RTI HEALTH SOLUTIONS®

Developing health economic models for assessing cost-effectiveness and product value

Prepared for

Health Economics 2006

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Agenda

- 9.30 – 11.00 (then break)
- Introductions (15 min)
- Goals (5 min)
- Process (5 min)
- Recommended Reading (5 min)
- Terms (30 min)
- Why Develop a Model? (20 min)
- Key Methodological Concepts (10 min)
- 11.15 – 12.30 (then lunch)
- Key Methodological Concepts cont.
- 13.30 – ?
- Case Studies

Introductions

- Relationship with Health Economic Models?
- Experience with Health Economic Models?
- Scientific Discipline?

Goals of Today's Workshop

- To Understand How an Economic Model Can Support Pricing & Reimbursement
- To Understand Key Methodological Concepts related to Economic Modeling

Process

- Interactive, Conversational, Share Experiences
- Flipchart for Questions & Issues
- Follow-up

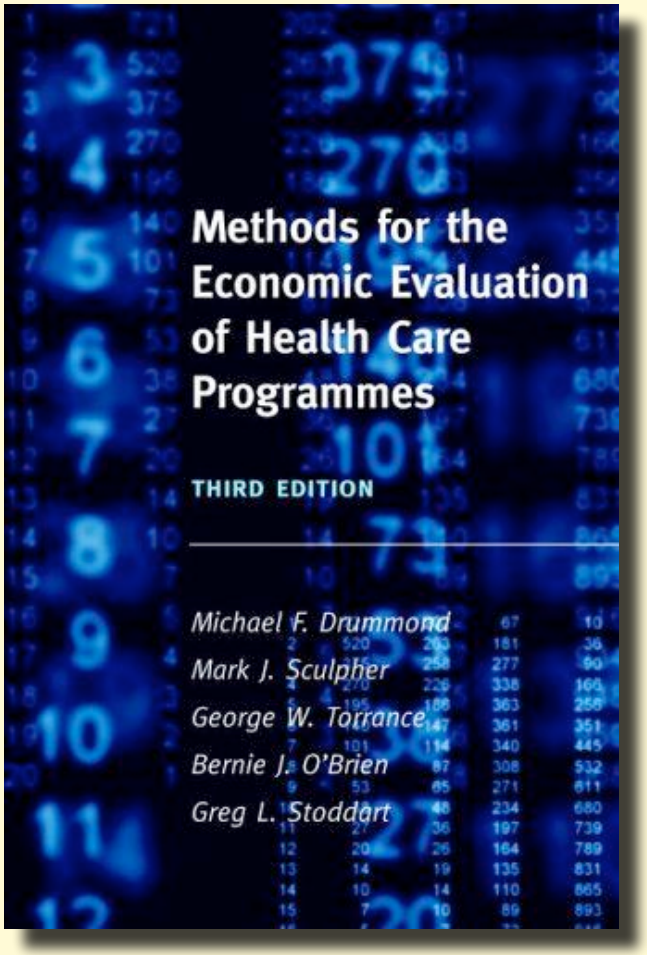
Recommended Reading (1 of 3)

Briggs A, K Claxton, M Sculpher (eds). Modeling methods for health economic evaluation. Oxford University press: 2006 (coming soon).

H Berger ML, Bingefors K, Hedblom EC, et al. (eds). Health care cost, quality, and outcomes. ISPOR book of terms. Oxford University Press: 2001.

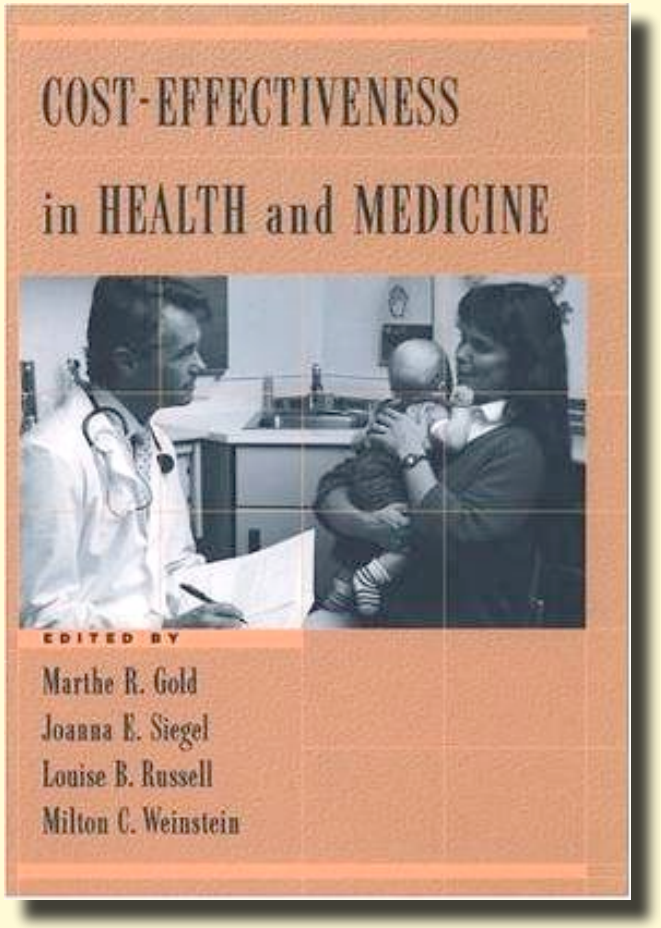
Recommended Reading (2 of 3)

Drummond M, MJ Sculpher, GW Torrance, BJ O'Brien, GL Stoddart (eds). Methods for the economic evaluation of health care programmes, 3rd edition. Oxford University Press: 2005.



Recommended Reading (3 of 3)

Golde MR, JE Siegel, LB Russell, MC Weinstein (eds). Cost-effectiveness in health and medicine. Oxford University Press,1996.



