Innovations in Medical Cost-Effectiveness Analysis

David Meltzer MD, PhD
The University of Chicago

Objectives

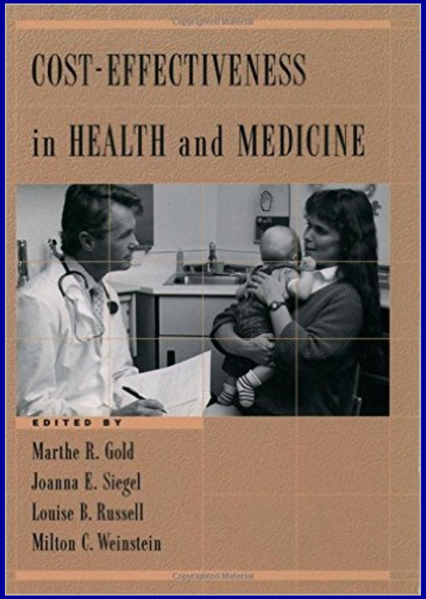
- To introduce important theoretical innovations in cost-effectiveness analysis
  - Perspective
  - Future costs
  - Self-selection in cost-effectiveness analysis
  - Empirical cost-effectiveness
  - The value of research

Background on Medical Cost-Effectiveness Analysis

- Origins in academic medicine in 1970s
- Seeks to maximize welfare/health (quality-adjusted life years (QALYs) given constrained resources
  - Incremental cost-effective ratio (ICER): cost/QALY
- Applications
  - Government, especially outside the U.S.
    - e.g., UK National Institute for Health and Clinical Excellence
    - US: Office of Technology Assessment, recent CMS, FDA interests, not Patient Centered Outcomes Research Institute (PCORI)
  - Private payers
  - Clinicians
  - Pharmaceutical companies
    - "Pharmacoeconomics"

Perspective

- Private
  - HMO, consumer
- Public
  - Medicare, Medicaid, state mental health system
- Societal
  - Include all costs and benefits no matter to whom they accrue
  - Policy analysts (i.e., US Panel on Cost-Effectiveness in Health and Medicine Reference Case)



JAMA®

The Journal of the American Medical Association

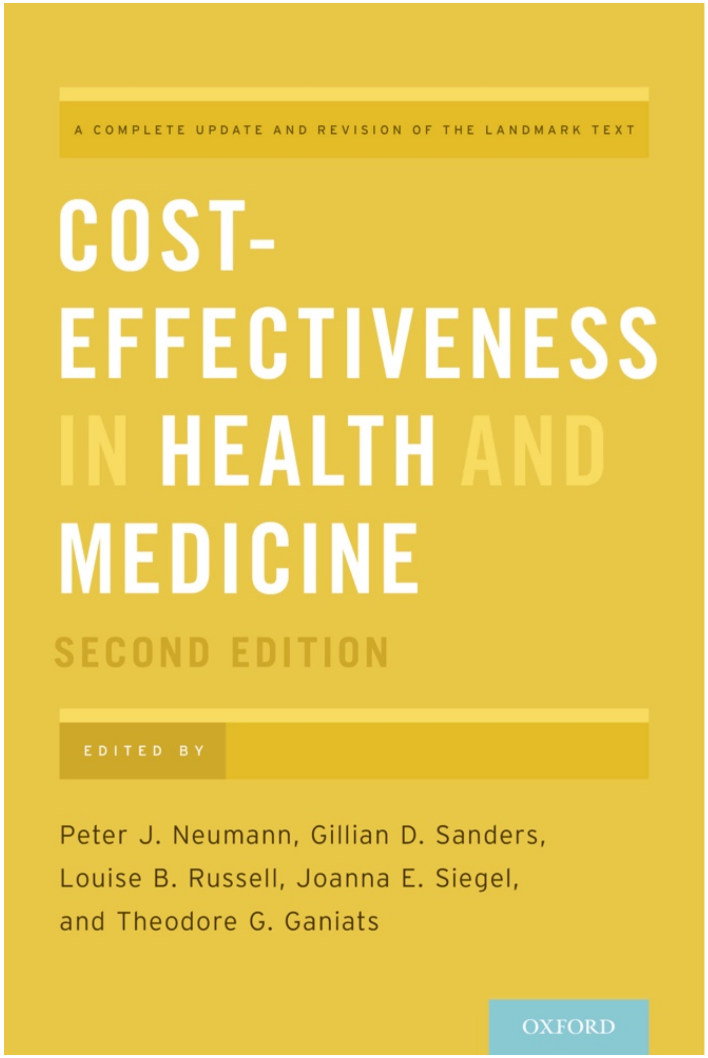
JAMA | Special Communication

Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses

Second Panel on Cost-Effectiveness in Health and Medicine

Gillian D. Sanders, PhD; Peter J. Neumann, ScD; Anirban Basu, PhD; Dan W. Brock, PhD; David Feeny, PhD; Murray Krahn, MD, MSc; Karen M. Kuntz, ScD; David O. Meltzer, MD, PhD; Douglas K. Owens, MD, MS; Lisa A. Prosser, PhD; Joshua A. Salomon, PhD; Mark J. Sculpher, PhD; Thomas A. Trikalinos, MD; Louise B. Russell, PhD; Joanna E. Siegel, ScD; Theodore G. Ganiats, MD

September 13, 2016



Experiences since the Original Panel

- Many CEAs, most not using the societal perspective
- Even when stating using societal perspective – important elements often omitted
- Decision makers using CEA – often have taken more focused perspective

Perspective: Second Panel's Considerations

- Appeal of societal perspective
- Potential to disregard revealed preferences of decision makers
- Is there a single "societal perspective"?
- Need to promote quality and comparability

Recommendation – Reference Cases:

- All studies represent a reference case analysis based on a **health sector perspective** and a reference case based on a **societal perspective**
- Measure health effects in QALYs
- Intended to enhance consistency and comparability

Recommendation: Health Sector Perspective

- Results should be summarized in ICER
- NMB and NHB may also be reported
- Range of CE thresholds should be considered

Recommendation: Impact Inventory

- Include impact inventory table which lists the health and non health impacts of an intervention
- Main purpose is to ensure that all consequences, including those outside the formal healthcare sector, are considered regularly and comprehensively
- Provides a framework for organizing, thinking about, and presenting various types of consequences

