Conducting and Implementing CEAs

Karen Kuntz, ScD

Recommendations of the
Second Panel on Cost-Effectiveness
in Health and Medicine

Decision Models

- Provide a framework for decision making under uncertainty
- Help structure the analysts' thinking and facilitate the communication of assumptions
- Provide a structural framework for synthesizing data from disparate sources and allows for extrapolations

Importance of Modeling as Framework

- Original Panel devoted little attention to modeling

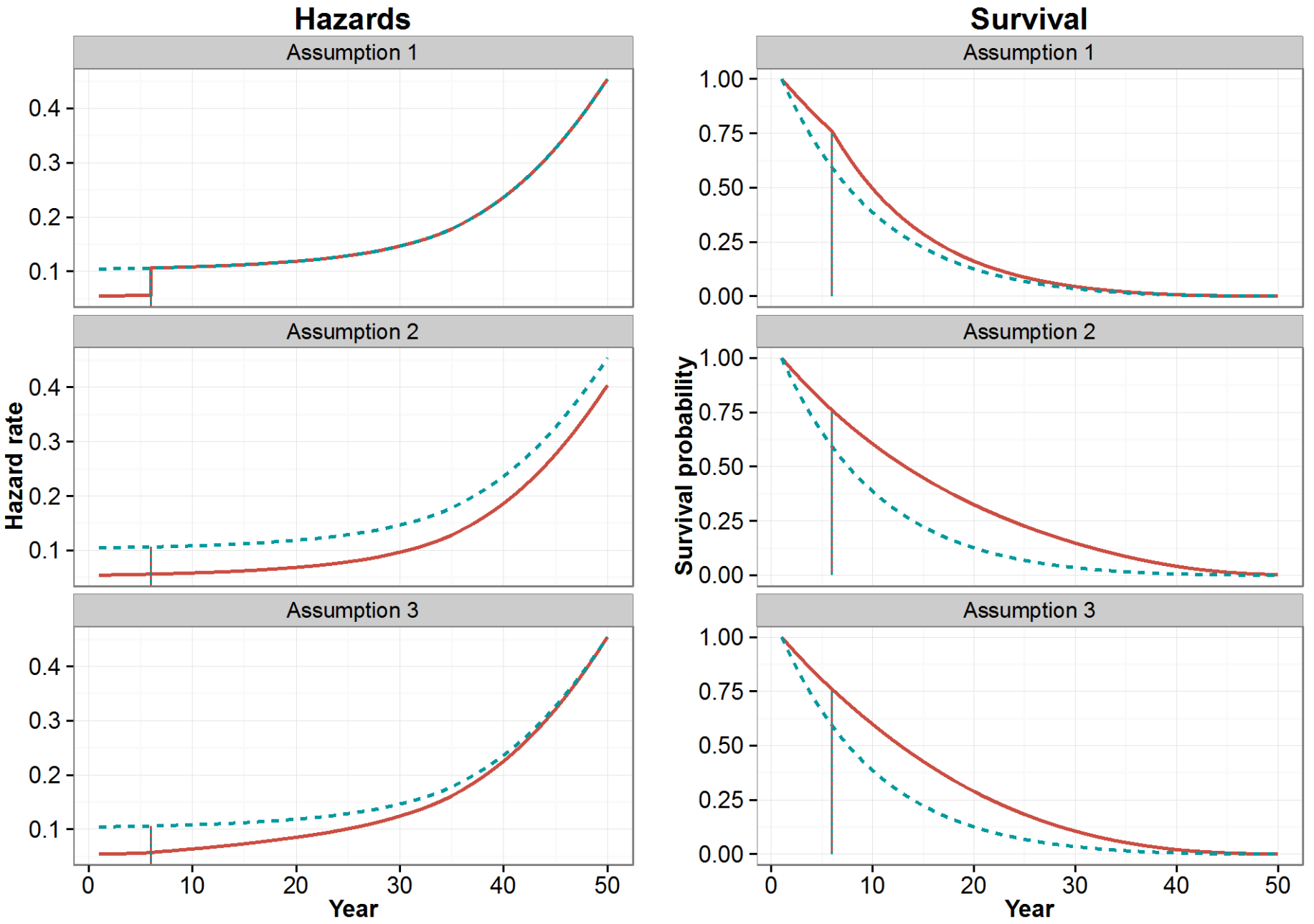
> "Where direct primary or secondary empirical evaluation of effectiveness is not possible (e.g., in important subpopulations or in different time frames), the use of modeling to estimate effectiveness is a valid model of scientific inquiry for CEAs"

