

# The Institute for Clinical and Economic Review (ICER)

Appraisal of IMRT vs. 3D-CRT

# Purpose of the Day

- What is the structure and role of the Evidence Review Group?
  - Independent
  - Constitution
  - Review of Draft Assessment
  - Confirm/comment on ratings of comparative clinical effectiveness and value

# Structure of the Day

- Policy and political background
- Introduction to ICER and purpose of today
- Introduction to IMRT
- Lunch
- Clinical Effectiveness
- Comparative Value
- Tying it all together

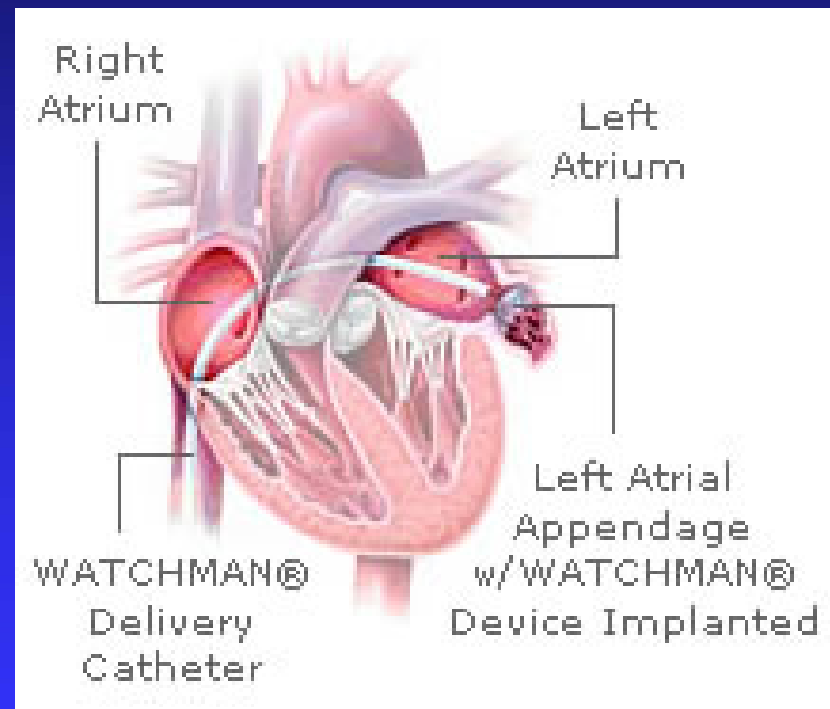
PLEASE HANG UP.

