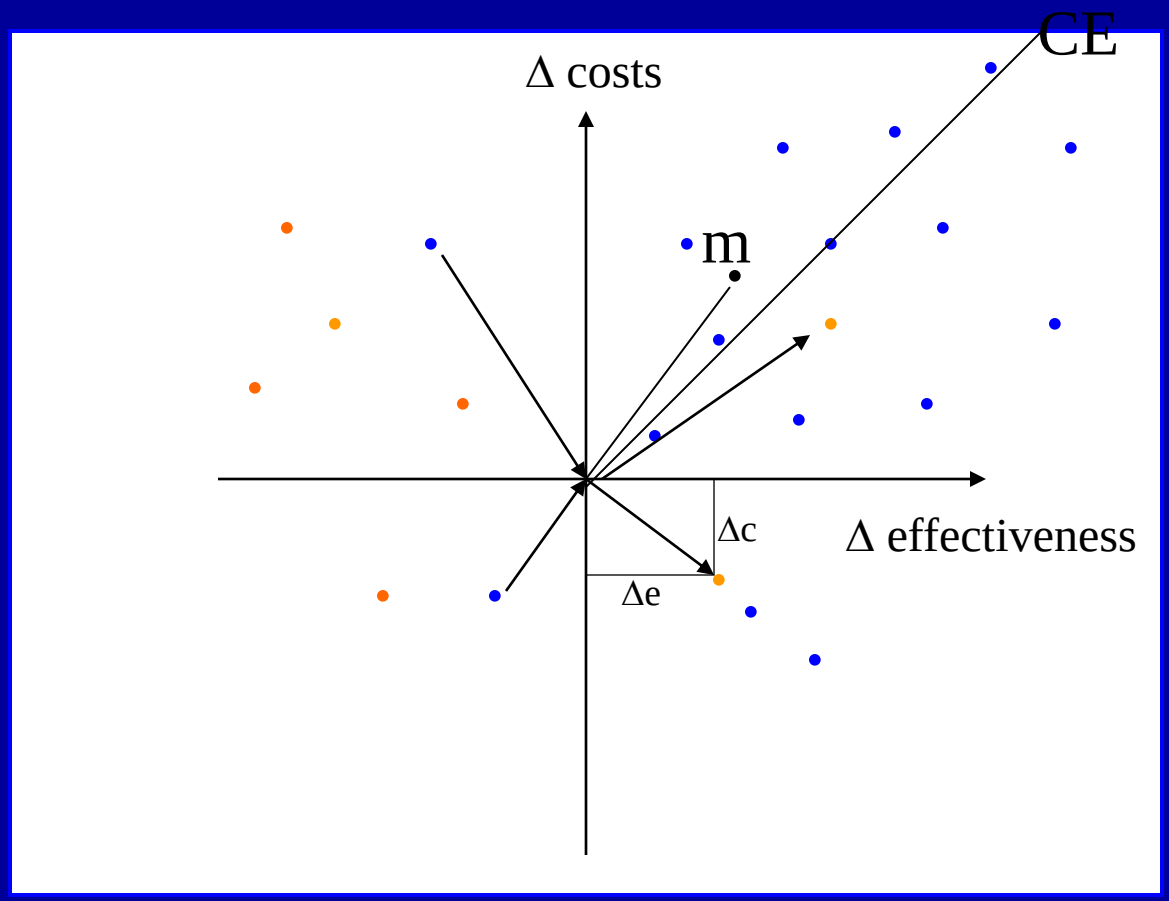


Blue Dots=Pts getting Tx; Orange Dots=Pts not getting Tx

Value of Decision Aid

- Effectiveness = $\Sigma_{\text{Pts }\Delta}\,\Delta e$
- Costs = $\Sigma_{\text{Pts }\Delta}\,\Delta c$
- Total Benefit

  Cost-Benefit = $(1/\lambda)\,\Sigma_{\text{Pts }\Delta}\,\Delta e + \Sigma_{\text{Pts }\Delta}\,\Delta c$

  Net Health Benefit = $\Sigma_{\text{Pts }\Delta}\,\Delta e + \lambda\,\Sigma_{\text{Pts }\Delta}\,\Delta c$

Per Capita Value of Identifying Best Population-level and Individual-level Care in Prostate Cancer

	Value
Best Population-level Therapy	$29
Best Individual-level Therapy	$2958

Fit of PCORI Research Criteria with VOI

Criterion	Fit wit VOI
Impact of condition on health of individuals and populations	Yes (Populations), Potentially (individuals)
Innovation and potential for improvement (Δ benefits, reduced uncertainty, p(implementation), durability)	Yes
Potential impact on health care performance	Yes
Potential for patient-centeredness	Yes, potential
Potential for inclusiveness of different populations	Yes, potential

VOI and Inclusiveness of Populations

- Can’t maximize population health if omit large parts of population
  - Especially parts with greatest health problems and potential to gain
- Can overweight health of priority populations
  - What research haws greatest VOI for specific priority populations?
  - In extreme, place zero weight on non-priority populations
- Can treat inclusiveness as separate criterion from VOI and use judgment to weigh them against each other

Conclusions

- VOI provides a mechanism to estimate the population health impact of specific research questions
- VOI can be burdensome to apply but methods exist for its practical application
  - Maximal modeling, full modeling, limited modeling, conceptual VOI
  - VOI approaches to assess value individualization
- Prioritize research studies and areas
  - Prioritizing studies more straightforward than prioritizing areas
  - VOI in areas may be bounded from above, estimated by aggregating studies
  - Studies in prioritized areas should still meet criteria for value; reserve $ for areas with high-value studies at margin
- Practical experience with VOI limited but increasing
  - Critical to integrate into and complement existing prioritization processes

Improving Research Prioritization Methods

Claire McKenna, PhD, MPhil, MSc
Centre for Health Economics, University of York, UK
Research Prioritization Methods Workshop
December 5, 2012

Patient-Centered Outcomes Research Institute

Expected health benefits of additional evidence: Principles, methods and applications

Karl Claxton, Susan Griffin, Hendrik Koffijberg†, Claire McKenna

Centre for Health Economics, University of York, UK

†Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Netherlands

December 5th, 2012

Patient-Centered Outcomes Research Institute

Purpose and principles

- Demonstrate the principles of what assessments are required when considering the need for additional evidence and the priority of proposed research
- Illustrate how these assessments might be informed by quantitative analysis based on standard methods of systematic review and meta-analysis
- Distinguish between the value of additional evidence and the value of implementing the findings of existing research
- Are the expected health benefits of additional evidence sufficient to regard a particular research proposal as potentially worthwhile?
  → Should it be prioritized over other research topics that could have been commissioned with the same resources?

White paper sets out

- What assessments are needed? How might these assessments be informed?

What assessments are needed?

- Value of evidence and the value of implementation
  - Improve patient outcomes by resolving uncertainty in the existing evidence about the effectiveness of the interventions available
  - How much does the uncertainty matter? Scale of the consequences of uncertainty
  - Will the findings of research be implemented into clinical practice?
- Minimum clinical difference (MCD) in outcomes required
  - Clinical practice is unlikely to change without it (effect size)
  - Other aspects of outcome not captured in the primary endpoint
  - Significant resource, system or patient cost implications
- Assessments in different contexts
- Variability in patient outcomes and individualized care

How might these assessments be informed?

- Value of information analysis applied to random or fixed effect meta-analysis
- Four contexts which are likely to arise are illustrated by case studies:

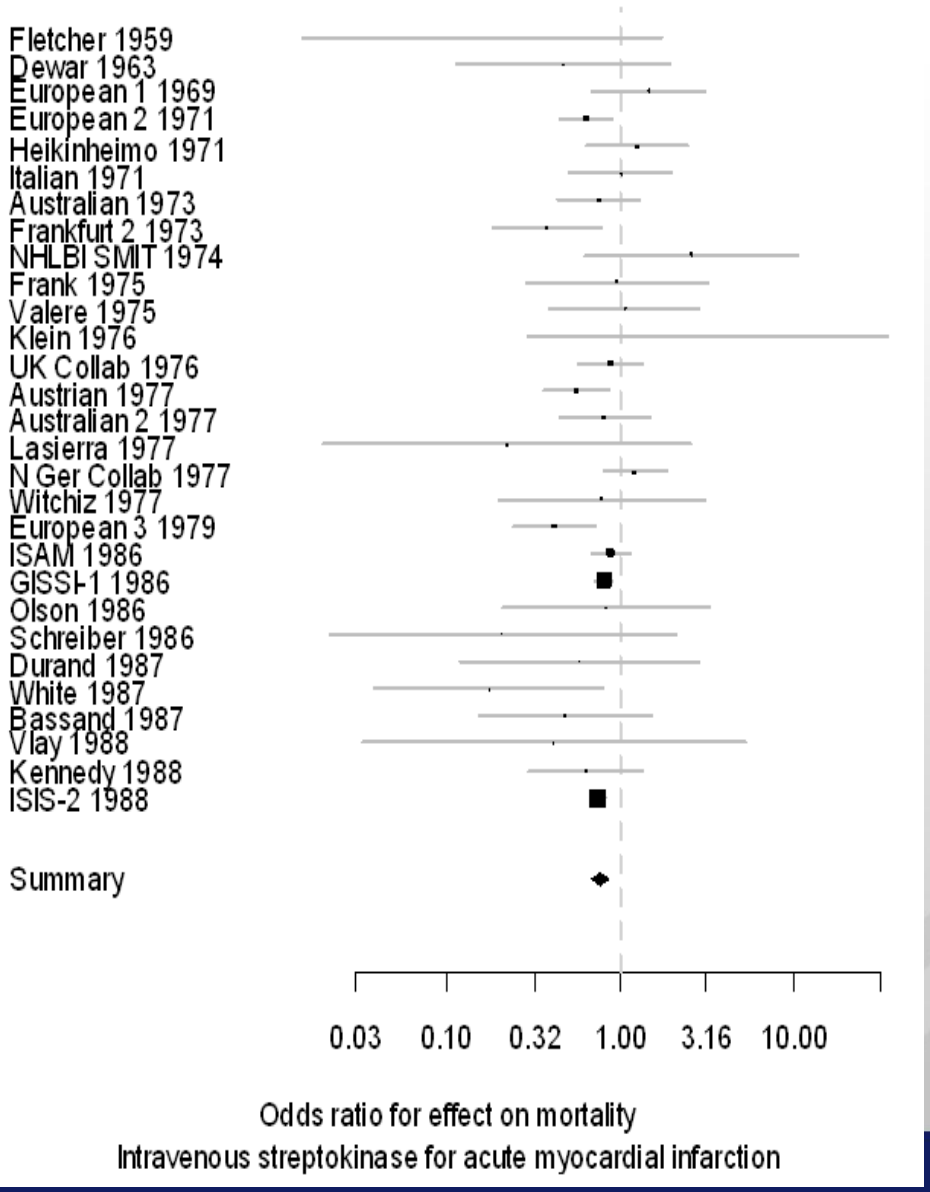
  i. Primary endpoint in the meta-analysis captures health effects (cumulative meta-analysis of streptokinase for the treatment of acute MI)

  ii. Primary endpoint in the meta-analysis needs to be linked to other aspects of outcome (steroids following traumatic head injury)

  iii. Different weights to reflect the relevance and potential bias of the existing evidence (probiotics in severe acute pancreatitis)

  iv. More than two treatment alternatives need to be compared (topotecan, PLDH and paclitaxel for advanced ovarian cancer)

Primary endpoint captures health effects (cumulative meta-analysis)



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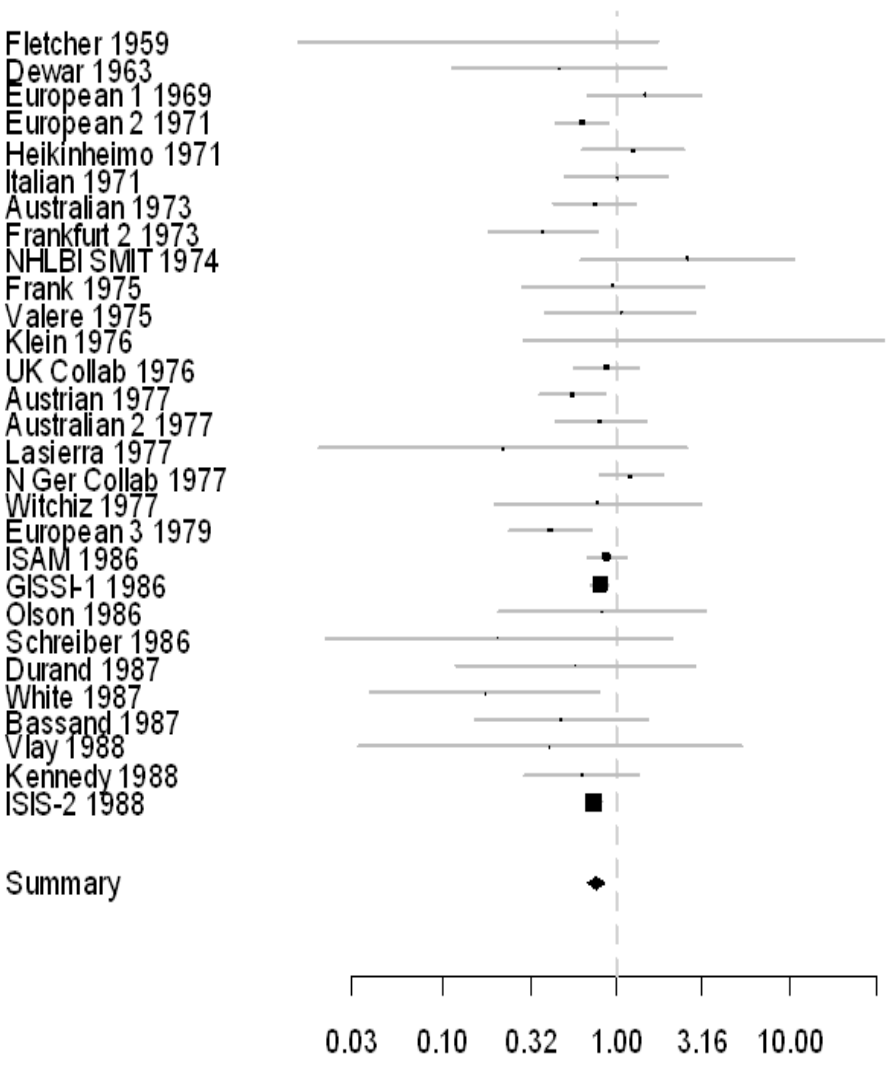
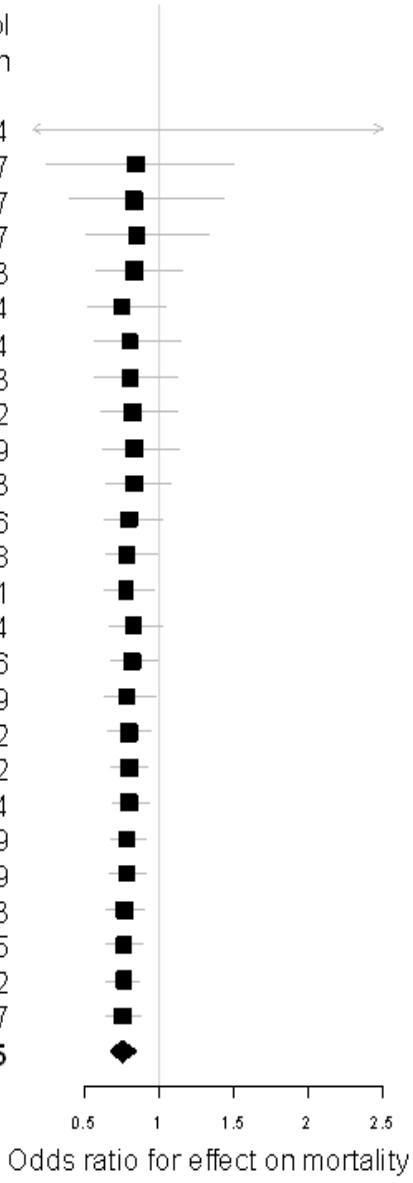
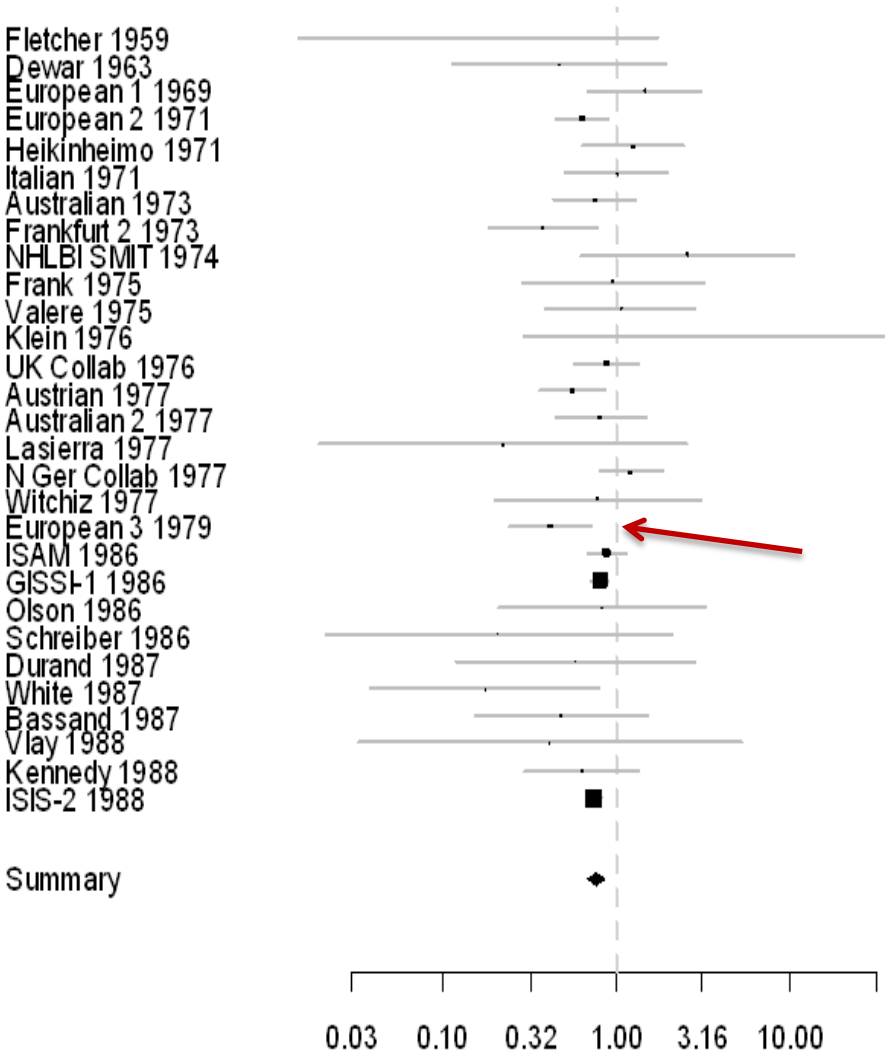