Terms

- Perspective (IMPORTANT)
- Costs
- Health Outcomes
- Economic Analysis
- Models

Terms: Perspective

- Society (?)
- Patient
  - Health Outcomes (Personal, Experiential)
  - Out-of-Pocket Cost
  - Ease of Obtaining Treatment
- Physician
  - Health Outcomes—Evidence-based Medicine
  - Equality vs Efficiency
  - Cost (esp with capitation or fundholder responsibilities)
  - Ease of Obtaining Treatment
- 3rd-party Payer
  - Health Outcomes (Population-based)
  - Budget Impact (Population-based)

Terms: Costs (1 of 5)

- Economists' conception of cost is one of opportunity cost: the value of a resource if it were employed in it's best alternative use.
- Economics is interested in the efficient allocation of (scarce) resources.
- The value of resources (i.e., costs) are typically approximated by a resource's market or transaction price—the price at which buyers and sellers agree to make an exchange. But money has little intrinsic value; it only serves to represent real goods and services. The resources that are created or destroyed are the real things of concern.

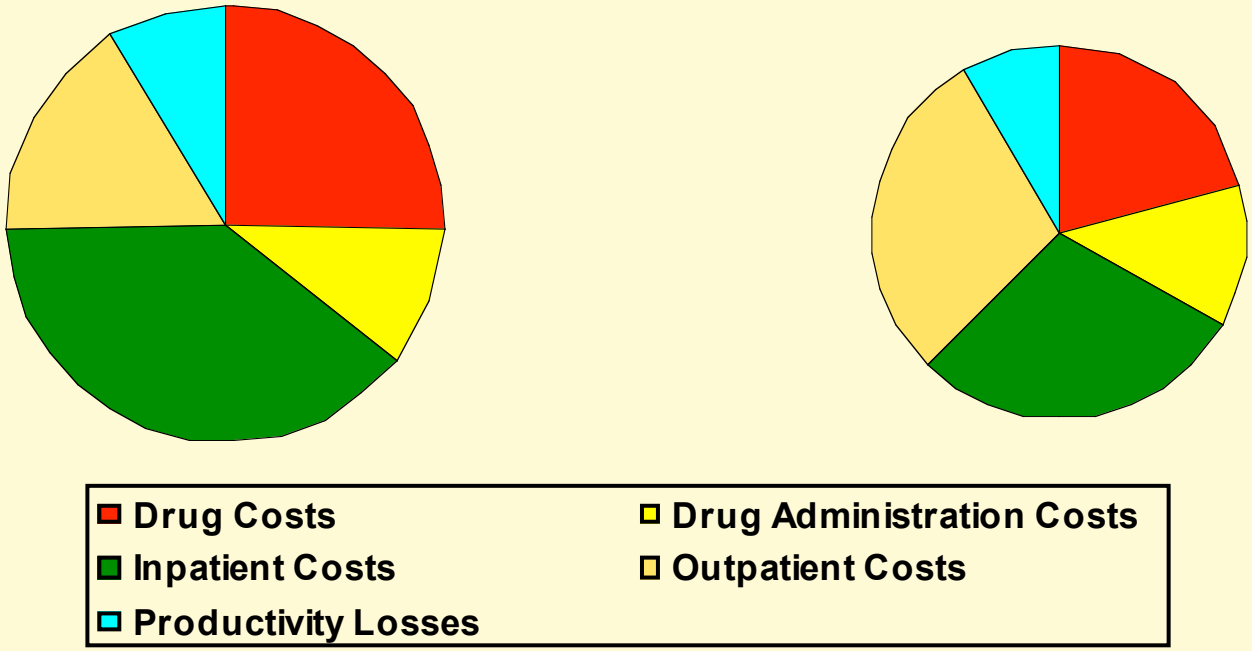
Terms: Costs (2 of 5)

- Net Total Cost—Alternative Terms
  - "Incremental cost"
  - "Marginal cost" (?)
- Depends on Perspective
- Increases in Cost
  - Drug
  - Drug administration
  - Monitoring
  - Treatment of adverse events
  - Improvement in health outcomes
- Cost Offsets
  - No need for alternative drug
  - Reduced administration and monitoring
  - Better side effect profile
  - Improvement in health outcomes

Terms: Costs (3 of 5)

- Drugs
  - OTC vs prescription
  - Subsidized/reimbursed vs not
  - Outpatient vs inpatient delivery
- Outpatient Visits
  - GP, Specialist, Nurse, Therapist, etc.
  - Laboratory services
  - Procedures
- ER
- Inpatient Hospitalization
- Surgeries
- Nursing Home Care
- Mental Health Care

Terms: Costs (4 of 5)
Cost Outcomes with the New Drug



Terms: Costs (5 of 5)

- Indirect Costs
  - Value of lost productivity
  - Various methods
  - Paid vs unpaid (volunteer)
  - Patient vs caregiver
- Not normally of interest to payers
  - Exception may be US employer-based MCOs; societal perspective

Terms: Health Outcomes

- Health Outcomes—Alternative Terms
  - "Health benefits"
  - "Effectiveness"
- Proxy vs Ultimate Outcomes
  - Change in LVEF vs recurrent AMI
  - Change in blood pressure vs CV Event
  - Response rate vs survival (?)
- Quality of life
  - Value as clinical trial endpoint
  - Profiles, indices
  - Generic, disease-specific
- QALY
  - Value as a tool for resource allocation

Terms: Economic Analysis

- Cost Consequences
  - Assess net total cost
  - Present portfolio of changes in health outcomes
- Cost-minimization/Benefit-maximization
- Cost-effectiveness analysis (CEA)
  - Ratio of net cost over net health outcomes
    - Incremental cost-effectiveness ratio “ICER”
  - Profiles, indices
  - Generic, disease-specific
- Cost-utility analysis (CUA)
  - A type of CEA in which the measure of effectiveness is a QALY

Example 1 (1 of 2)

Suppose you were the medical director at a large HMO. A subset of your beneficiaries suffers from Serious Disease. There are two treatments for Serious Disease, Miracle Drug and Status Quo. You must choose one to include on your formulary. Miracle Drug and Status Quo are equally effective in curing Serious Disease. They have similar side effect profiles. They are both oral tablets, taken twice a day. In a blinded, randomized cross-over clinical trial, patients reported no preference for one drug over the other. Both improve quality of life to about the same extent. Miracle Drug costs twice as much as Status Quo.