Decision Models in CEA

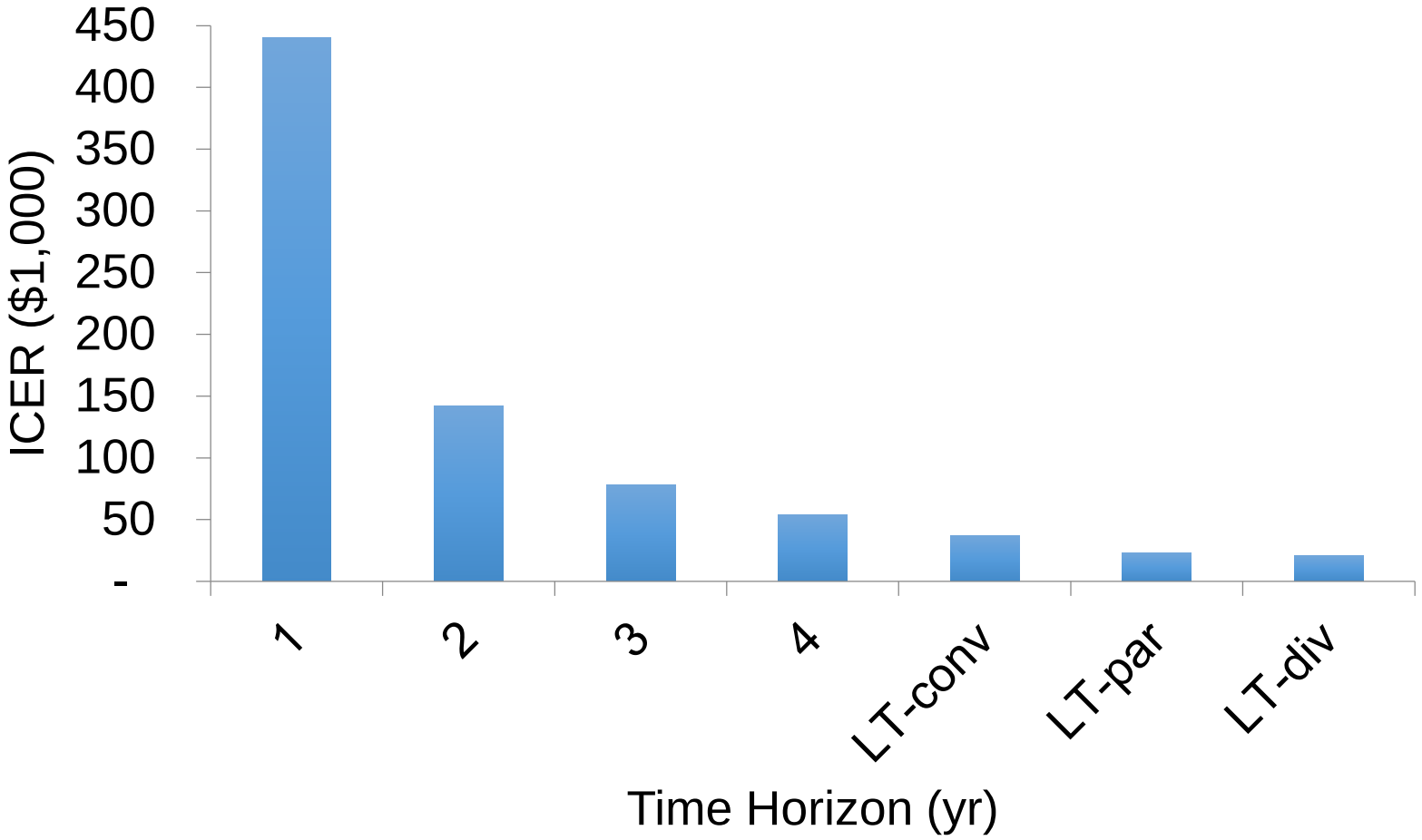
- Analysts often face situations for which modeling can be informative
- Many country-specific guidelines for conducting CEAs for health technology appraisals include recommendations for developing decision models
- Several publications related to best practices for decision models