# Pratt's HEALING OINTMENT FOR MAN AND BEAST



**WE BOTH USE IT!**

# Innovation: The Challenges



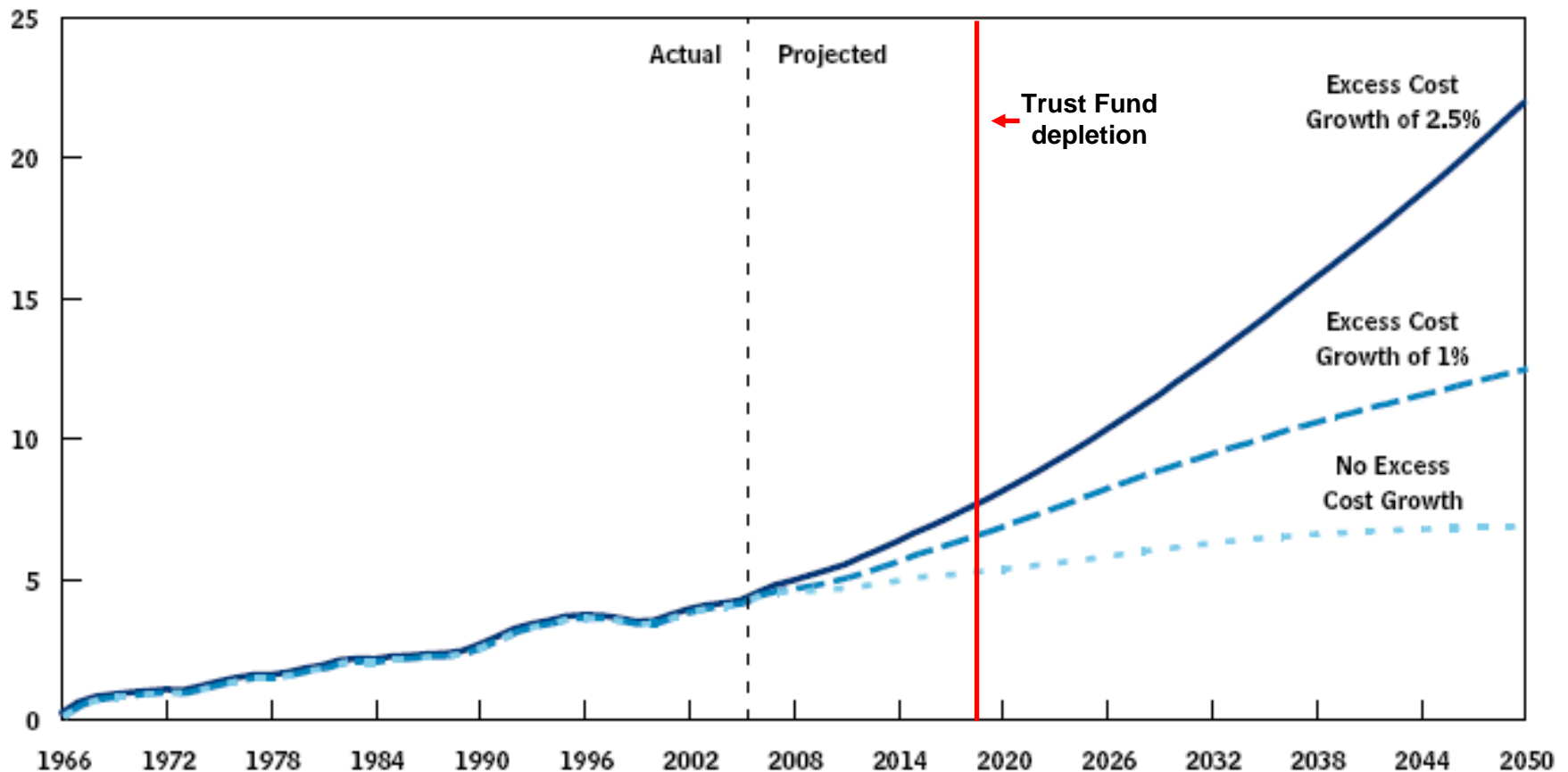
# Health Care Costs

- Today the US spends on health care  
 $\$2,100,000,000,000$
- 16% of GDP, \$1 of every \$7 spent
- If nothing changes, by 2030 health care will consumer \$1 out of every \$3 of GDP

**Figure 1-7.**

## Total Federal Spending for Medicare and Medicaid Under Different Assumptions About Excess Cost Growth, 1966 to 2050

(Percentage of gross domestic product)



Source: Congressional Budget Office.

# US Health Technology Assessment

- Poor coordination
- Weak legitimacy
- Limited usefulness
- Incomplete integration



# Proposed Agency

- A new Comparative Effectiveness Research agency has been proposed in Congress
- The agency would provide information on the relative clinical (and cost) effectiveness of alternative health care interventions
  - Drugs, devices, diagnostics, procedures
- Funding at the level of \$5 billion dollars

# Goals of ICER

- Stimulate broader national policy to integrate value considerations into comparative effectiveness initiatives
- Test new methods for making technology assessments more accessible and actionable
- Integrate assessment of comparative clinical effectiveness with “comparative value”

# ICER

- Blue Shield of California Foundation
- Collaborative academic model
- Pilot appraisals
  - IMRT for localized prostate cancer
  - Virtual colonoscopy
  - Pegfilgrastim

# ICER Appraisal Process

- Topic selection
- Scoping committee
- Technology assessment
  - Clinical effectiveness
  - Comparative value
- Presentation to Evidence Review Group (ERG)
- Final Report with Integrated Evidence Rating