The Impact Inventory

Sector	Type of Impact (list category within each sector with unit of measure if relevant)[a]	Included in This Reference Case Analysis From...Perspective?		Notes on Sources of Evidence
		Health Care Sector	Societal	
Formal Health Care Sector				
Health	Health outcomes (effects)			
	Longevity effects	☐	☐	
	Health-related quality-of-life effects	☐	☐	
	Other health effects (eg, adverse events and secondary transmissions of infections)	☐	☐	
	Medical costs			
	Paid for by third-party payers	☐	☐	
	Paid for by patients out-of-pocket	☐	☐	
	Future related medical costs (payers and patients)	☐	☐	
	Future unrelated medical costs (payers and patients)	☐	☐	
Informal Health Care Sector				
Health	Patient-time costs	NA	☐	
	Unpaid caregiver-time costs	NA	☐	
	Transportation costs	NA	☐	
Non–Health Care Sectors (with examples of possible items)				
Productivity	Labor market earnings lost	NA	☐	
	Cost of unpaid lost productivity due to illness	NA	☐	
	Cost of uncompensated household production[b]	NA	☐	
Consumption	Future consumption unrelated to health	NA	☐	
Social Services	Cost of social services as part of intervention	NA	☐	
Legal or Criminal Justice	Number of crimes related to intervention	NA	☐	
	Cost of crimes related to intervention	NA	☐	
Education	Impact of intervention on educational achievement of population	NA	☐	
Housing	Cost of intervention on home improvements (eg, removing lead paint)	NA	☐	
Environment	Production of toxic waste pollution by intervention	NA	☐	
Other (specify)	Other impacts	NA	☐	

Accounting for Future Costs in Medical Cost-Effectiveness Analysis

Background: Accounting for Future Costs

- Save patient with medical care today who requires care in the future. Should we count that as a cost?
  - Related illness?
    - Angioplasty today, count bypass in future?
  - Unrelated illness?
    - Influenza vaccine today, count dialysis in future?
  - Non-medical costs and benefits?
    - Suicide prevention today, earnings in future? Consumption in future?

Traditional Treatment of Future Costs and Benefits in CEA

- Analyses generally include:
  - Future benefits
    - Length of life/Quality of life = QALYs
  - Future medical costs for related illnesses
- Analyses generally exclude:
  - Future medical costs for unrelated illnesses
    - Few exceptions: Weinstein, OTA
  - Future non-medical costs
- Controversies reflect weak theoretical foundation of CEA

Theoretical Background: Phelps & Garber (1997)

- Use lifetime utility maximization model
- Conclude: Obtain same relative rankings of interventions if you include or exclude future medical costs for unrelated illness as long as they are:
    - treated consistently
    - truly unrelated = “conditional independence”

Theoretical Background: Meltzer (1997)

- Use lifetime utility maximization model
- Conclude:
  - Must include all future net resource use
    - Medical costs - both related and unrelated - and future non-medical costs net of earnings
    - “Net resource use”= consumption + medical expenditures - earnings
    - From -$10,000/ year @ age 25 to +$20,000/year @ age 85
  - Relative rankings of interventions not independent of future costs
    - Analyses that omit future costs favor interventions that extend life over those that improve quality of life
  - Phelps/Garber inadvertently assume net annual resource use is zero

Lifetime Utility Maximization Model: Utility Function and Budget Constraint

$$\sum_{t=0}^{T} \beta^{t} S_{t}(\vec{m}_{t})\, u(c_{t}, h_{t}(\vec{m}_{t})) \qquad (1)$$

$$\sum_{t=0}^{T} \frac{1}{(1+r)^{t}} S_{t}(\vec{m}_{t})(c_{t} + m_{t}) = \sum_{t=0}^{T} \frac{1}{(1+r)^{t}} S_{t}(\vec{m}_{t})(i_{t}) \qquad (2)$$

Lifetime Utility Maximization Model: First Order Conditions

$$\frac{\frac{1}{(1+r)^{t}} S_{t}(\vec{m}_{t}) + \sum_{\tau=t}^{T} \frac{1}{(1+r)^{\tau}} \frac{\partial S_{\tau}(\vec{m}_{t})}{\partial m_{t}} (c_{\tau} + m_{\tau} - i_{\tau})}{\sum_{t=\tau}^{T} \left[\beta^{\tau} \frac{\partial s_{\tau}(\vec{m}_{t})}{\partial m_{t}} u(c_{\tau}, h_{\tau}(\vec{m}_{\tau})) + s_{\tau}(\vec{m}_{t}) \frac{\partial u(c_{\tau}, h_{\tau}(\vec{m}_{\tau}))}{\partial m_{t}} \right]} \tag{3}$$

Theoretical Background: Meltzer (1997)

- Use lifetime utility maximization model
- Conclude:
  - Must include all future net resource use
    - Medical costs - both related and unrelated - and future non-medical costs net of earnings
    - "Net resource use"= consumption + medical expenditures - earnings
    - From -$10,000/ year @ age 25 to +$20,000/year @ age 85
  - Relative rankings of interventions not independent of future costs
    - Analyses that omit future costs favor interventions that extend life over those that improve quality of life
  - Phelps/Garber inadvertently assume net annual resource use is zero

Intuition

- Consider two interventions with equal current cost that both produce one QALY
    - ***A*** increases life expectancy by one year at QOL=1
    - ***B*** increases life expectancy by two years at QOL=0.5
- Which is preferred?
    - From utility side: Indifferent
    - From cost side: ***A*** preferred since it saves the costs of supporting an extra year of life
    - Hence, ***A*** preferred overall
- Omitting future costs favors interventions that extend life (***B***) versus those that increase QOL (***A***)