Need for a Decision Model: Extrapolating

- Beyond the time horizon of available data
- From intermediate (surrogate) outcomes to long-term outcomes
- To population subgroups not observed in studies
- Long-term outcomes associated with diagnostic test strategies
- To strategies that have not been studied in head-to-head comparisons


Hazards
Survival
Assumption 1
Assumption 2
Assumption 3
Hazard rate
Survival probability
0.1
0.2
0.3
0.4
0.00
0.25
0.50
0.75
1.00
0
10
20
30
40
50
Year
Group
Intervention
Control

ICERs Vary by Time Horizon



Hlatky et al. Clinical Trials 2006;3:543-51.

Key Modeling Recommendations

- Initial conceptualization of model should be independent of data identification phase
- Full documentation and justification of structural assumptions should be provided
- Analyst should specify starting population whether they are analyzing a cohort or population
- Validation of model should occur throughout the conduct of a CEA

Uncertainty Analysis

- Propagation of input uncertainty informs on decision uncertainty
- Correlations among parameters should be considered
- Structural uncertainties should be explored (in scenario analyses if necessary)
- EVI should be used to guide decision making under uncertainty

Structural Uncertainty

- How to model the effects of an intervention beyond the time horizon of the data
- How different states of health and pathways of care are characterized in a model
- How disease progression is modeled over time (extrapolated) beyond the follow-up period of study
- Judgments about the relevance and appropriateness of different sources of evidence

Sensitivity Analysis

- Examining model outputs while conditioning on specific inputs provides insight about model behavior
  - One-way and multi-way sensitivity analyses
  - Threshold analyses
- Can be used as a means of understanding the implication of heterogeneity

Evidence Synthesis for Informing Cost Effectiveness Analysis

Tom Trikalinos, MD

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Principle of ‘total evidence’

- Maximizing use of the relevant evidence increases the likelihood of good quality decisions

- Evidence synthesis is about identifying, culling, and using relevant evidence in a CEA

How does evidence synthesis inform CEA model parameters?

1. Learn an evidence synthesis model that describes the relationships between study characteristics and bias-free study estimates
2. Use the evidence synthesis model to predict the value of the parameter of interest in the context of the CEA model

How does evidence synthesis inform CEA model parameters?

Contexts comprise salient differences between studies	Observed data: what each study observed	Estimate: what each study's analysis found	Estimand: what each study aimed to find
$\text{Context}_1 : \mathbf{x}_1$	y_1	θ_1	θ_1^*
…	…	…	…
$\text{Context}_k : \mathbf{x}_k$	y_k	θ_k	θ_k^*
…	…	…	…
$\text{Context}_K : \mathbf{x}_K$	y_K	θ_K	θ_K^*

Net study bias:
Difference between estimand and estimate

$$b_k = \theta_k^* - \theta_k, \ \forall\, k \in \{1, \ldots, K\}$$

Evidence synthesis model:
Describes the relationship between estimands and contexts, given observed contexts and study results, and analysts' opinions about bias

$$f\left(\theta^* \mid \underbrace{\mathbf{x}_1,\ldots,\mathbf{x}_K}_{\text{contexts}}, \underbrace{y_1,\ldots,y_K}_{\text{observed data}}, \underbrace{b_1,\ldots,b_K}_{\text{analysts' opinion about bias}}\right)$$