# Integrated Evidence Rating

Comparative Clinical Effectiveness

Superior A

Incremental B

Comparable C

Pot/Unprov P/U

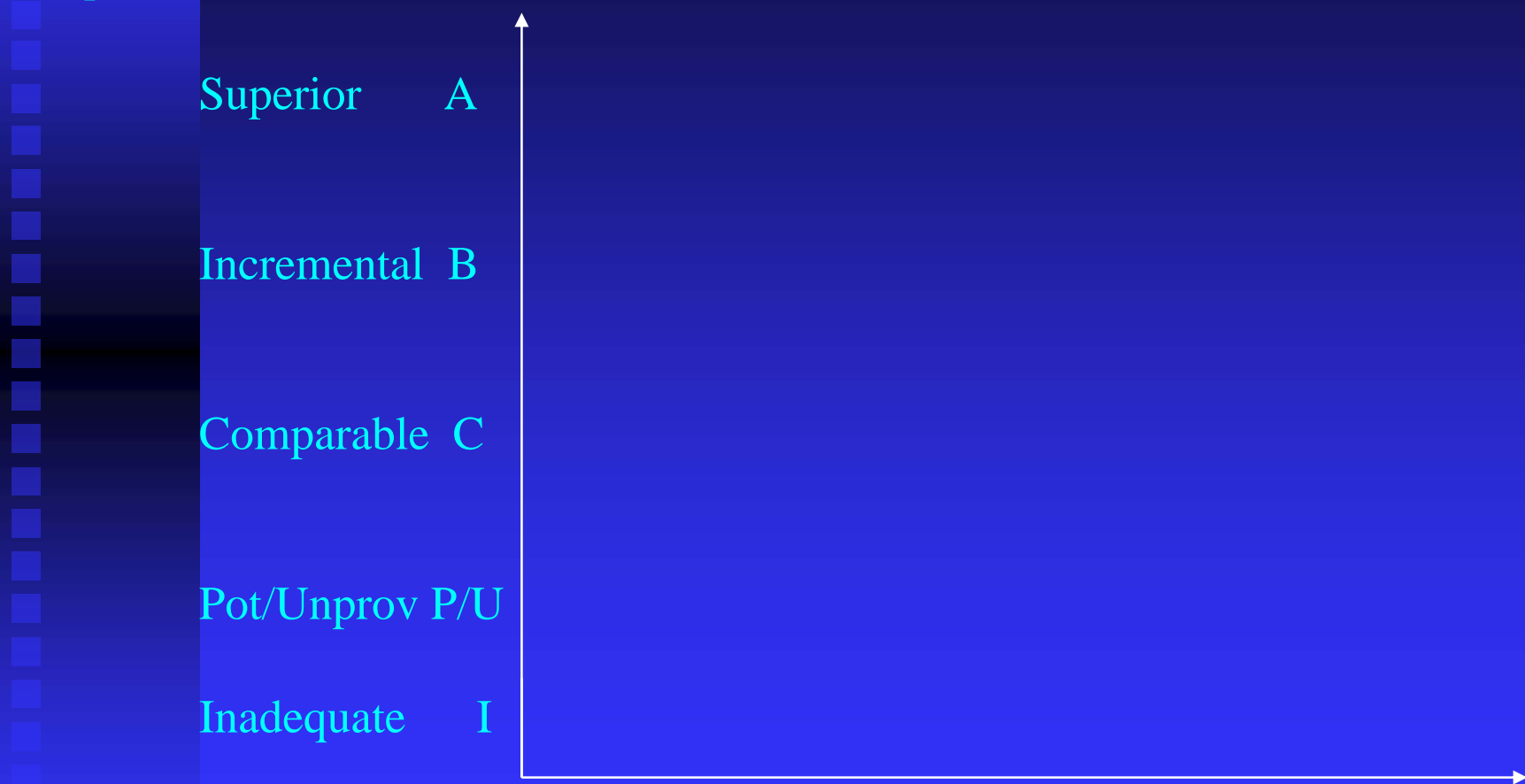
Inadequate I

Comparative Value

a  
High

b  
Reasonable/  
Comparable

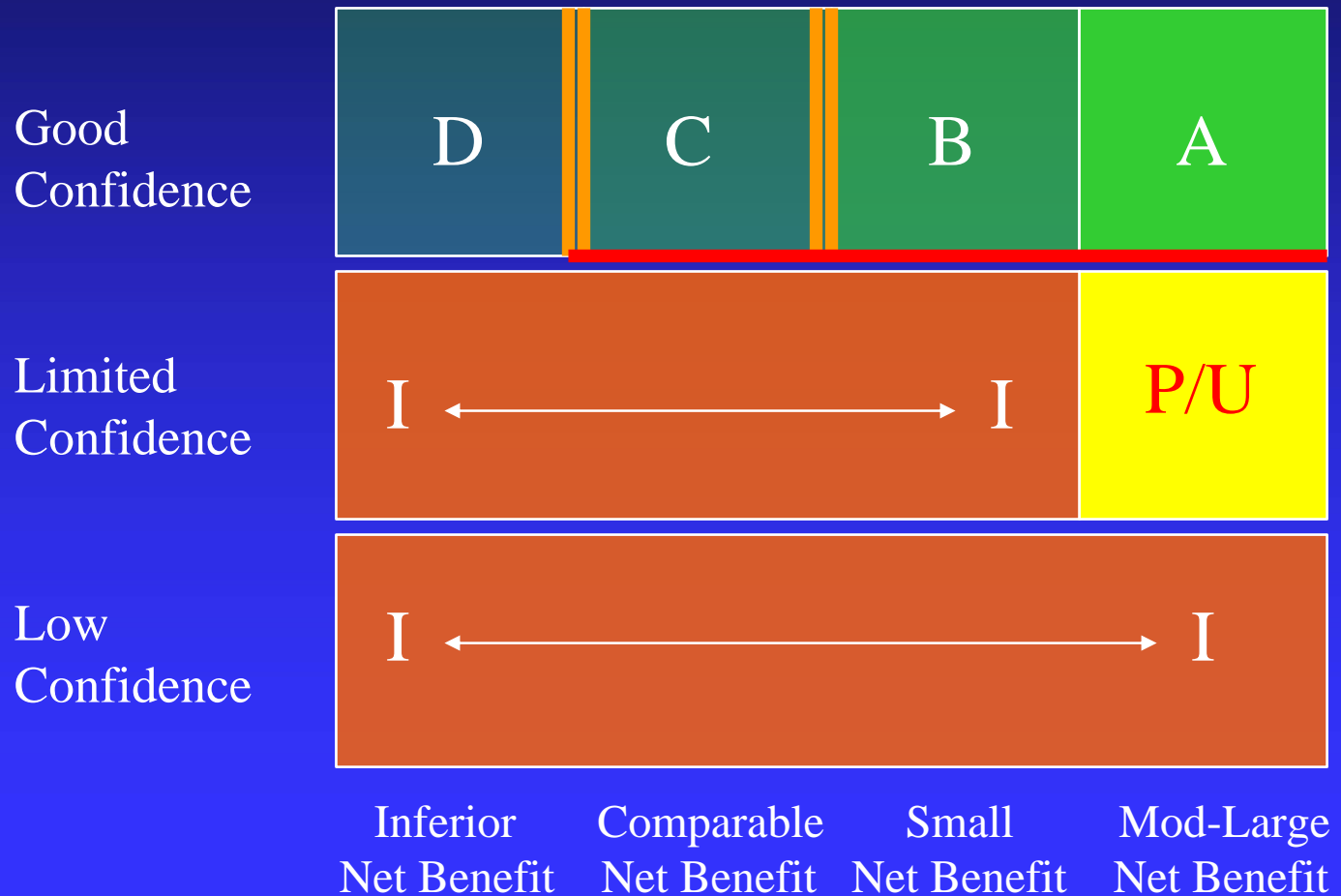
c  
Low



# Comparative Clinical Effectiveness

## Comparative Clinical Effectiveness

Comparing tech \_\_\_ vs. \_\_\_



# Integrated Evidence Rating

Comparative Clinical Effectiveness

Superior A

Incremental B

Comparable C

Pot/Unprov P/U

Inadequate I

Comparative Value

a  
High

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c  
Low



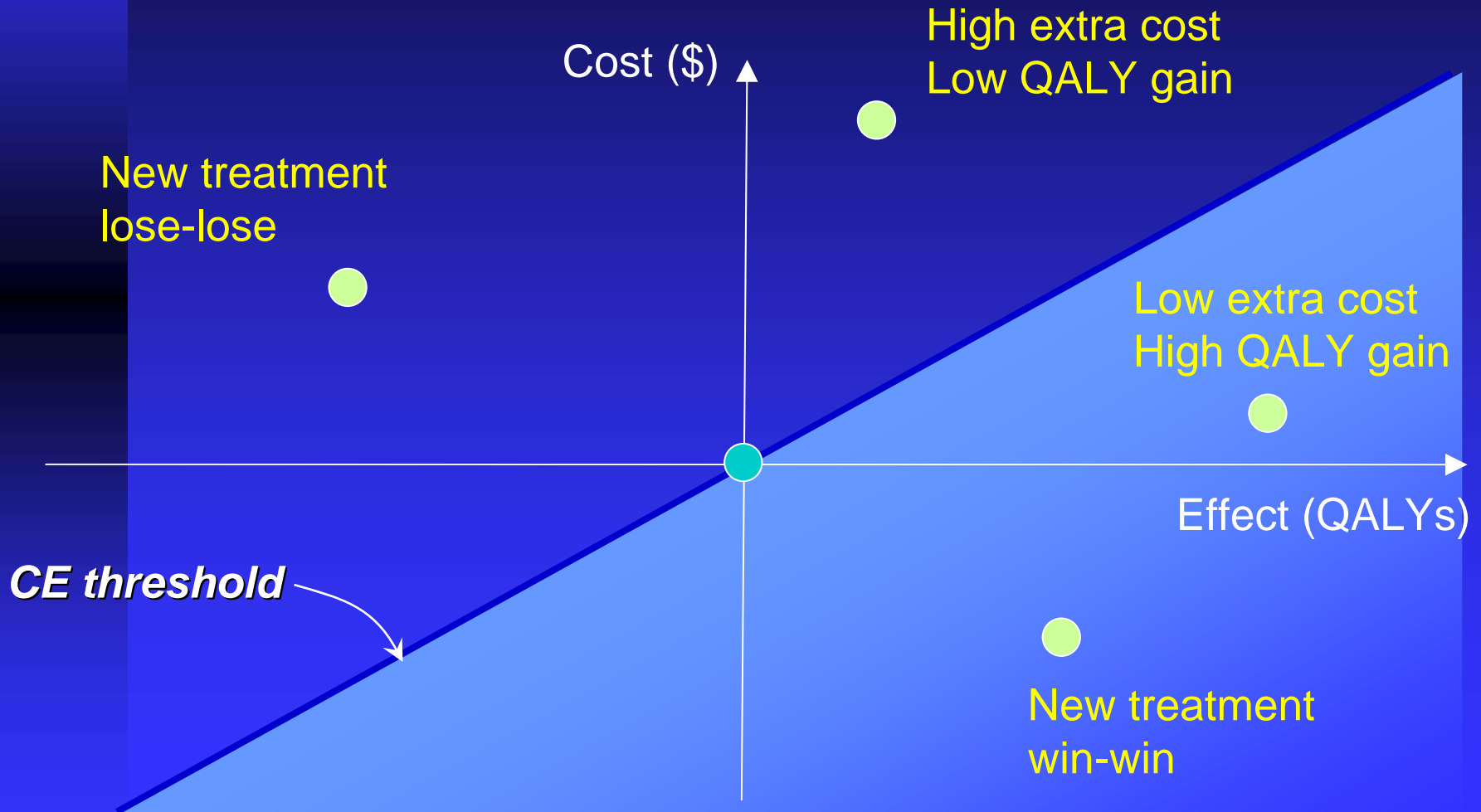
# Economic Evaluation

“... the comparative analysis of alternative courses of action in terms of both their costs and consequences.”

Drummond, Stoddart & Torrance, 1987