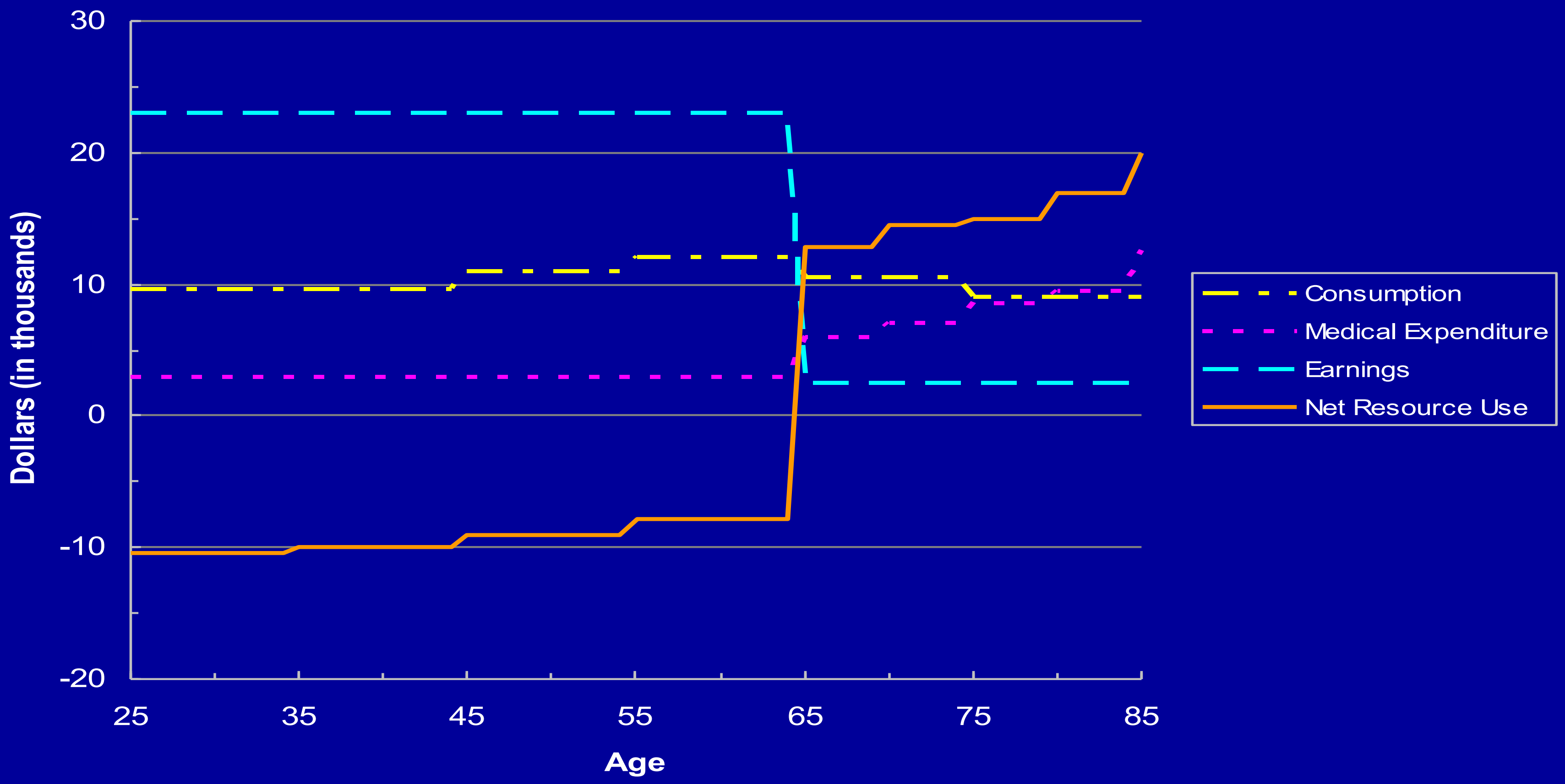
Accounting for Future Costs

$$\frac{\Delta \text{cost}}{\Delta \text{QALY}} = \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + \frac{\Delta \text{future cost}}{\Delta \text{QALY}}$$

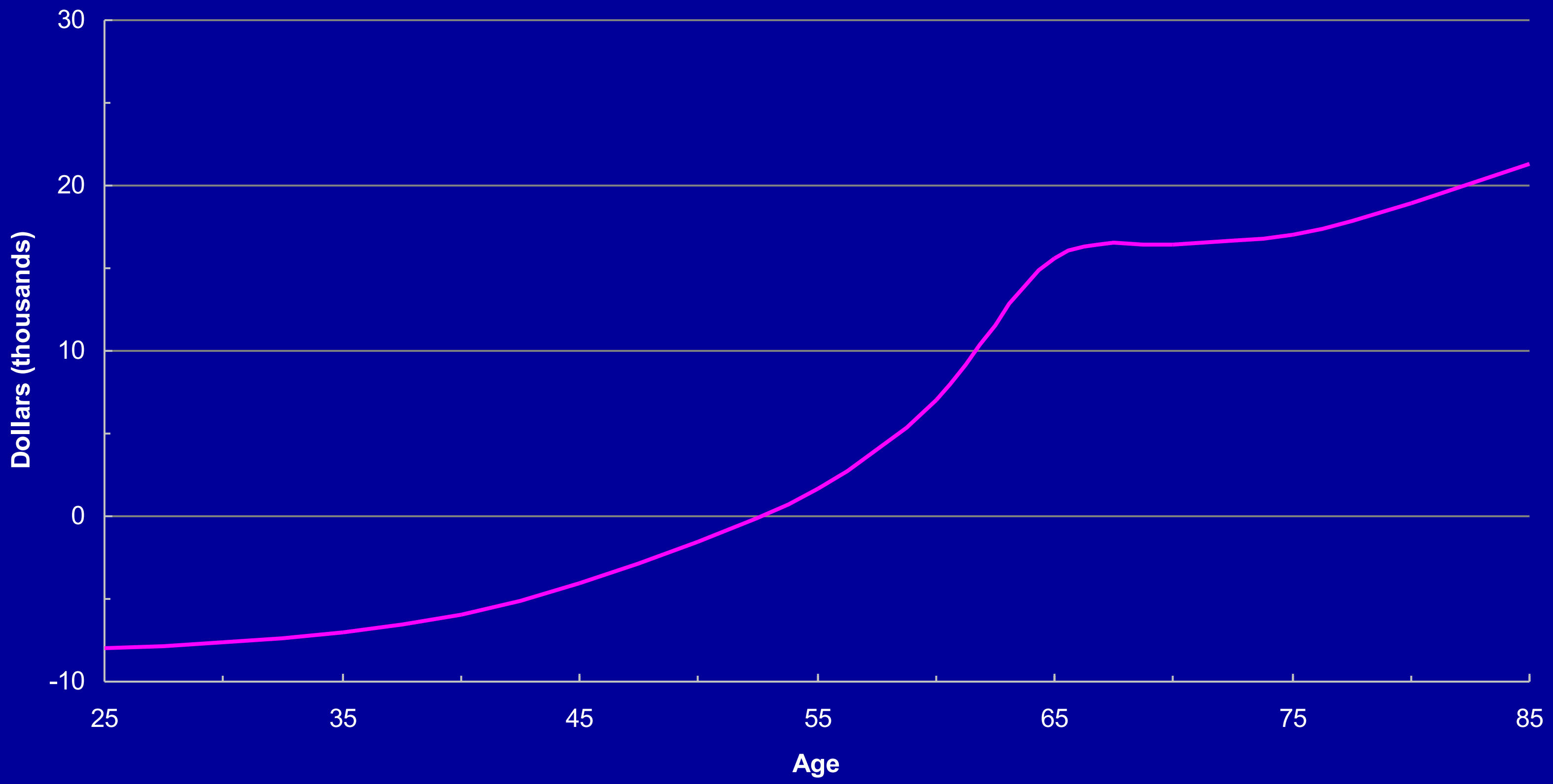
$$= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + \frac{C * \Delta \text{LY}}{\Delta \text{QALY}}$$

$$= \frac{\Delta \text{present cost}}{\Delta \text{QALY}} + C * \frac{\Delta \text{LY}}{\Delta \text{QALY}}$$