Study	Strep deaths/n	Control deaths/n
European 1	20/83	15/84
European 2	69/373	94/357
Heikinheimo	22/219	17/207
Italian	19/164	18/157
Australian	26/264	32/253
Frankfurt 2	13/102	29/104
NHLBI SMIT	7/53	3/54
Frank	6/55	6/53
Valere	11/49	9/42
Klein	4/14	1/9
UK Collab	48/302	52/293
Austrian	37/352	65/376
Australian 2	25/112	31/118
Lasierra	1/13	3/11
N Ger Collab	63/249	51/234
Witchiz	5/32	5/26
European 3	25/156	50/159
ISAM	124/859	142/882
GISSI-1	628/5860	758/5832
Olson	5/28	5/24
Schreiber	1/19	4/19
Durand	3/35	4/29
White	2/79	12/93
Bassand	5/52	10/55
Vlay	1/13	2/12
Kennedy	12/191	17/177
ISIS-2	**791/8592**	**1029/8595**



Intravenous streptokinase for acute myocardial infarction

Primary endpoint captures health effects (cumulative meta-analysis)



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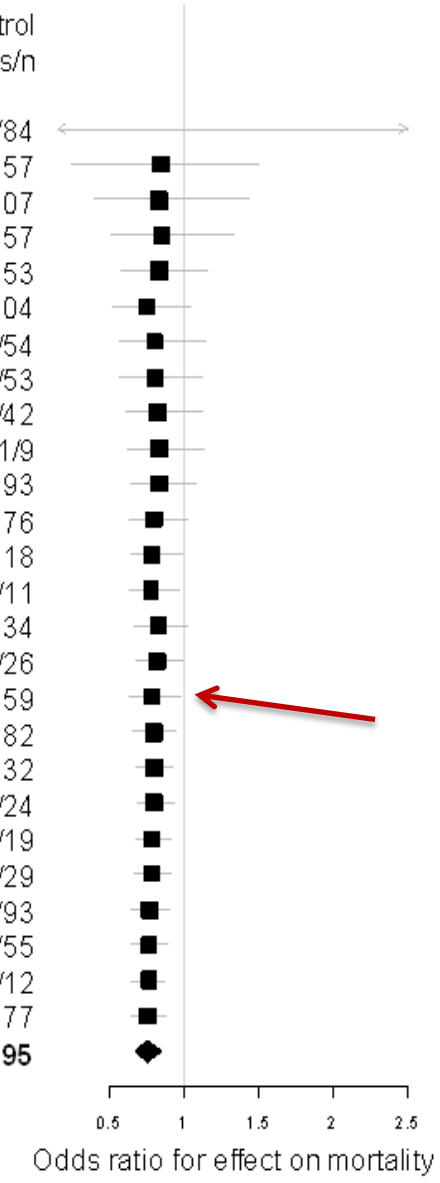
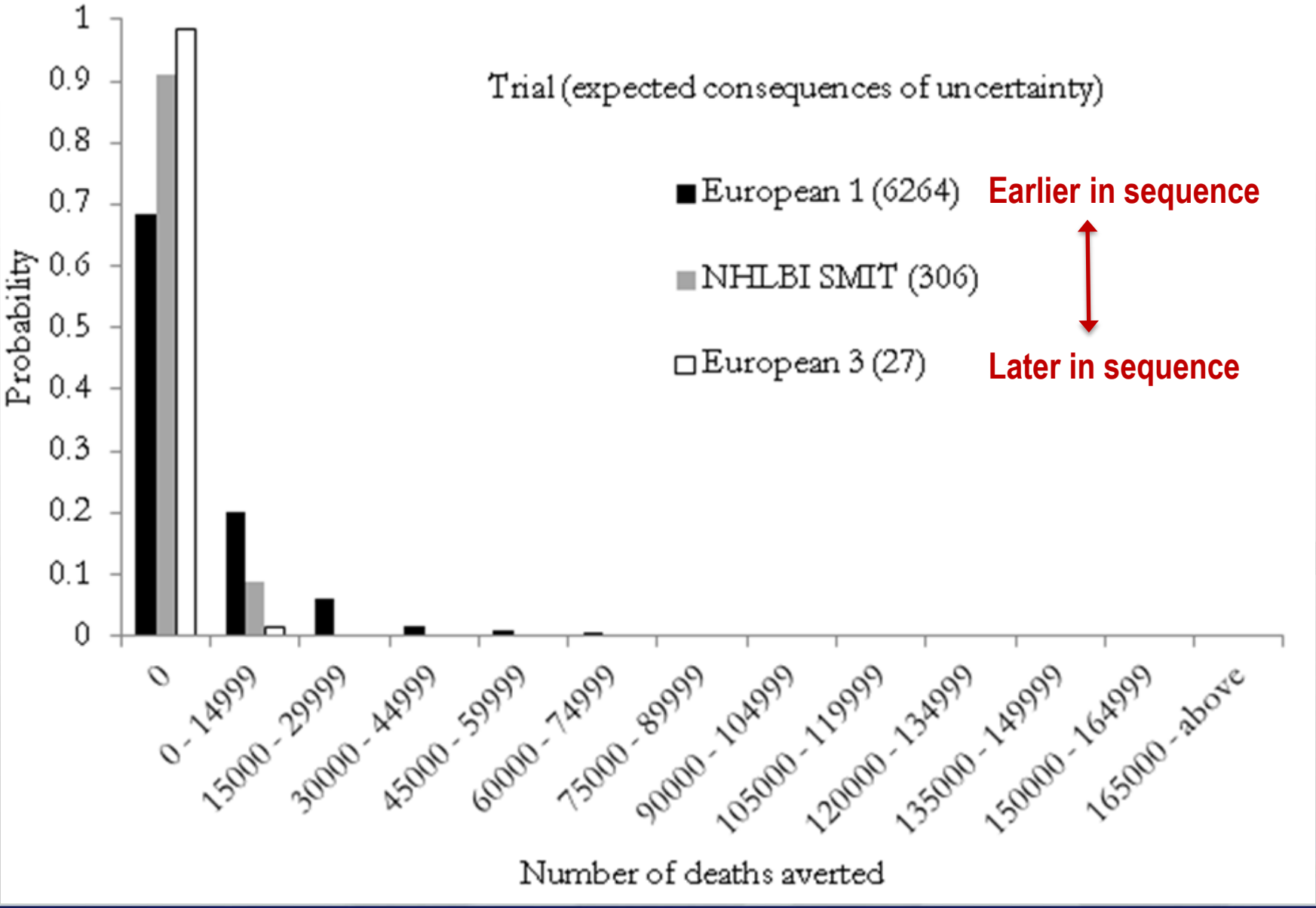
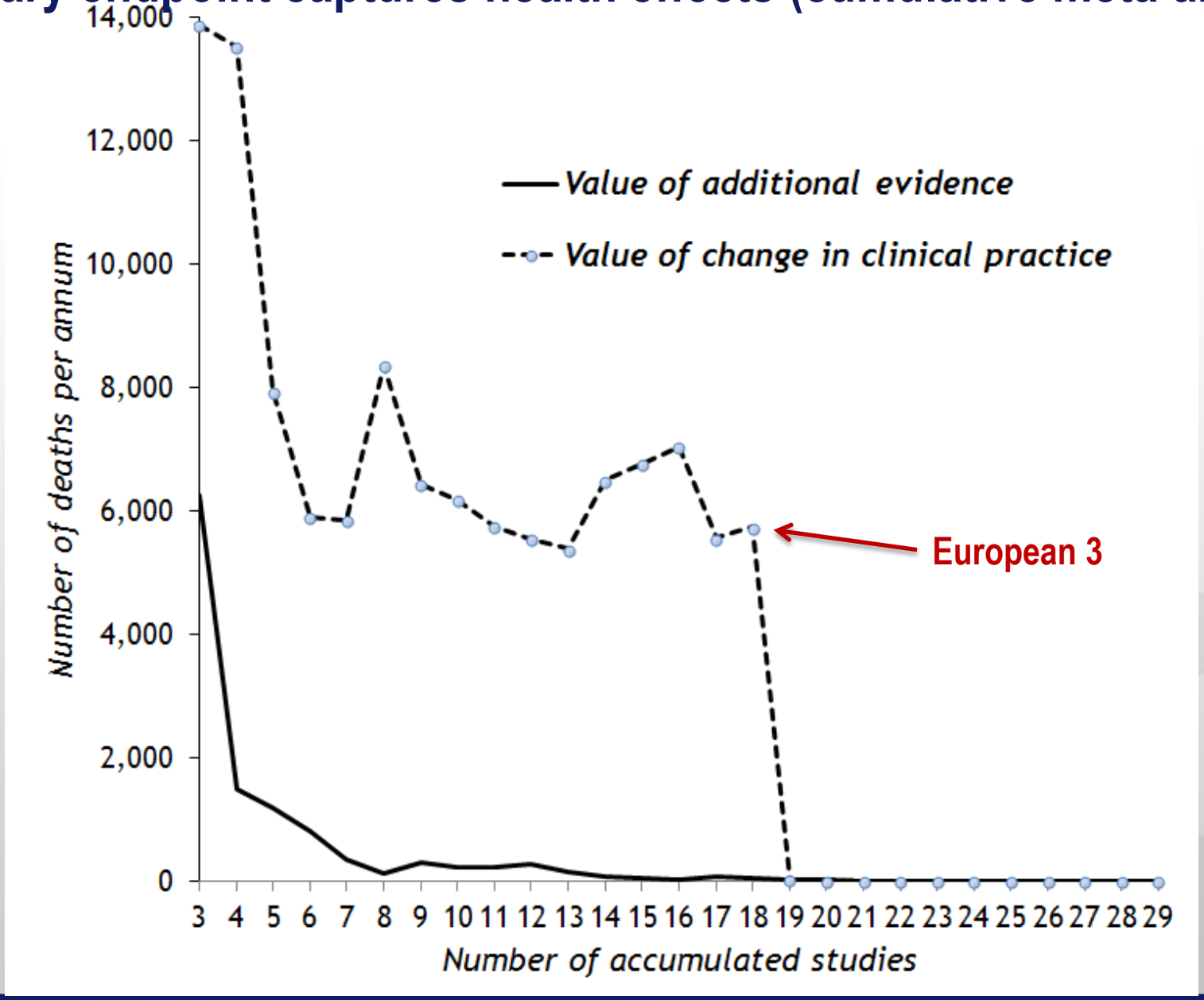