Example 1 (2 of 2)

Alternatives to Treat Serious Disease	Average Cost per Person	Average Life-Years Saved (LYS) per Person	Side Effects	Delivery Method/ Schedule	Quality of Life Effects	Patient Preference
Status Quo	$500	5	20% mild nausea, treated with inexpensive OTC products	Oral tablets taken twice daily	Improves by about the same amount as with Status Quo	No preference compared to Miracle Drug
Miracle Drug	$1,000	5	20% mild nausea, treated with inexpensive OTC products	Oral tablets taken twice daily	Improves by about the same amount as with Miracle Drug	No preference compared to Status Quo

- Which drug would you endorse for use in your patients?
- What economic evaluation technique did you employ to make your decision?

Example 2

Now suppose that Miracle Drug and Status Quo actually cost the same amount, and are similar in every respect except that Miracle Drug is more effective.

Alternatives to Treat Serious Disease	Average Cost per Person	Average Life-Years Saved (LYS) per Person	Side Effects	Delivery Method/ Schedule	Quality of Life Effects	Patient Preference
Status Quo	$1,000	5	20% mild nausea, treated with inexpensive OTC products	Oral tablets taken twice daily	Improves by about the same amount as with Miracle Drug	No preference compared to Miracle Drug
Miracle Drug	$1,000	8	20% mild nausea, treated with inexpensive OTC products	Oral tablets taken twice daily	Improves by about the same amount as with Status Quo	No preference compared to Status Quo

- Now which drug would you endorse for use in your patients?
- What economic evaluation technique did you use?

Example 3: Cost-Consequences Analysis

For this example, suppose that the following differences exist between the drugs. Which drug would you endorse?

Alternatives to Treat Serious Disease	Average Cost per Person	Average Life-Years Saved (LYS) per Person	Side Effects	Delivery Method/ Schedule	Quality of Life Effects	Patient Preference
Status Quo	$1,000	5	60% mild nausea, treated with inexpensive OTC products	Oral tablets taken six times daily	Improves, but not by as much as with Miracle Drug	Strong preference for Miracle Drug
Miracle Drug	$2,000 + $40 in regular monitoring labwork	5	3% mild nausea, treated with inexpensive OTC products; 0.001% acute renal failure	Oral tablets taken twice daily	Improves by a good bit more than Status Quo	Strong preference for Miracle Drug

Terms: Models

- An attempt to Mimic the “Real-World”
  - Understand and predict
  - Accurate yet simple
  - Analytical or visual
  - Mathematical or statistical
  - Deterministic or probabilistic
- Decision Trees
- Markov Models

Why Develop a Model?

- Internal Decision-making
- Decision-makers Will Consider Costs
- Manufacturer Has Best Information and Resources
- Clinical Trials are Limited

Why Develop a Model? Internal Decision-making

- Pricing
  - Threshold analysis can clarify trade-offs between price and effectiveness, given a payer's threshold ICERPricing
- Early models can identify likely cost impact of new drug, contributing to efficient clinical trial design, including
  - Collection of medical resource utilization data
  - Selection of comparators
  - Prospective definitions of subgroups
  - Ancillary studies required
  - Design of post-marketing studies

Why Develop a Model? Decision-makers Will Consider Costs

- UK
  - NICE recommendations to NHS
  - Physician fundholders
- France
  - CT, HAS
  - Pricing Committee
- Australia (e.g.)
  - Therapeutic group pricing, including generics
- US
  - MCOs (for profit, cost-containment given competitive offering, class vs within-class comparisons)
  - Public payers (e.g., CMS, state Medicaid)

Why Develop a Model? Manufacturer Has Best Information and Resources

- Must invest in this area, regardless of the expected payer decisions
- Be sure that modeling team appreciates the commercial reasons for the model
  - Ensure perspective is correct
  - Ensure model is transparent
  - Ensure model is credible and well-documented
  - Ensure model is user-friendly

Why Develop a Model? Clinical Trials Are Limited

- Clinical Trials are Limited
  - Surrogate outcomes
  - Efficacy vs effectiveness
  - Trial vs actual patients
  - CE may vary by subgroup

Key Methodological Concepts (KMC)

1. Economic Models Commonly Used in Pharmaceutical Evaluation
2. Presenting and Interpreting Economic Model Results
3. Addressing and Conveying Uncertainty
4. Linking Cost-effectiveness and Budget Impact
5. Patient-reported Outcomes
6. Data Sources for Economic Models
7. Country Adaptations
8. Critical Appraisal of Economic Models