Consumption, Medical Expenditure, Earnings and Net Resource Use by Age



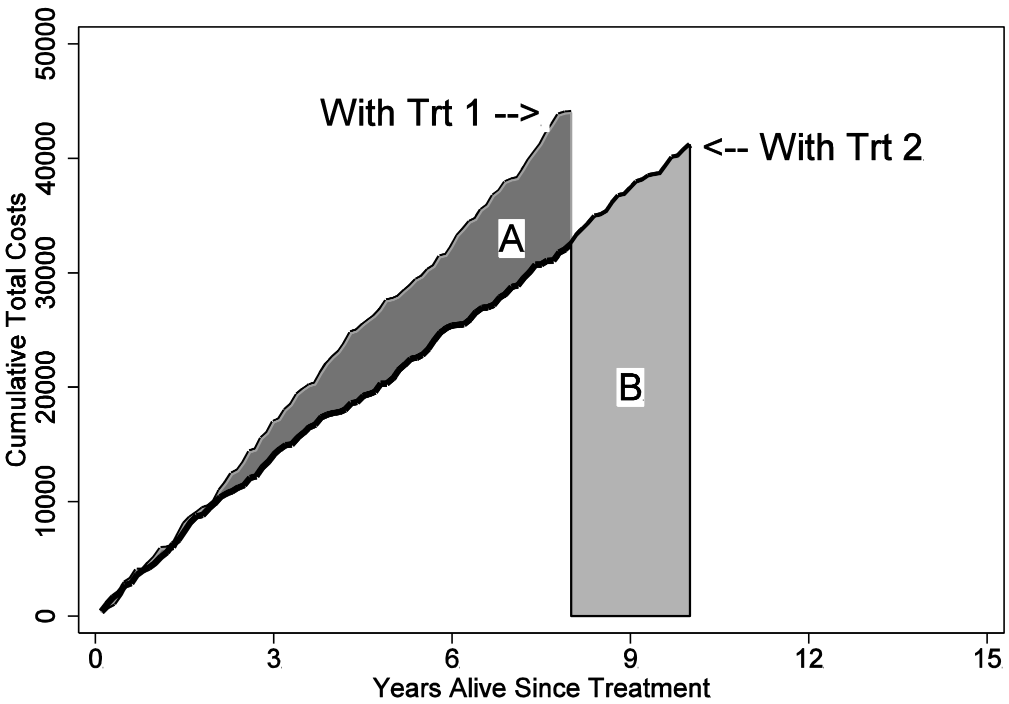
Present Value of Future Net Resource Use Per Year of Life Saved by Averting Death (by Age)



Approximate Effects of Future Costs

Intervention	Cost/QALY without future costs	C	ΔLE/ΔQALY	C∗(ΔLE/ΔQALY)	Cost/QALY with future costs
Treatment Severe Hypertension Men Age 40	$18,000	-$5,000	1.03	-$5,200	$12,800
Treatment Severe Hypertension Men Age 60	$60,000	$8,000	1.07	$8,500	$68,500
Adjuvant Chemo Duke's C Colon CA Men Age 60	$67,000	$8,000	18	$144,000	$211,000
Hemodialysis for ESRD Men Age 60	$117,000	$8,000	1.5	$12,000	$129,000

Future Costs Recommendation



Trt: Treatment

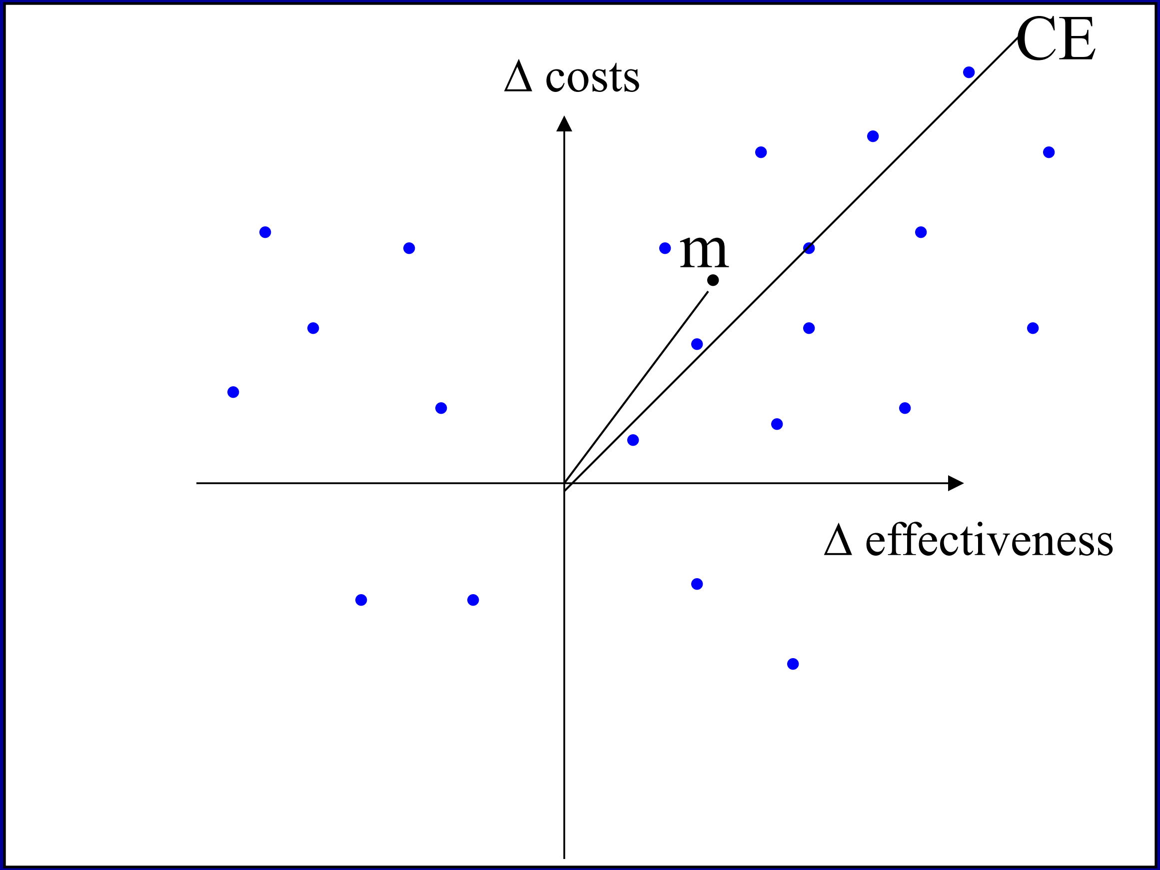
All healthcare costs, related or unrelated, should be considered either when survivals under alternative interventions are not the same or when cost components cannot be readily identified as related to the target condition.