Intravenous streptokinase for acute myocardial infarction

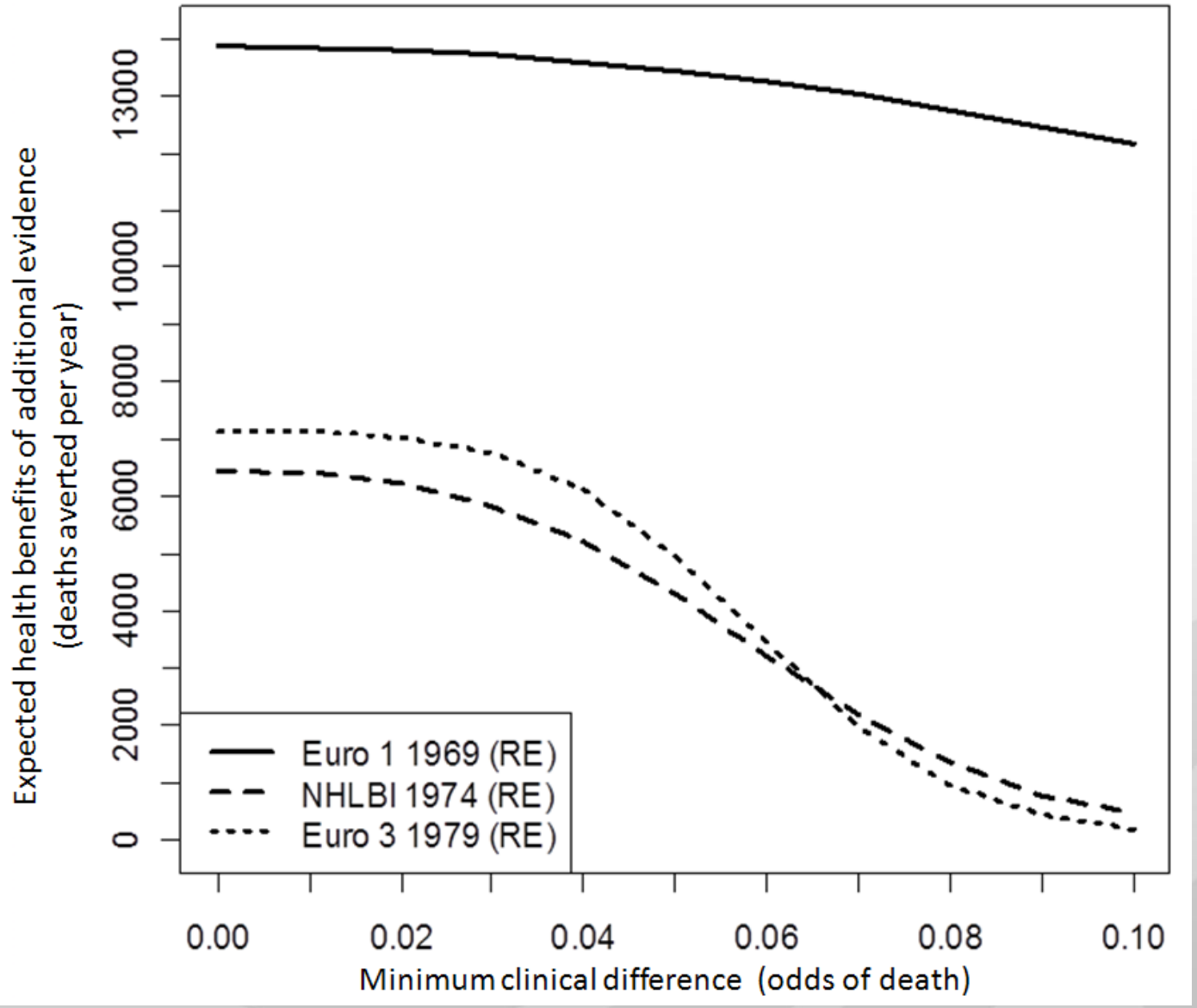
Primary endpoint captures health effects (cumulative meta-analysis)



Primary endpoint captures health effects (cumulative meta-analysis)



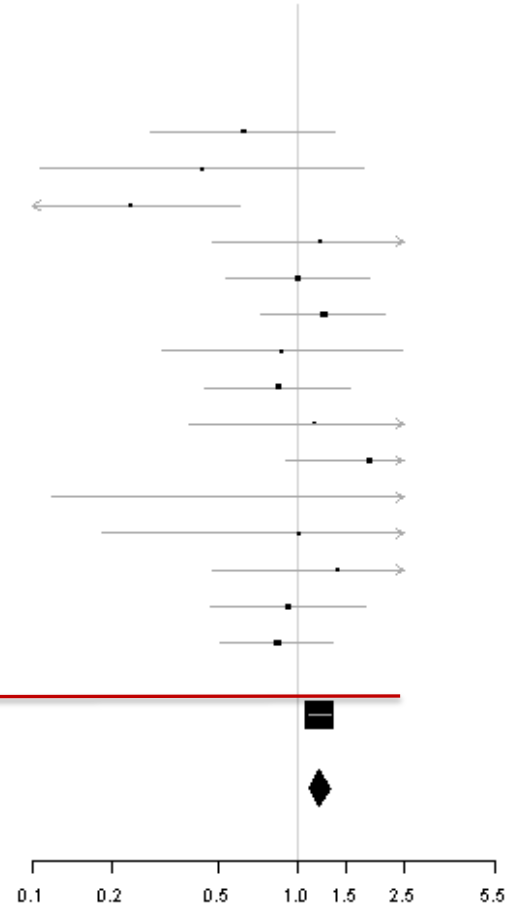
Primary endpoint captures health effects (cumulative meta-analysis)