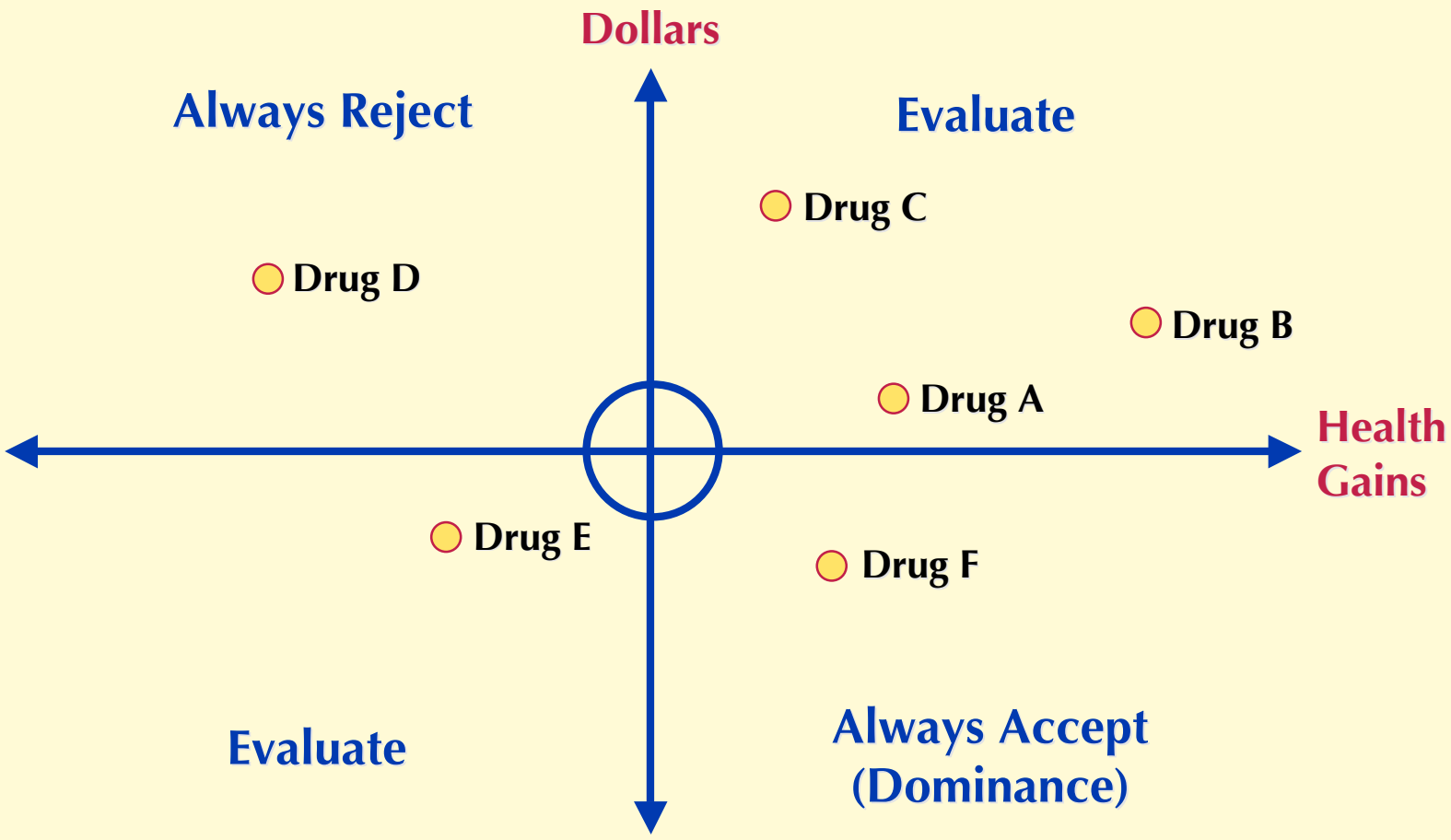
KMC 1: Economic Models Commonly Used in Pharmaceutical Evaluation

- Selecting the Appropriate Modeling Approach
  - Disease (e.g., Markov in cancer; decision tree for pain)
  - Drug
  - Market (e.g., cost-utility for NICE)
- Common Software Packages
  - Excel (build it!)
  - TreeAge (www.treeage.com; free trial version online)
  - @RISK (www.palisade.com; free tutorial online)

KMC 2: Presenting and Interpreting Economic Model Results

- Cost-effectiveness Plane
- ICER
- ICER League Table
- Cost-effectiveness Acceptability Curves (CEACs)
- Dominance
- Net-benefit

KMC 2: Cost-effectiveness Plane



KMC 2: ICER (1 of 6)

- Most commonly applied economic evaluation technique with pharmaceuticals
- Facilitates comparisons across diseases
- Places decision in hands of decision-maker rather than economist

KMC 2: ICER (2 of 6)

- Incremental Cost-Effectiveness Ratio:

$$\frac{Cost\ Drug\ A - Cost\ Drug\ B}{Eff\ \ Drug\ A - Eff\ \ Drug\ B}$$

- Average Cost-Effectiveness Ratio:

$$\frac{Cost\ \ Drug\ \ A}{Eff\ \ Drug\ \ A}$$

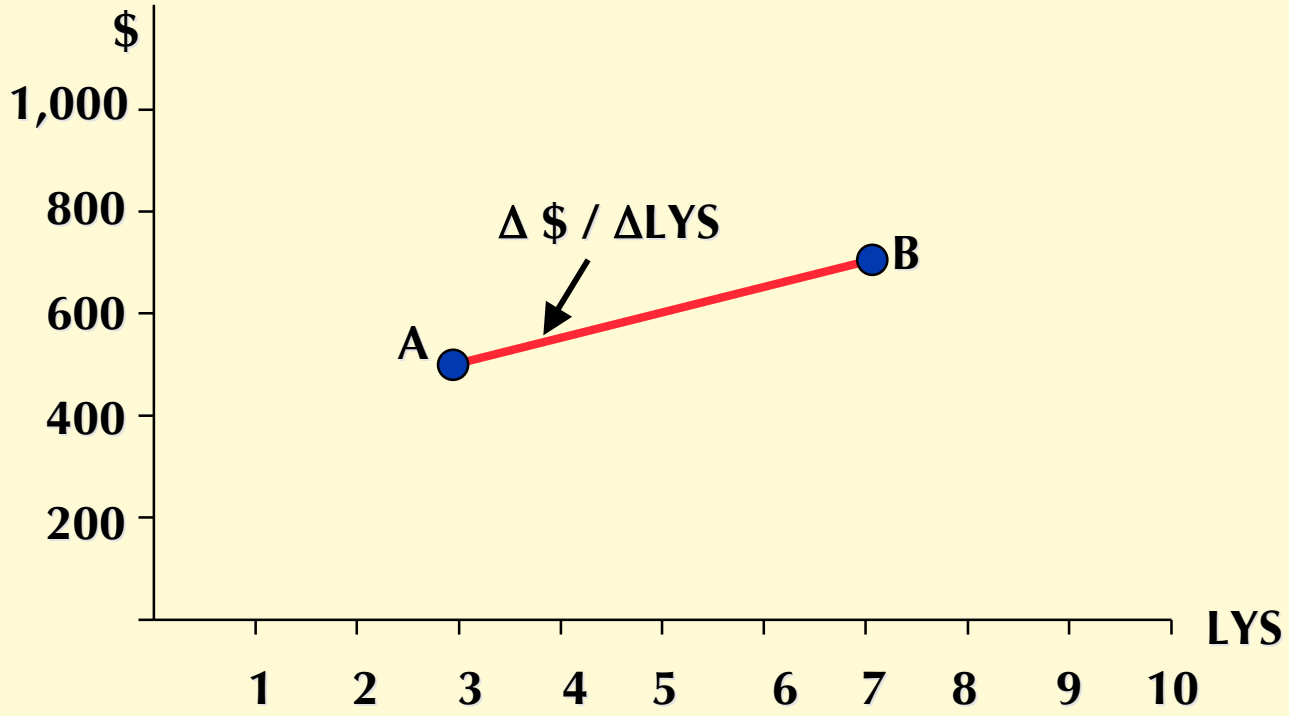
KMC 2: ICER (3 of 6)