Effects of Self-Selection on Cost-Effectiveness

Background

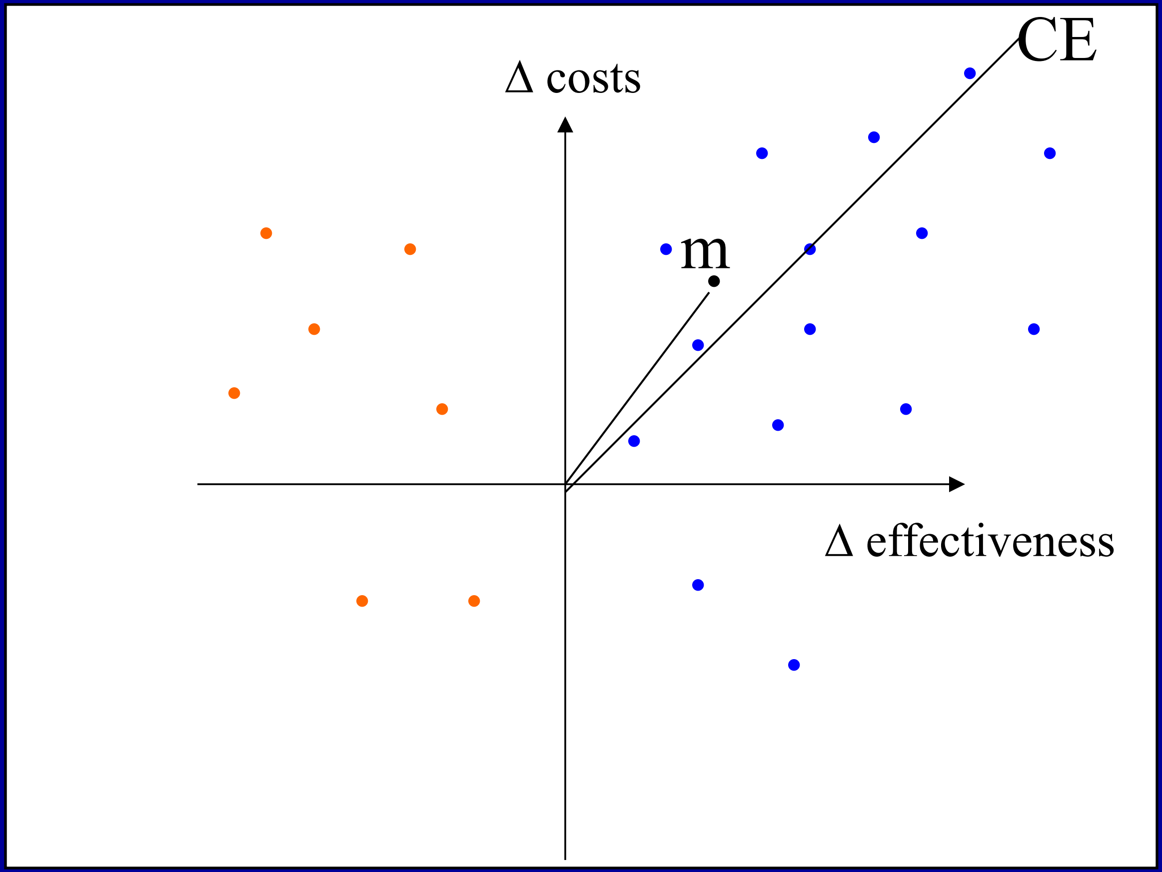
- Traditional CEA uses preferences (utilities) that average across individuals
- However, utilities may vary across individuals or populations and influence expected benefits of treatment
  - Implies cost-effectiveness can vary for individuals or populations that differ in preferences
- Preferences can also affect treatment choice
  - Specifically, patients whose preferences favor an option may be more likely to choose it
- How might "self-selection" affect cost-effectiveness?