Primary endpoint linked to other outcomes (steroids in head injury)

Meta-analysis of existing evidence

Study	Steroids deaths/total	Control deaths/total	OR	95%CI
Alexander 1972	16/55	22/55	0.62	(0.28 - 1.36)
Ransohoff 1972	9/17	13/18	0.43	(0.11 - 1.76)
Faupel 1976	16/67	16/28	0.24	(0.09 - 0.60)
Cooper 1979	26/49	13/27	1.22	(0.48 - 3.12)
Hernesniemi 1979	35/81	36/83	0.99	(0.54 - 1.84)
Pitts 1980	114/201	38/74	1.24	(0.73 - 2.12)
Saul 1981	8/50	9/50	0.87	(0.31 - 2.47)
Braakman 1983	44/81	47/80	0.83	(0.45 - 1.56)
Giannotta 1984	34/72	7/16	1.15	(0.39 - 3.42)
Dearden 1986	33/68	21/62	1.84	(0.91 - 3.74)
Chacon 1987	1.5/6	0.5/6	3.67	(0.12 -113.74)
Zagara 1987	4/12	4/12	1.00	(0.18 - 5.46)
Stubbs 1989	13/104	5/54	1.40	(0.47 - 4.16)
Gaab 1994	19/133	21/136	0.91	(0.47 - 1.79)
Grumme 1995	38/175	49/195	0.83	(0.51 - 1.34)
Zarate 1995	0/30	0/30		
CRASH 2005	1248/4854	1075/4819	1.21	(1.10 - 1.32)
Summary OR			**1.21**	**(1.10 - 1.33)**



Before CRASH:

Odds ratio of dead = 0.93 (0.71, 1.18)

Odds ratio of dead, vegetative and severely disabled = 1.10 (0.81, 1.53)

Primary endpoint linked to other outcomes (steroids in head injury)

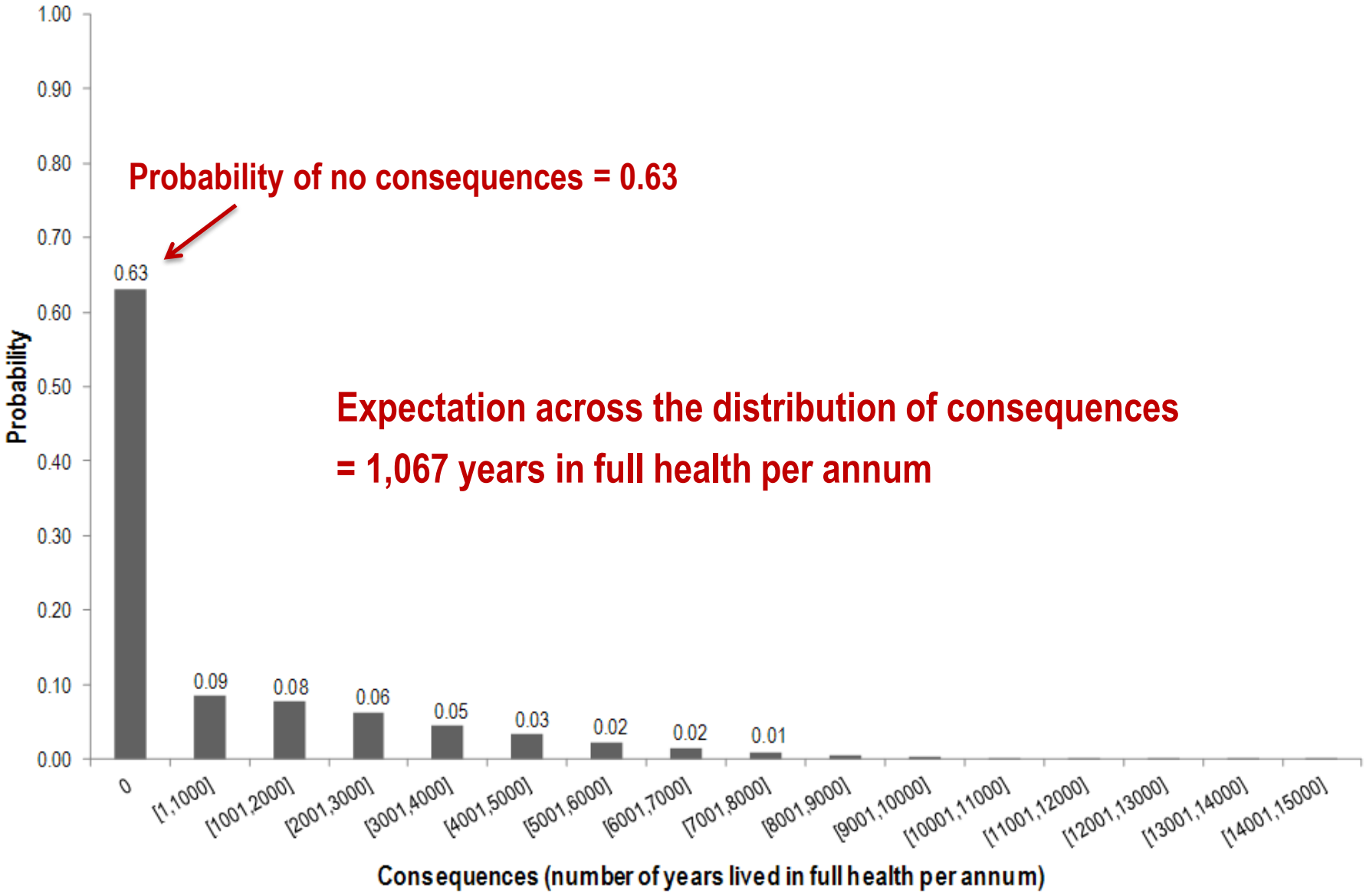
Before CRASH:

Glasgow Outcome Scale outcome	Percentage of individuals (95% CrI) by treatment	
	Steroids	No steroids
Dead	33.5 (22.8, 45.2)	35.3 (24.8, 46.9)
Vegetative	4.8 (2.8, 7.5)	3.8 (2.4, 5.9)
Severe disability	13.5 (8.3, 20.1)	10.7 (7.1, 15.8)
Moderate disability	11.6 (8.6, 14.8)	12.1 (9.2, 15.1)
Good recovery	36.5 (28.1, 44.8)	38.0 (30.1, 45.6)

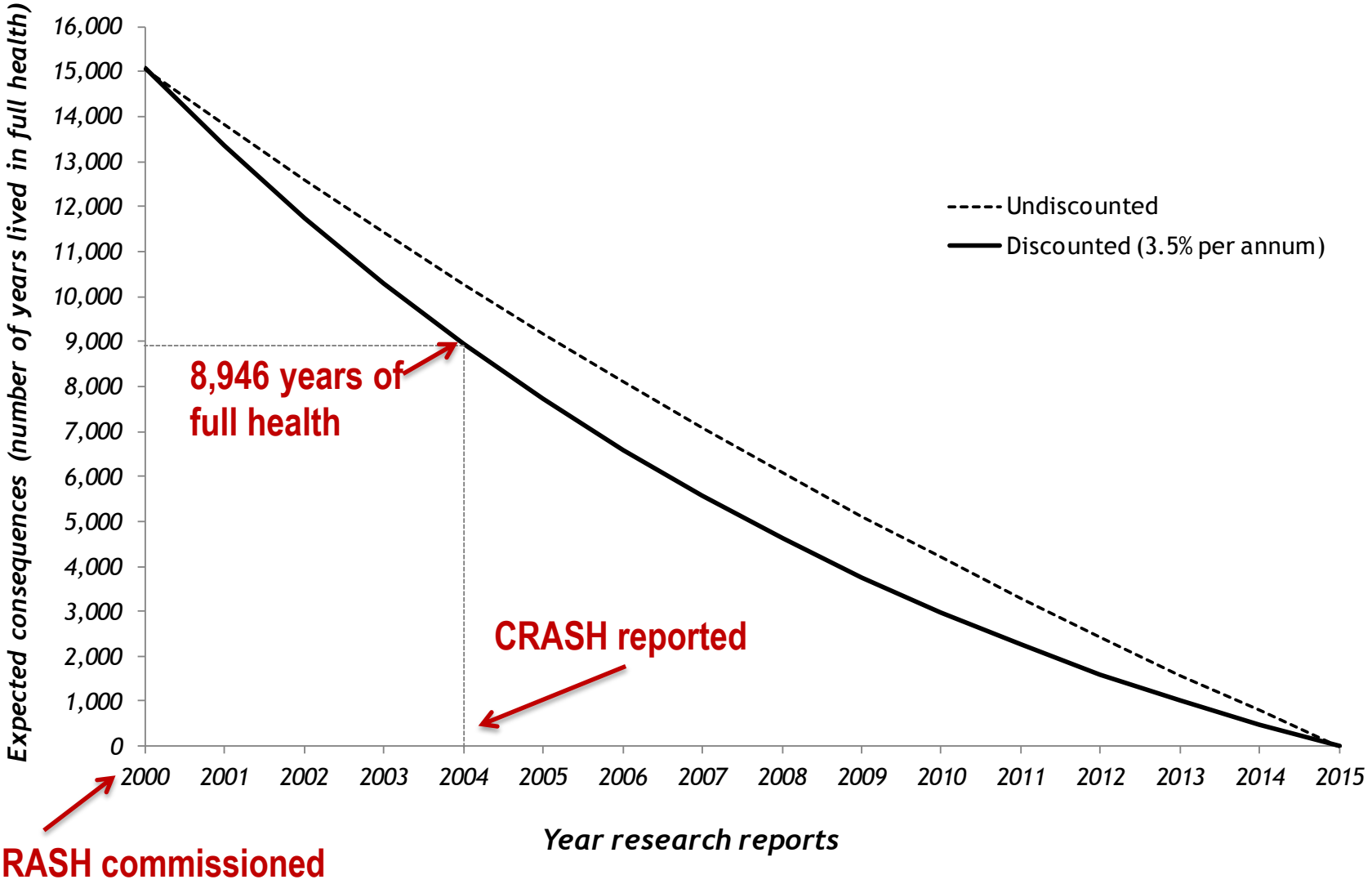
- Life expectancy given survival and estimates of quality of life associated with GOS outcomes → **Equivalent years of full health**