- An Incremental Cost-Effectiveness Ratio is NOT the Difference between Two Average Cost-Effectiveness Ratios

KMC 2: ICER (4 of 6)

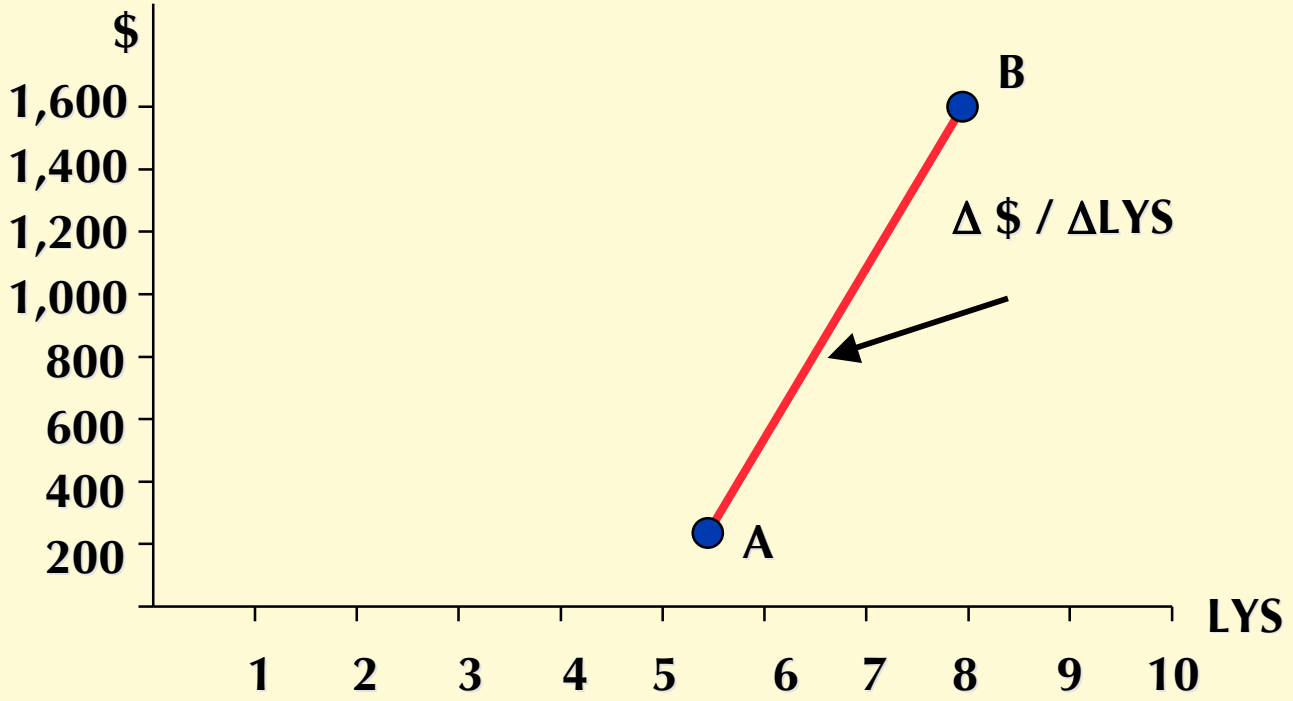
- ICER is a SLOPE (Rise over Run)
- Look at it's sign (positive or negative) and it's magnitude
- A negative ICER indicates the presence of a DOMINANT therapy
- The higher the ICER, the less cost-effective is the therapy compared to the alternative