Standard CEA with Heterogeneous Individuals



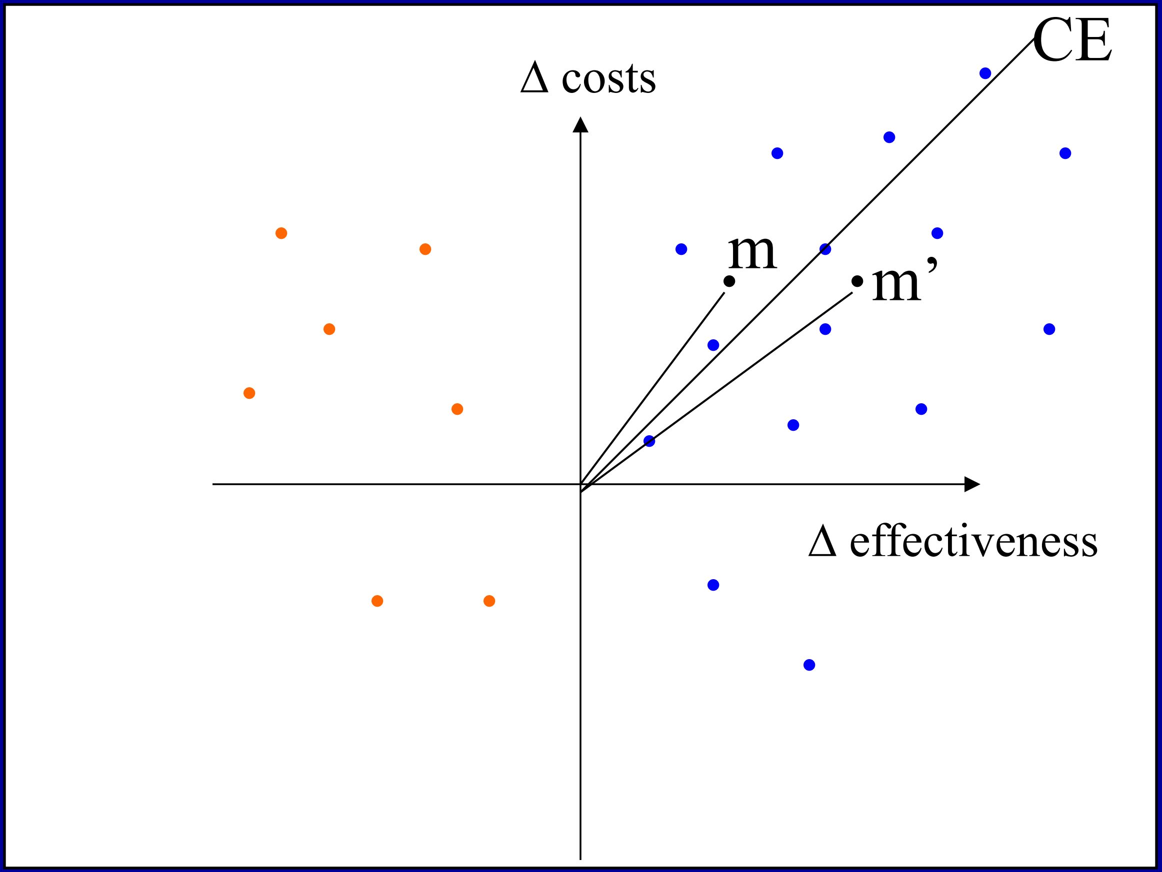
Blue Dots = Treated Patients

Perfect Self-Selection



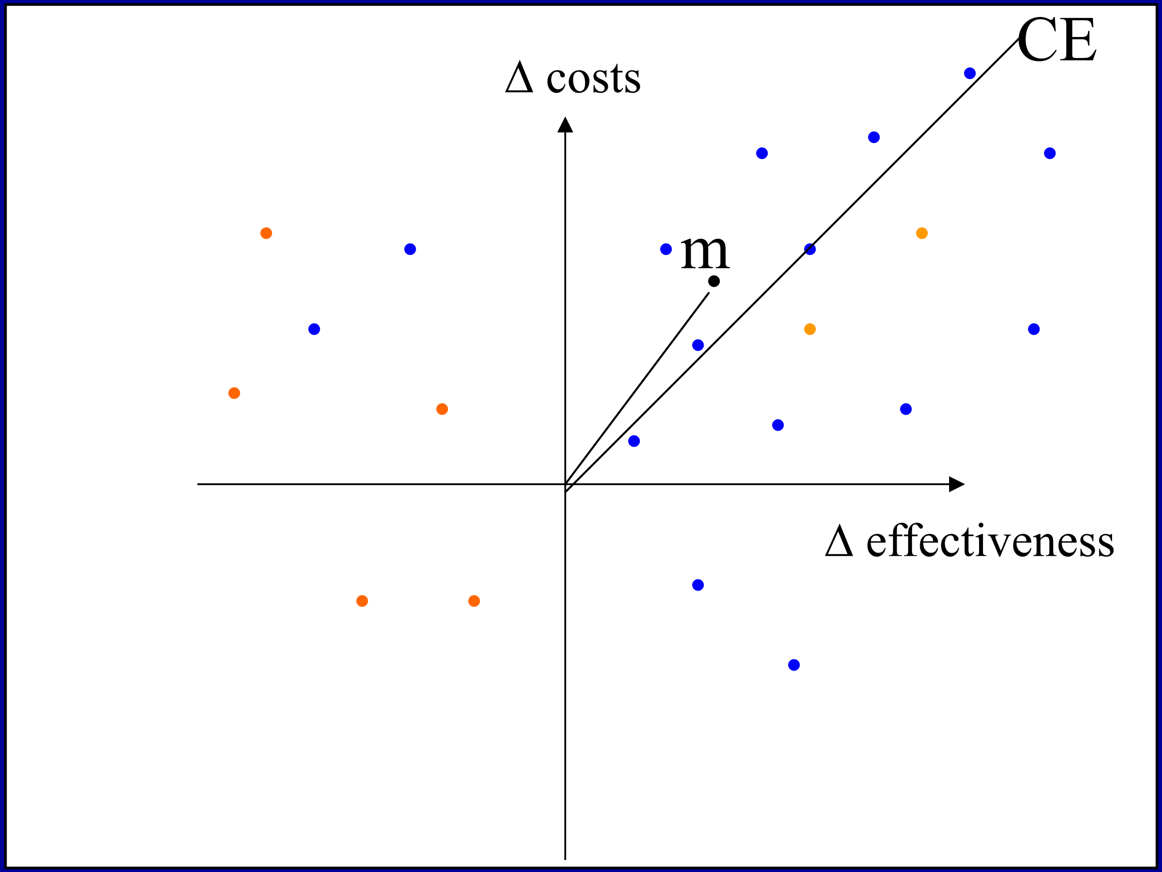
Blue Dots=Pts gain from Tx; Orange Dots=Pts lose from Tx

Effect of Perfect Self-Selection on CEA



Blue Dots=Pts gain from Tx; Orange Dots=Pts lose from Tx (reject)

Empirical Self-Selection



Blue Dots=Pts choose Tx; Orange Dots=Pts reject Tx

Background: Diabetes in the Elderly

- Diabetes care guidelines call for intensive lowering of glucose among younger patients
- However, unclear if this should apply to older patients
  - Gains in life expectancy smaller
  - Side effects of treatment may dominate
  - CE models of intensive therapy in older patients:
    - Minimal or even negative effects on QALYs
    - Not cost-effective
  - Know many patients refuse intensive therapy
- Suggests self-selection may have important effects on CEA in diabetes

Methods

- Interviewed 500 older diabetes patients to obtain data on preferences
  - Conventional and intensive glucose lowering (using insulin or oral medications)
  - Blindness, end-stage renal disease, lower extremity amputation
- Collected data on treatment choices and patient characteristics by medical records review
- Used CDC simulation model of intensive therapy for type 2 diabetes and patient-specific demographic, health, and preference data to get person-specific estimates of lifetime costs and benefits
- Analyses of cost-effectiveness of intensive vs. conventional therapy contrasting all patients vs. perfect self-selection vs. empirical self-selection

Results: Intensive vs. Conventional Therapy

CE Approach	Group	N	Change in Costs ($)	Change in QALYs	CE Ratio ($/QALY)
Standard	Full Population	543	8076	-0.49	--
Perfect Self-Selection	ΔQALY>0	403	8165	0.40	20K
	ΔQALY<0	131	7906	-3.25	--
Empirical Self-Selection	Self-identified intensive insulin therapy	154	7948	0.17	47K
	All others	364	8164	-0.80	--

Implications

- Results of standard CEA may be misleading
  - CEAs should consider the importance of self-selection
- Provides framework to value guidelines, decision-aids, or improved patient-doctor communication to make care more consistent with patient preferences
- Suggests framework to design co-payment systems to enhance cost-effectiveness of therapies
- Provides insight into policy making for voluntary vs. involuntary interventions

Empirical Cost-Effectiveness Analysis

Non-selective Use and Empirical Cost-effectiveness

- Cost-effectiveness analyses of interventions often stratify cost-effectiveness by indication
- Yet technologies are often used non-selectively
- The actual (empirical) costs and effectiveness of an intervention may be strongly influenced by patterns of use