  (Impact on life years expected to be lived due to the effects on mortality risk adjusted for the quality in which they are likely to be lived)

Primary endpoint linked to other outcomes (steroids in head injury)



Primary endpoint linked to other outcomes (steroids in head injury)



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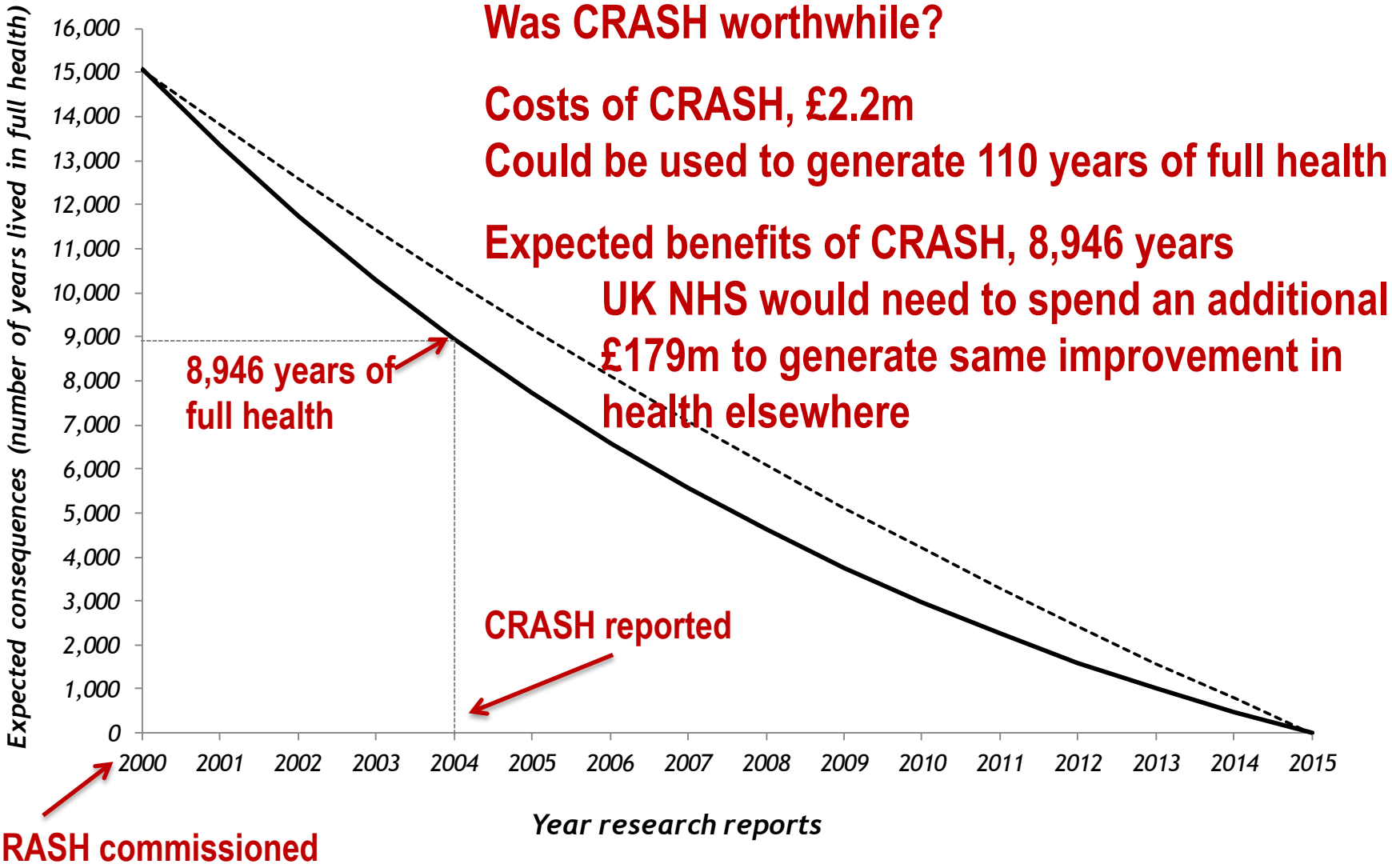
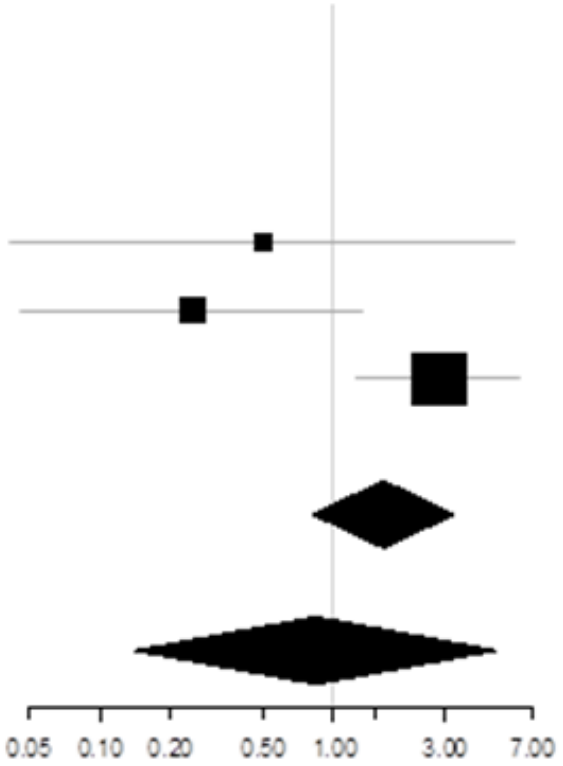