Informing a CEA model parameter amounts to predicting what the estimand would be in the context of the CEA model, using the learnt evidence synthesis model

$$f\left(\theta_{CEA}^* \mid \mathbf{x}_{CEA}, \mathbf{x}_1,\ldots,\mathbf{x}_K, y_1,\ldots,y_K, b_1,\ldots,b_K\right)$$

Evidence synthesis for informing a CEA vs for summarizing evidence

Differences exist in

- The acceptable degree of comprehensiveness
- The goals of the evidence synthesis
- The willingness to learn across study designs
- The need to grade the “Strength of Evidence”
- Statistical modeling choices
- Priming transparency vs objectivity

Evidence synthesis for informing a CEA vs for summarizing evidence

Characteristic	ES for describing evidence	ES for informing CEA
Comprehensiveness	Mandatory attribute	Desirable attribute
Goals of ES	Describe evidence	Predict estimate in modeled setting
Cross-design synthesis	Uncommon	Common
'Strength of evidence' assessments	Common	Superfluous
Statistical modeling	Simple	Advanced
Objectivity vs transparency	Objectivity	Transparency

ES: Evidence synthesis

Phases of evidence synthesis for CEAs

- Pre-analytical phase
  - Assemble team
  - Define target question
  - Identify evidence
  - Extract information
- Analytical phase
  - Conduct qualitative analysis
  - Conduct quantitative synthesis
  - Assess and account for risk of bias
  - Assess and account for (non)-transferability
- Post-analytical phase
  - Obtain predictions of parameters in the modeled setting
  - Report process, sensitivity analyses, miscellanea

Recommendations

1. Follow established guidance for systematic reviews and meta-analyses, modified as per **Recommendations 2** through **8**

Recommendations

2. The CEA team and the Evidence Synthesis team (if separate) should coordinate to **refine the scope and goals of the evidence synthesis.**

Recommendations

3. Identify the **important model parameters**. Important parameters are those that are **(i) influential on model results, or (ii) critical to the (perceived) validity of the model.** Estimates of important parameters should be informed through evidence synthesis.

Recommendations

4. Provide an **analytical description and a critique** of the evidence base.

Recommendations

5. Quantitative evidence synthesis should use methods that
   (i) model **the statistical variability of data**,
   (ii) allow **between-study heterogeneity**, and
   (iii) yield **consistent estimates for all model parameters informed by the synthesis**

Recommendations

6. The evidence synthesis must be explicit about **whether and how bias in each study and across studies was handled.**
   The goal of the synthesis should be to produce bias-corrected estimates.

Recommendations

7. The evidence synthesis must be explicit about **whether and how estimates were adjusted for transferability.**
   The goal of the synthesis should be to produce estimates applicable to the modeled setting.

Recommendations

8. Enumerate scenarios for **sensitivity analysis for (i) structure and (ii) parameter values** based on the findings of the qualitative analysis and assumptions made when accounting for/dealing with biases and transferability of estimates in the quantitative synthesis.

The Cost Effectiveness of Home Palliative Care For Patients at the End of Life

Ba' Pham, PhD

Murray Krahn, MD MSc

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End-of-Life Care

- EOL care consumes ~9% of the Ontario healthcare budget

- 2014 policy review:

  Health Quality Ontario Expert Panel on End-of-Life Care

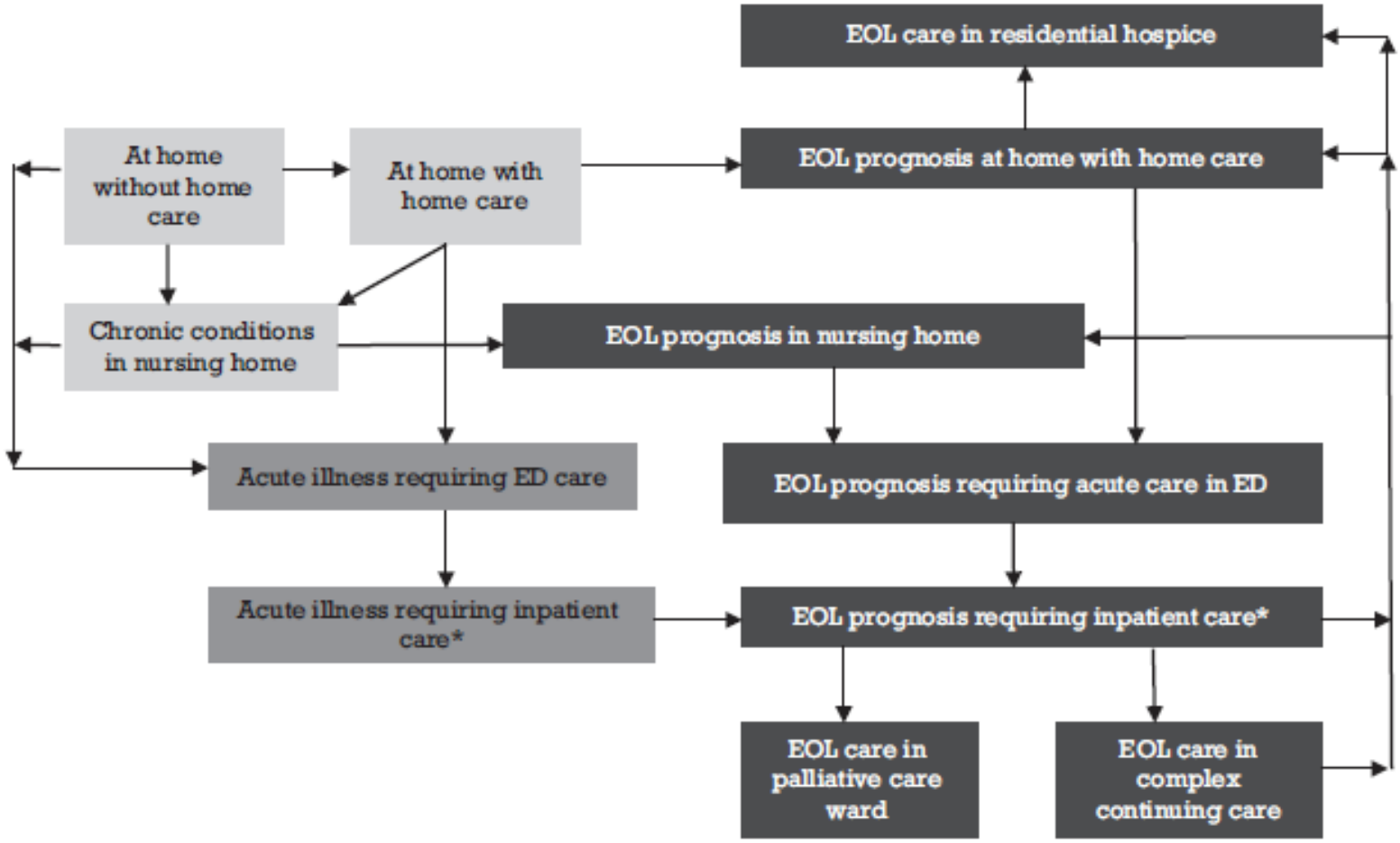
- Research question
  - What is the cost-effectiveness of Home Palliative Care relative to Usual Care for EOL patients in Ontario?