Example: Cox-2 Inhibitors vs. NSAIDs

	ΔQALY	ΔCOST	$/QALY	Fraction Users
High Risk	0.085	4721	56K	39%
Low Risk	0.026	14123	537K	61%
Overall	0.042	11584	276K	

Cost-Effectiveness of Pap Smears

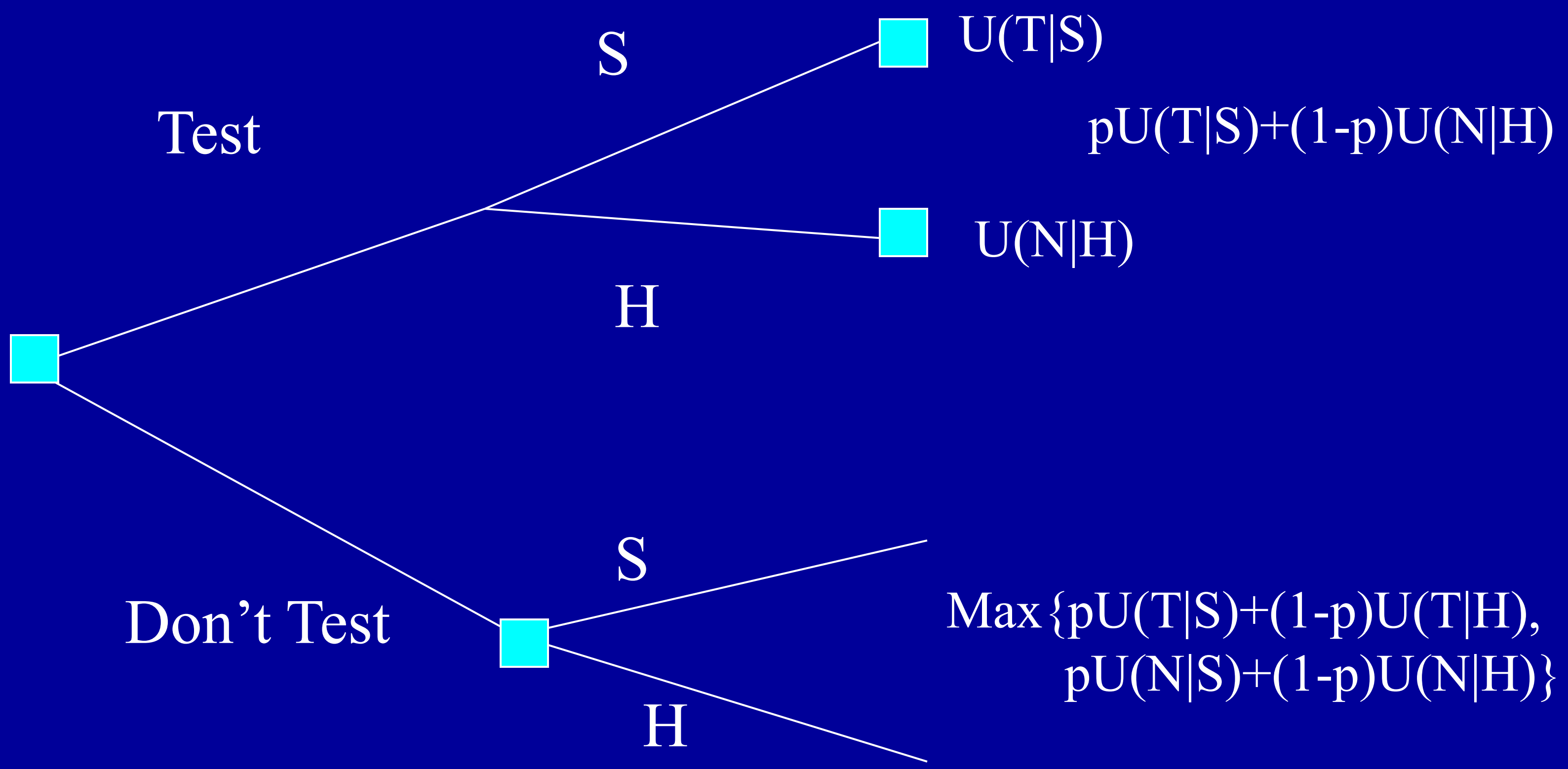
Frequency	Increase in LE vs. no screening	Increase in Cost vs. no screening	Average Cost per Life-Yr Saved	Marginal Increase in LE	Marginal Increase in Cost	Marginal Cost per Life-Yr Saved	Percent US Women who get Pap smears who get them at this Frequency	Percent of Pap Smears in US given at this Frequency
3 years	70 days	$500	$2,600/LY	70 days	$500	$2,600/LY	0.18	0.07
2 years	71 days	$750	$3,900/LY	1 day	$250	$91,000/LY	0.19	0.16
1 year	71 days 8 hours	$1,500	$7,300/LY	8 hours	$750	$830,000/LY	0.63	0.77
Average in the US			$6,400/LY					