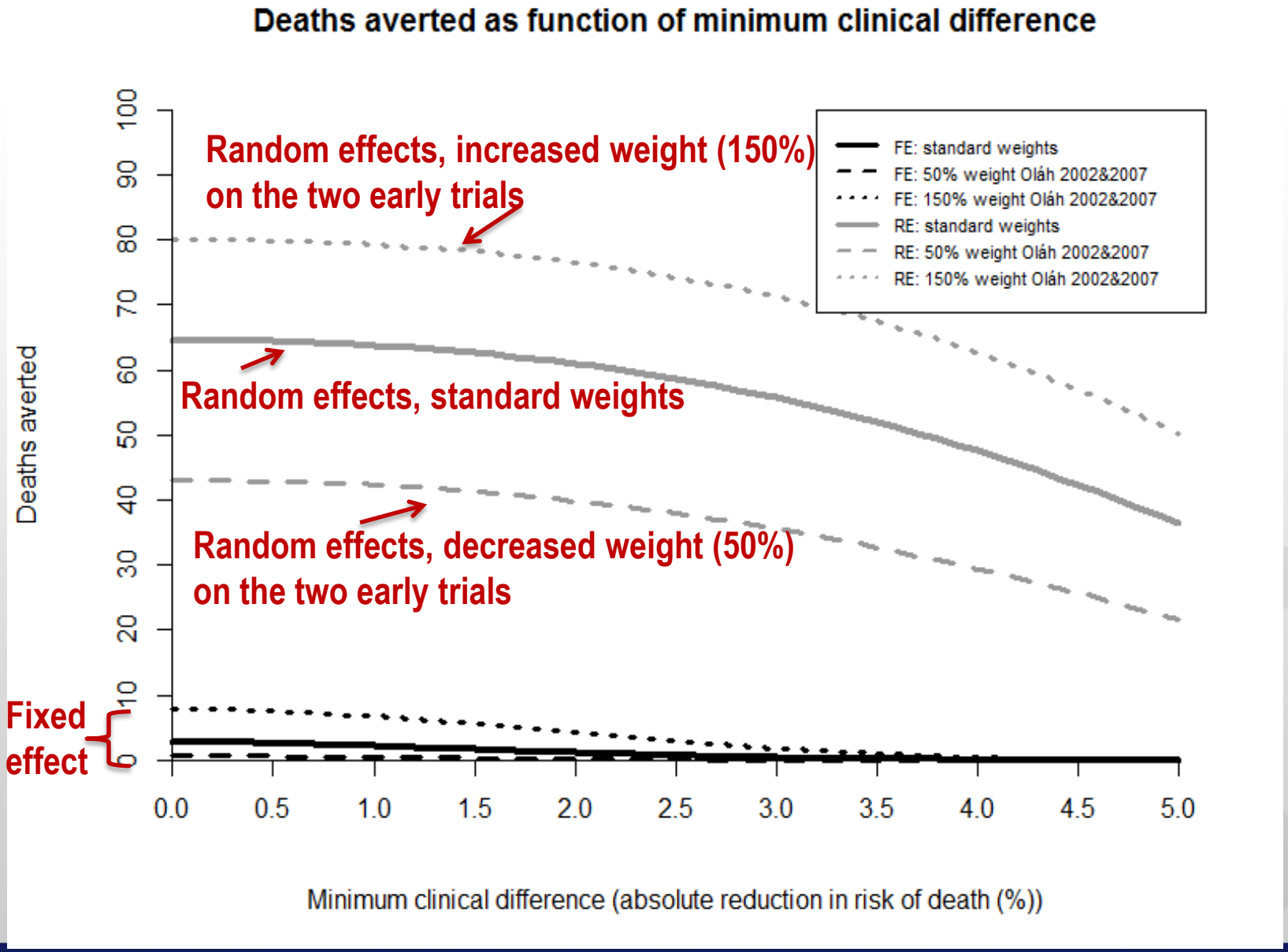
Different weights to reflect the relevance of evidence (probiotics)

Study	N	OR of death probiotics vs usual care	OR 95%CI
Oláh (2002)	45	0.50	(0.04 - 5.94)
Oláh (2007)	62	0.25	(0.05 - 1.34)
Besselink (2008)	296	2.81	(1.26 - 6.28)
Fixed effect summary		**1.62**	**(0.81 - 3.26)**
Random effects summary		**0.83**	**(0.14 - 4.83)**



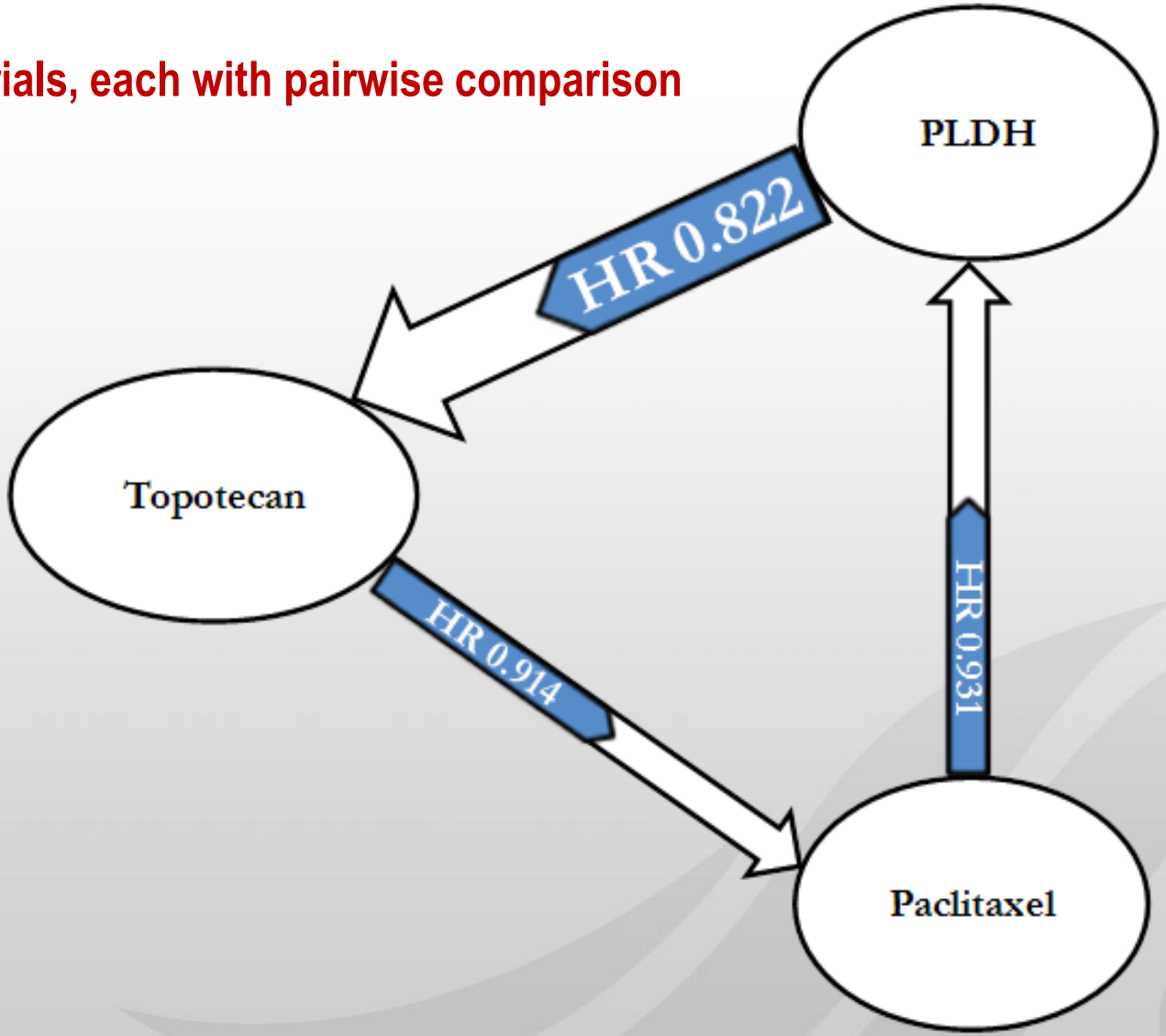
Odds ratio of death for probiotics compared to usual care

Different weights to reflect the relevance of evidence (probiotics)