Methods

- Cost-utility analysis

- Perspective
  - Healthcare payer
  - Health sector
  - Societal

- Time horizon: Last year of life
- Costs in $CAD 2014



State transition, microsimulation model

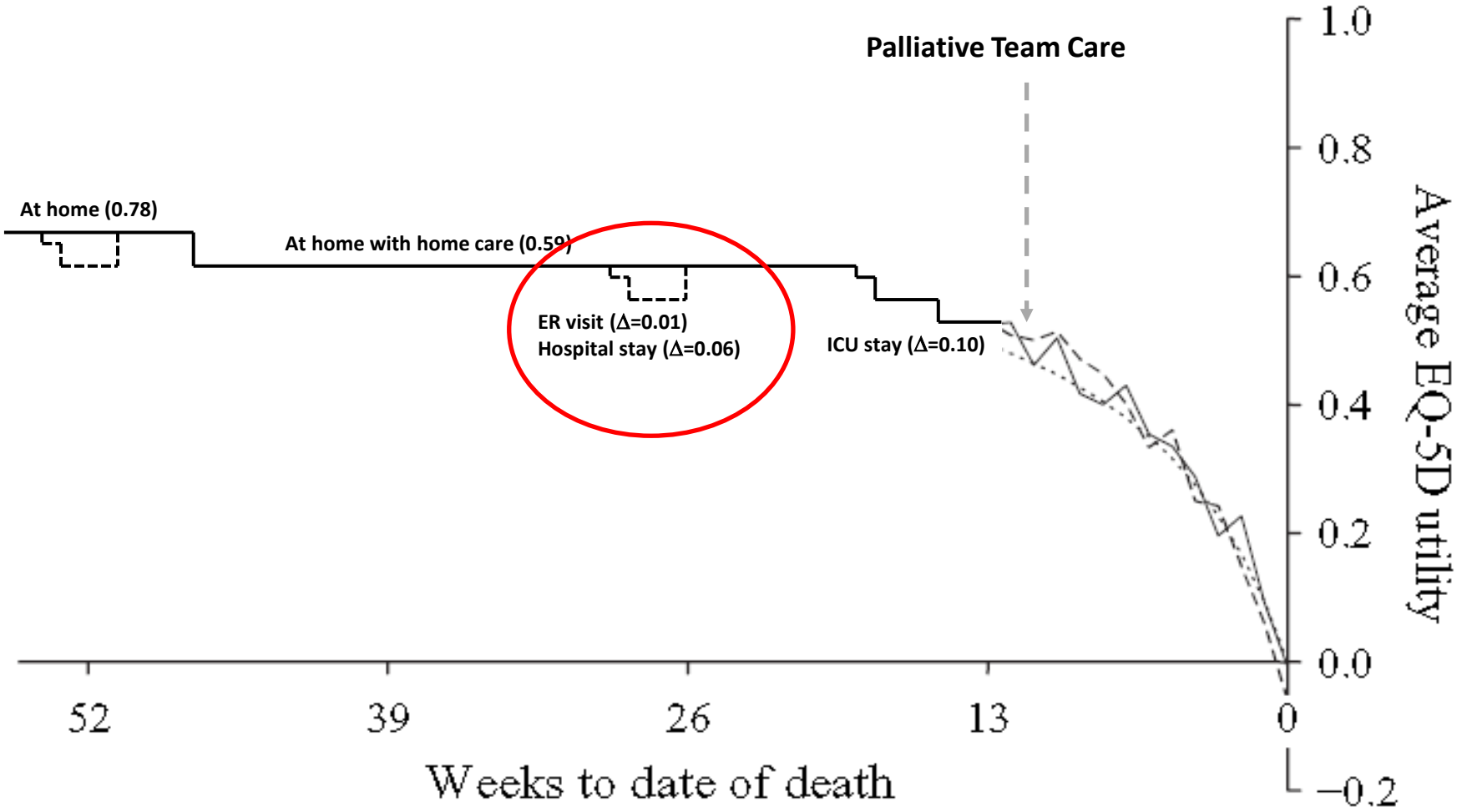
Data sources

- Effectiveness:
  - 6 systematic reviews

- Prognosis:
  - administrative data study 256,284 decedents (2007-09)

- Costs-
  - Intervention ($19/day)
  - Caregiver time ($5000-$20,000/month)
  - Out of pocket costs