KMC 2: ICER (5 of 6)
Example 1



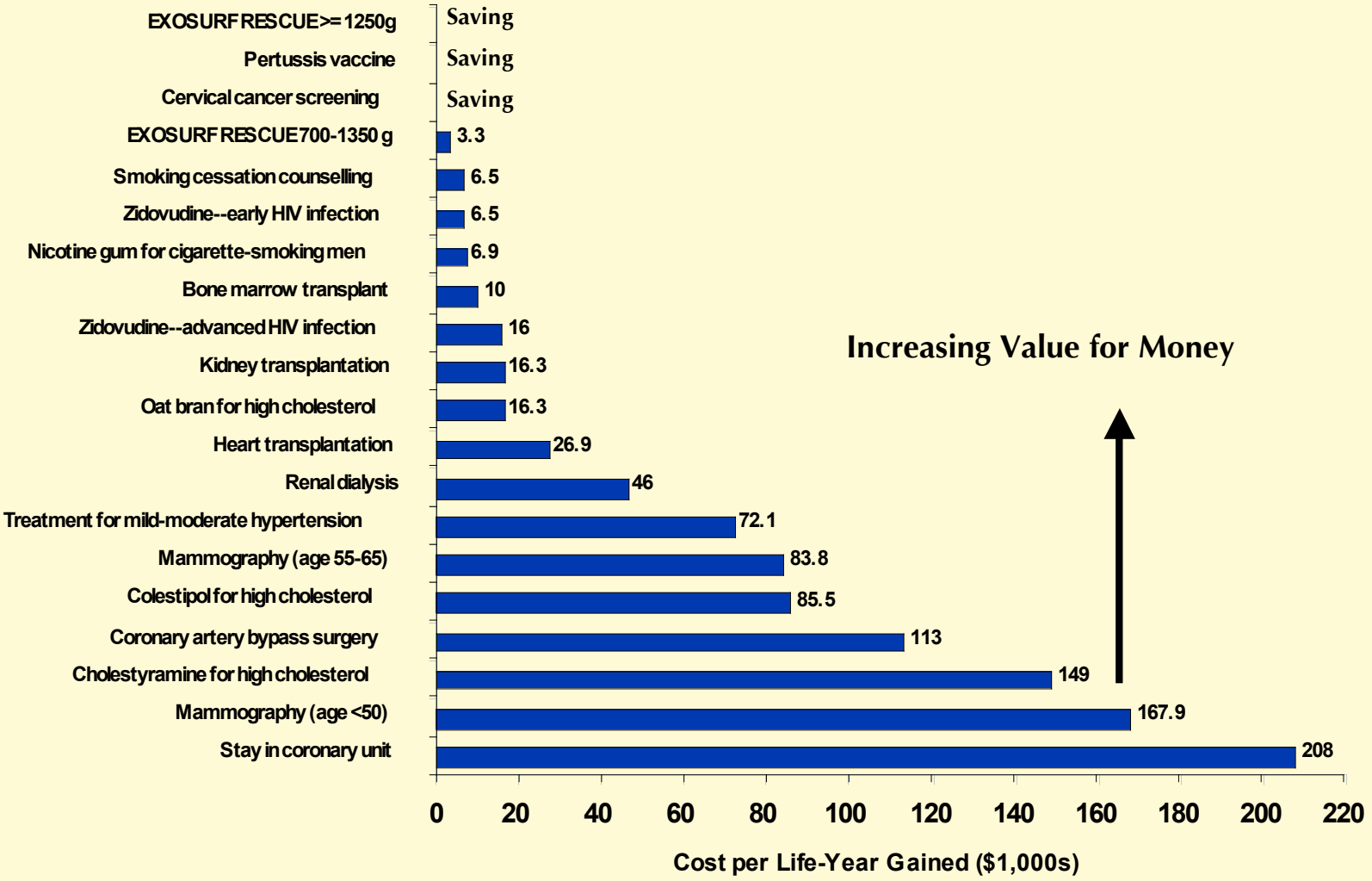
	$	LYS	Avg CER	Inc CER
Drug A	500	3	167	—
Drug B	700	7	100	50