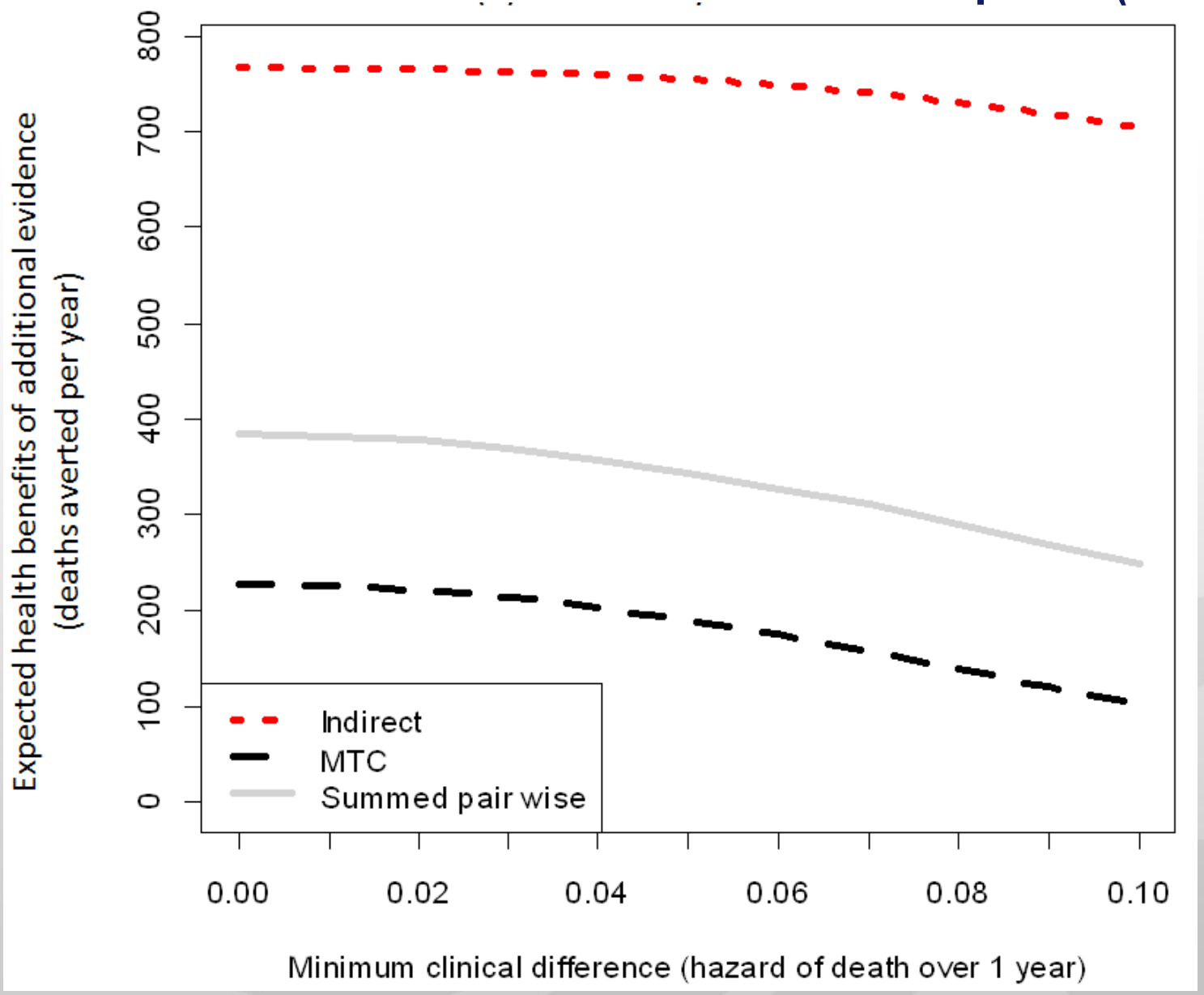


More than two alternative interventions to be compared (ovarian)

Three trials, each with pairwise comparison



More than two alternative interventions to be compared (ovarian)



Considerations

- Quantitative analysis based on systematic review and meta-analysis provides a practical and useful starting point for research prioritization and commissioning
- Adds transparency and accountability but does not capture all scientific and social value judgments

Some considerations:

- Should this type of analysis be required or recommended?
- Should it be required for all suggested topics and proposals?
- Who should be responsible for conducting the analysis?
- Can access to information that might commonly be required be provided?
- What process might make best use of developing methods of analysis?

PCORI Methodology Workshop for Prioritizing Specific Research Topics

December 5, 2012

TWITTER: #PCORI EMAIL: getinvolved@pcori.org

Patient-Centered Outcomes Research Institute

Panel: Experts' Reactions to PCORI's Proposed Research Prioritization Process

Jean Slutsky, PA, MSPH (Moderator)

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Patient-Centered Outcomes Research Institute

Panel: Experts' Reactions to PCORI's Proposed Research Prioritization Process

Robert Dubois, MD, PhD
Chief Science Officer
National Pharmaceutical Council

Patient-Centered Outcomes Research Institute

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Veronica Goff, MS
Vice President
National Business Group on Health

Patient-Centered Outcomes Research Institute

Panel: Experts' Reactions to PCORI's Proposed Research Prioritization Process

Sally Morton, PhD

Professor and Chair, Department of Biostatistics

University of Pittsburgh

Patient-Centered Outcomes Research Institute

How Can PCORI Prioritize Topics Based on the Eight PCORI Criteria?

- Proposed approach is consistent with PCORI mission:

  *"… evidence-based information that comes from **research guided by** patients, caregivers and the broader health care community."*

- Approach must also be
  - Fair
  - Inclusive
  - Trusted
  - Efficient
  - Scalable
  - Sustainable
  - Flexible
  - Reproducible

Inherent Objectives: Fair, Inclusive, Trusted

- **Transparency** will be key to credibility
  - How are stakeholders' voices heard?
  - How are topics gathered?
  - How are topics chosen for prioritization?
  - How does prioritization take place?

- **Simplicity** is desirable
  - Implicit procedures are simple to explain but subjective
  - Explicit procedures are objective but hard to explain, open to manipulation, and not robust to changes in formula

Advice to Achieve Inherent Objectives

- **Release individual raters' data** with individual's identification masked
- **Construct topic briefs** in common format, similar metrics, and easy-to-understand language
- **Divide 8 criteria** into subgroups:
  - *Required* – Topic is discarded if it does not meet a threshold
    - Example: Patient centeredness
  - *Automatic* – Topics are rated based on common statistics (with exceptions for rare diseases)
    - Example: Impact
  - *Essential* – Raters must score each topic
    - Example: Implementation in practice

Extrinsic Objectives: Efficient, Scalable, Sustainable, Flexible, Reproducible

- **Simplicity** is desirable given practical considerations
  - If a topic is not chosen when first rated, is it rated again?
  - Can “urgent” topics be integrated quickly into the approach?
  - Is the approach scalable?

- **Continual quality improvement** and **topic balance** desirable too

Advice to Achieve Extrinsic Objectives:

- Include **reproducibility** in approach and research agenda
  - Have all topics rated by at least two committees
  - Conduct reliability experiments
- Assess rater **variability (disagreement)** and interpret results in that context. An example:
  - Topic A ratings: (15, 15, 15, 15, 15, 15, 15, 15, 15) average is 15
  - Topic B ratings: (0, 0, 0, 15, 15, 15, 30, 30, 30) average is also 15
  - “Raters disagree if at least 1 ‘low’ rating and at least 1 ‘high’ rating”

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Patient-Centered Outcomes Research Institute

Panel: Pilot Group Feedback on Research Prioritization Process

Paul Wallace, MD (Moderator)

TWITTER: #PCORI EMAIL: getinvolved@pcori.org

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Research Topic Prioritization Pilot: One Perspective

Fouza Yusuf, MS, MPH
Medical College of Wisconsin

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Pilot Group Composition and Selection

- Diversity
  - Personal and professional experiences
  - Expertise in science/research
  - Representation from research, academia, advocacy groups, etc.
- Self selection by online application
  - Limited to those familiar with PCORI
  - Exclusion of others
  - Is some diversity lost by this process?

Future Group Selection

- Recruitment
  - A PCORI pipeline for recruitment – media, advocacy groups, partnerships to spread the word (including us)
  - Invite participation from public officials/legislators or their staff
- Selection and Composition
  - Systematic selection process
  - Group/panel not static
    - Representation of experience on the topics being prioritized
  - Pair up based on knowledge of topic or research/science

Survey Gizmo

- Pros
  - Head to head comparison
  - Simpler to use
  - Less time
- Cons
  - Some subjectivity
  - 8 criteria, 10 topics – challenging to consider all at once
- Helpful solution
  - Table with summary information from topic briefs
  - Columns – Topic; Rows – Criteria information

Expert Choice

- Pros
  - Objective
  - Easier to rank
- Cons
  - Long (80 decisions)
  - Scale long (11-item) and ambiguous wording; hard to distinguish between certain levels
  - Lacks head to head comparison of topics
- Helpful Solution
  - Table with criteria and topic, assigned ranks (1-10) for each criterion

Suggestions for Future Prioritization

- Expert Choice
  - Currently takes a topic and ranks on the criteria
  - Consider taking one criterion and ranking all topics on it before going to the next criterion
    - Allow head to head comparisons
- Use both tools to validate the rankings.
  - Top and bottom ranked topics were similar in pilot group. Would that be the same for other future groups?
- Some face to face interaction during process

Research Topic Prioritization Pilot: One Perspective

Kirk Allison, PhD, MS
Program in Human Rights and Health
University of Minnesota School of Public Health

Patient-Centered Outcomes Research Institute

Research Topic Prioritization Pilot: One Perspective

Dan Cherkin, PhD

Group Health Research Institute / Bastyr University Research Institute

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Research Topic Prioritization Pilot: One Perspective

Liz Jacobs, MD

University of Wisconsin School of Medicine and Public Health

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Research Topic Prioritization Pilot: One Perspective

Lisa Hopp, PhD, RN, FAAN

Indiana Center for Evidence Based Nursing Practice

Patient-Centered Outcomes Research Institute

Research Topic Prioritization Pilot: One Perspective

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patient and caregiver

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Panel: Pilot Group Feedback on Research Prioritization Process

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Public Feedback on Proposed Research Prioritization Process

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PCORI Perspectives on Input into Research Prioritization Process

Joe Selby, MD, MPH

Rachael Fleurence, PhD

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Closing Remarks

Joe Selby, MD, MPH

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