Quality of Life - Patients



* Van den Hout et al. 2006

Estimated Spillover Disutility: ~0.1

Results

Perspective	UC Cost♦	UC QALY	HPC+UC Cost♦	HPC+UC QALY	HPC+UC vs UC ΔC	HPC+UC vs UC ΔQALY	ICER	INMB*	Acceptability†
Payer	$49,467	0.5996	$47,192	0.6015	-$2,275	0.0018	Dominant	$2,366/$2,457	0.64 / 0.65
Healthcare sector	$50,006	0.5996	$47,737	0.6015	-$2,269	0.0018	Dominant	$2,360/$2,451	0.64 / 0.65
Societal	$107,405	0.5996	$106,351	0.6015	-$1,054	0.0018	Dominant	$1,145/$1,236	0.59 / 0.60

* Incremental net monetary benefit was calculated at cost-effectiveness threshold of $50k and $100k per QALY, respectively.
† Probability that the HPC+UC strategy is more cost-effective than the UC strategy at thresholds of $50k and $100k per QALY.

Sector	Type of Impact (List category within each sector with unit of measure if relevant)	Included in this analysis from ... perspective?			Notes on Sources of Evidence
		Payer	Health care Sector	Societal	
FORMAL HEALTHCARE SECTOR					
HEALTH	*Health Outcomes (Effects)*				
	Longevity effects, days	✓	✓	✓	See assumptions
	Health-related quality of life effects, QALYs	✓	✓	✓	
	Chance of dying at home, % dying at home	✓	✓	✓	
	Time at home, days at home	✓	✓	✓	
	Spillover effect,† QALYs	✓	✓	✓	
	Quality of death	×	×	×	See Discussion
	Satisfaction of care	×	×	×	See Discussion
	Medical Costs				
	Paid for by third-party payers, $	✓	✓	✓	Covered by (OMHLTC)*
	Paid for by patients out-of-pocket		✓	✓	
	Future related medical costs (payers and patients)	×	×	×	Not applicable to EOL population
	Future unrelated medical costs (payers and patients)	×	×	×	Not applicable
INFORMAL HEALTHCARE SECTOR					
HEALTH	Patient time costs, $			✓	
	Unpaid caregiver time costs, $			✓	
	Transportation costs				

NON-HEALTHCARE SECTORS (with examples of possible items)					
PRODUCTIVITY	Labor market earnings/productivity, $ Cost of lost productivity due to illness and to seeking and receiving care			✓ ✗	See Discussion
CONSUMPTION	None				
SOCIAL SERVICES	Cost of social services as part of HPC‡			✗	See Methods
LEGAL/ CRIMINAL JUSTICE	None				
EDUCATION	None				
HOUSING	None				
ENVIRONMENT	None				
OTHER (Specify)	Cost of non-medical household expenses for the patient, $			✓	

Ethical Issues in CEA– Ch 12

Norman Daniels, PhD

Chan School of Public Health

Background

- When we invest limited resources, we should get more benefits than other alternatives would give– that is why we must examine the opportunity costs of an investment
- CEA is the main tool for examining the opportunity cost of a given investment in the health of a population.
- CEA is about maximizing an objective function The content of that function is what raises ethical concerns. In thoery, the objective function can include distribute concerns In practice, the aggregate impact on health and not the distribution of that health is the focus of the objective function.
- Chapter 12 is divided into ethical issues about constructing CEA and issues about using CEA

Ethical Issues in constructing CEA

- Whose preferences should be used in evaluating health states? Should we value more the experience (ex post) a condition vs ex ante the societal experience?
- Does age matter? Is a QALY a QALY wherever it goes within a life?
- What costs and benefits should count in CEA?

Ethical issues in the use of CEA

- Should priority be give to the sickest or worst off? (the priority problem)
- When should large benefits to a small number of people outweigh small benefits to a large number of people? (the aggregation problem)
- When should best outcomes outweigh fair changes at some benefit? (the fair chances/best outcomes problem)
- Does CEA discriminate against people with disabilities?
- Why not use equity weights in CEA?
- Can we justify using cost/qaly thresholds?