Implications of Empirical CEA for Choice of Interventions

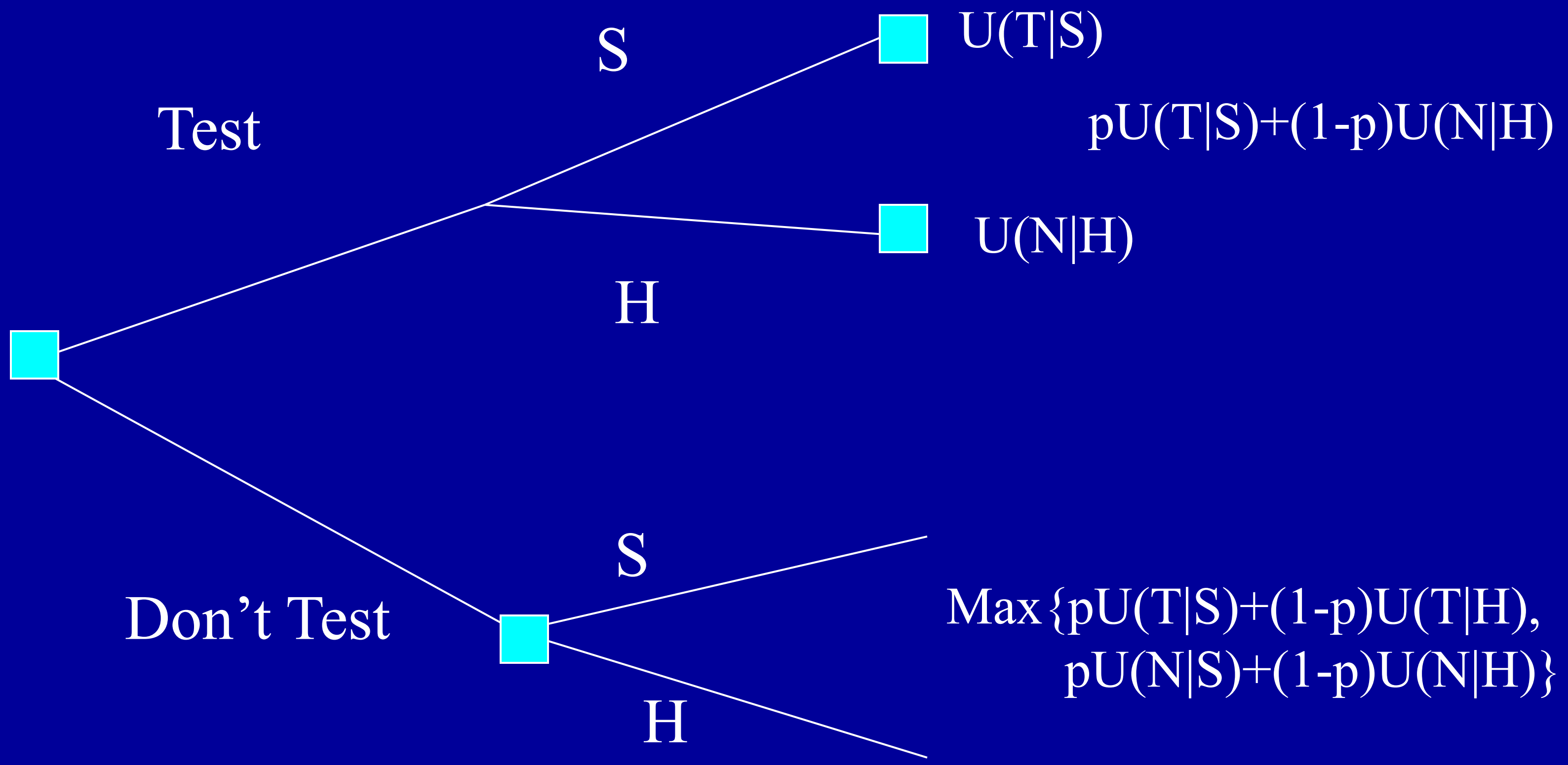
- Need to consider how an intervention will be used in deciding if it will be welfare improving
- Highlights importance of efforts to promote selective use
- Suggests that “inferior” technologies may sometimes be preferred if their use can be better controlled

Value of Research

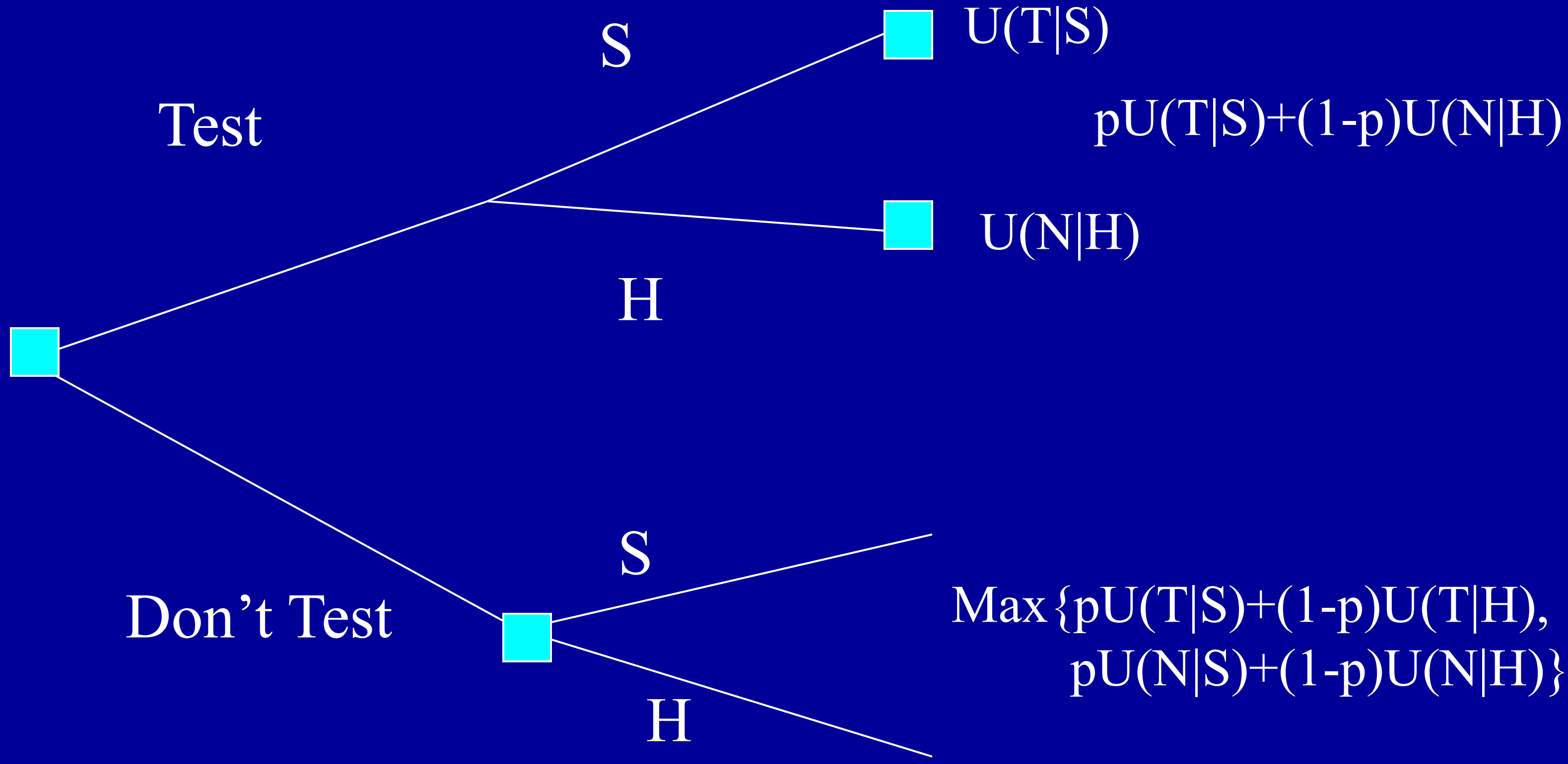
Value of Diagnostic Testing



Testing as Value of Information



Research as Value of Information



Value of Information Approach to Value of Research

- Without information
  - Make best compromise choice not knowing true state of the world (e.g. 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

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)

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

Thank you!