KMC 2: ICER (6 of 6)
Example 2

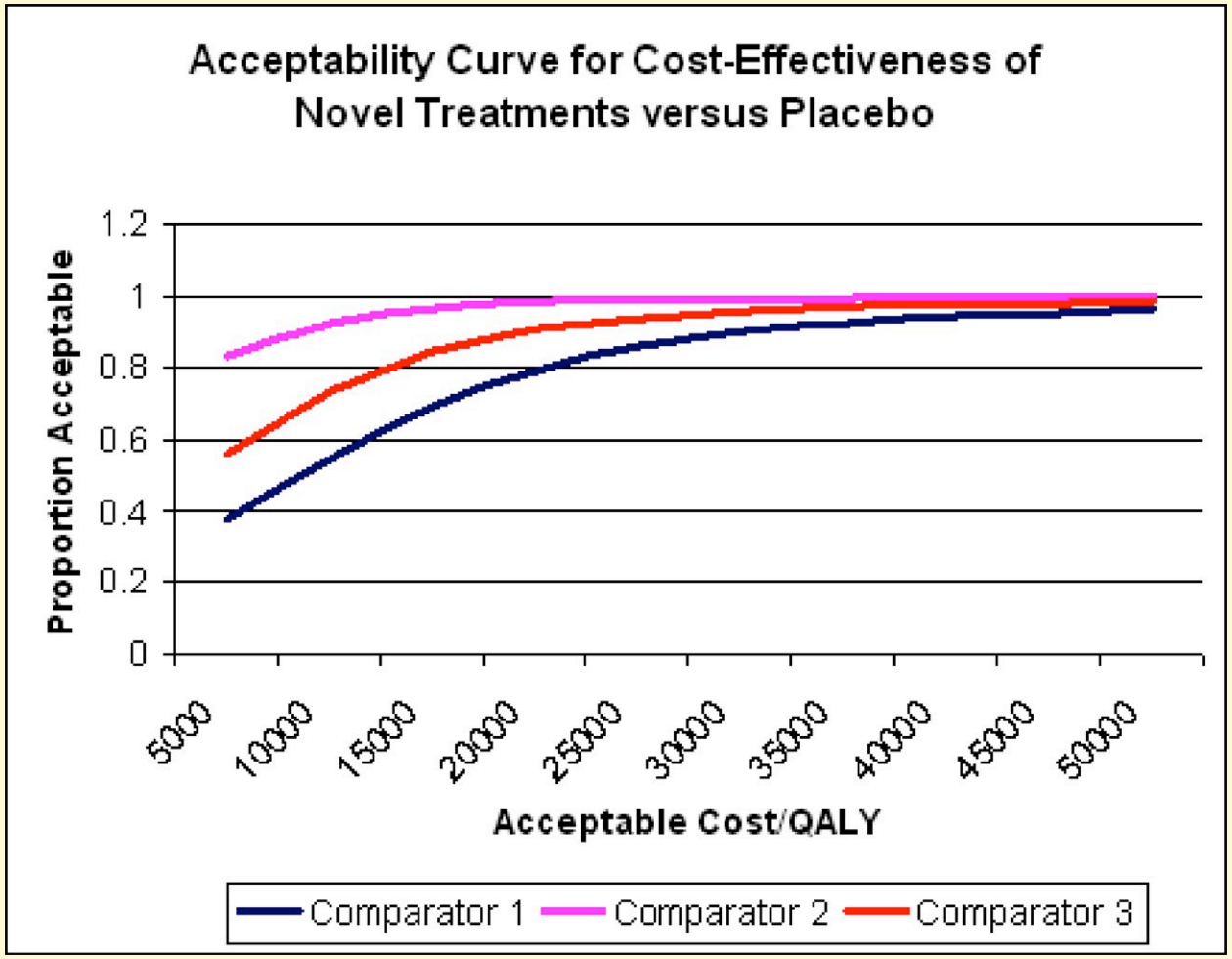


	$	LYS	Avg CER	Inc CER
Drug A	250	5.5	45	—
Drug B	1,600	8	200	540/LYS

KMC 2: ICER League Table



KMC 2: CEACs


Acceptability Curve for Cost-Effectiveness of Novel Treatments versus Placebo
Proportion Acceptable
1.2
1
0.8
0.6
0.4
0.2
0
5000
10000
15000
20000
25000
30000
35000
40000
45000
50000
Acceptable Cost/QALY
Comparator 1
Comparator 2
Comparator 3

KMC 2: Dominance

- Dominance occurs when one drug is both more effective and less costly than another
- Extended dominance

KMC 2: Net-benefit

- Alternative to ICER
- Expressed in monetary units (net monetary benefit) or in units of efficacy or utility (net health benefit)
- Need to know threshold decision levels

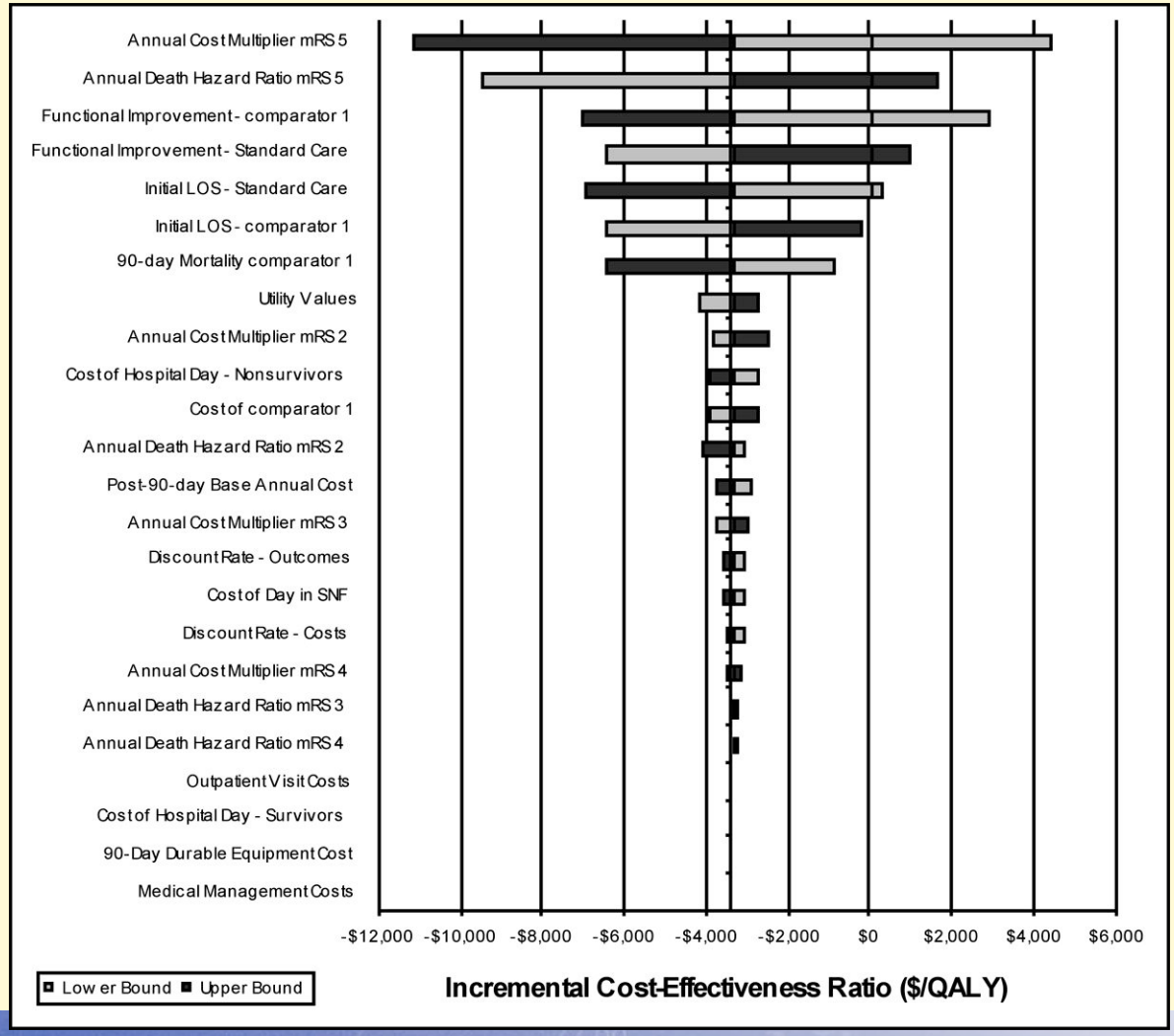
KMC 3: Addressing and Conveying Uncertainty

1. Sensitivity Analysis (1- and multi-way)
2. Tornado Diagrams
3. Threshold Analysis
4. Bootstrapping
5. Monte Carlo simulation

KMC 3: Sensitivity Analysis (1-way and Multi-way)

- 1-way SA examines the extent to which your model results change, given changes (over a reasonable range) in a single variable
- Multi-way SA examines the extent to which your model results change , given changes in multiple variables at once

KMC 3: Tornado Diagram



KMC 4: Linking Cost-effectiveness and Budget Impact

- Must Do Cost-effectiveness Model First
- Population Costs and Benefits
  - Incidence and Prevalence
  - Duration of Costs and Benefits
- Match Cost Parameters to Perspective (e.g., Nursing home paid by Medicaid, not MCOs; mental health benefits not paid by MCOs; factor in copays)
- Ensure Relevance of Timeline for Health Benefits vs Expenditures (e.g., smoking cessation drug cost now; health benefits in 25 years)

KMC 5: Patient-reported Outcomes

- Descriptive Health Status Assessment vs Utility Assessment
  - When to use each in economic analysis
  - How to use each in economic analysis
- Modeling Utilities from Health Status Measures
- Preferences of Pricing & Reimbursement Authorities for PRO Data

KMC 6: Data Sources for Economic Models

- Clinical Trials
- Published Literature
- Database Analysis
- Registries
- Validating Model Predictions with Subsequent Head-to-head Studies

KMC 7: Country Adaptations

- Currency conversion insufficient
- Perspective
- Comparators
- Adaptation of Treatment Patterns
  - To adjust medical resource utilization (Good)
  - To adjust model structure (Better)
- Unit Costs
- Adjustments to Baseline Patient Population Parameters, if Applicable

KMC 8: Critical Appraisal of Economic Models

- Applying Guidelines (and Common Sense)
- Case Studies:
  - Oncology
  - Schizophrenia
  - GERD
  - Migraine

Economic Evaluation of NVB vs NVB+CIS vs VDS+CIS

Deirdre M. Neighbors

1999

Objective

- To estimate the incremental cost-effectiveness of 3 regimens for advanced NSCLC.
- Advanced NSCLC cause of 82% of lung cancer deaths.
- Chemotherapy for advanced NSCLC represents a controversial use of societal resources, argued to be expensive, toxic, and offering little survival benefit.

Methods

- Modeled incremental cost-effectiveness analysis ($\Delta C/\Delta E$) using clinical trial survival and toxicity estimates for 3 chemotherapeutic regimens and academic medical center costs for patients on similar protocols.
- Societal perspective.
- No discounting, as 90% dead at 2 years.

Results

- NVB least expensive because of lower requirement for antiemetics and laboratory monitoring and lower chemotherapy costs (without CIS).
- Mean survival least with NVB compared to combination regimens.
- Most effective regimen also cost-effective.

Incremental CE Analysis

Variable	Vinorelbine + Cisplatin *vs* Vindesine + Cisplatin	Vindesine + Cisplatin *vs* Vinorelbine alone	Vinorelbine + Cisplatin *vs* Vinorelbine alone
Incremental mean survival (days)	37	19	56
Incremental cost per patient ($)	1,570	1,150	2,700
Incremental cost-effectiveness			
$/day of life gained	42	60	48
$/year of life	15,550	22,100	17,700

Sensitivity Analysis

- Utility of chemotherapy 0.7 for NVB, 0.6 for CIS
- NVB+CIS vs NVB: 241,000
- NVB+CIS vs VDS+CIS: 25,800
- VDS+CIS vs NVB: -29,000

Are the results valid?

- Full economic comparison of strategies?
- Costs and outcomes properly measured and valued?
- Estimates of costs and outcomes related to baseline risk?

Full Economic Comparison?

- No inclusion of cost savings of response.
- No inclusion of costs of disease progression (which have been shown to differ across regimens).
- Toxicity costs underestimated (only vomiting and febrile neutropenia; relied on incidence rates).
- No costs of 2nd-line chemotherapy.

Costs and Outcomes Properly Measured?

- No resource utilization data collected in trial.
- No utility or QOL data collected in trial.
- Cost data from MCV not representative.
- European trial with one non-US regimen (VDS+CIS).

What were the results?

- What were the incremental costs and outcomes?
- Do they differ among subgroups?
- Effect of uncertainty on results?

Effect of Uncertainty on Results?

- Not sensitive to reasonable changes in survival.
- Highly sensitive to utility estimates.
- Sensitive to costs of CIS administration.
- Also used sensitivity analysis to examine CE of similar US regimen (CIS+ETOP).

Will the results help?

- Are the treatment benefits worth the harms and costs?
- Could patients expect healthy outcomes?
- Could you expect similar costs?

Benefits worth the harms and costs?

- Debate re:chemo vs best supportive care. Does analysis support chemo?
- How important is QOL? Should more value be placed on cost-utility analysis?

Benefits worth the harms and costs (cont)?

- "The results of this study are similar to different types of thrombolytic therapy for AMI with short-term absolute reductions in mortality of one to three persons per 100 treated, lesser long-term effect on mortality, and a cost-effectiveness of $28,000 per year of life gained for the more effective but costlier tPA compared with streptokinase."

Could you expect similar costs?

- MCV data not representative.
- Analysis sensitive to CIS administration.
- Trial patients differ from typical patients.

Case Studies, Additional References—add primers

- Richter A et al. 2002. A Monte Carlo simulation for modeling outcomes of AIDS treatments. Pharmacoeconomics 20(4):215-24.
- Karnon J et al. 2006. Cost-effectiveness of extended adjuvant letrozole in postmenopausal women after adjuvant tamoxifen therapy: the UK perspective. Pharmacoeconomics 24(3):237-50.
- Thompson M et al. 2005. An economic evaluation of rizatriptan in the treatment of migraine. Pharmacoeconomics 23(8):837-50.
- Edwards NC et al. 2005. Cost effectiveness of long-acting risperidone injection versus alternative antipsychotic agents in patients with schizophrenia in the USA. Pharmacoeconomics 23 Suppl 1:75-89.
- Haycox A. 2005. Pharmacoeconomics of long-acting risperidone: results and validity of cost-effectiveness models. Pharmacoeconomics 23 Suppl 1:3-16.
- Bala M and J Mauskopf. 2006. Optimal assignments of treatments to health states using a Markov decision model: an introduction to basic concepts. Pharmacoeconomics 24(4):345-54.
- Phillips Z, et al. 2006. Good practice guidelines for decision-analytic modeling in health technology assessment: a review and consolidation of quality assessment. Pharmacoeconomics 24(4):355-71.