# Weighing up costs and effects



# Comparative Value Rating



Other considerations:

- Cost per key outcome(s)
- Relative cost to similar treatments/situations

# Integrated Evidence Rating

Comparative Clinical Effectiveness

Superior	A	Aa	Ab	Ac
Incremental	B	Ba	Bb	Bc
Comparable	C	Ca	Cb	Cc
Pot/Unprov P/U		Pa	Pb	Pc
Inadequate	I	I	I	I

Comparative Value

a  
High

b  
Reasonable/  
Comparable

c  
Low

# Applications of ICER ratings

- Coverage decisions
- Value-based insurance design
- Reimbursement platforms
- Physician compensation
- Patient-clinician decision support tools

# Purpose of the Day

- Review of Draft Assessment
- Comment on ratings of comparative clinical effectiveness and value
- NOT an NIH consensus committee
- NOT to make coverage recommendations
- Help us improve the ICER process

# Appraisal of IMRT vs. 3D-CRT

# Appraisal of IMRT

## ■ Scope

- Patient population(s)
- Comparator(s)
- Key questions
  - ◆ Differences in disease-free and overall survival
  - ◆ Differences in side effects → quality of life
  - ◆ Patient characteristics that most influence clinical and cost-effectiveness of IMRT

# Background

- Localized prostate cancer
  - Classification
  - Treatment options
  - Importance of side effects



# IMRT and 3D-CRT

- Origins
- Potential advantages of IMRT
  - Decrease in toxicity
  - Ability to deliver “ultra high” doses  $>81$  with acceptably low toxicity
- Potential disadvantages of IMRT
  - “Cold spots” within the field
  - Increased risk of secondary malignancy
  - Inadequate quality assurance of methods of delivery

# Clinical Guidelines

- NCCN
  - Low risk → 70-75 Gy
  - Intermediate risk → 75-80 Gy
- NCI
- ASTRO
  - IMRT is “preferred method” for Rx

# Ongoing Research

- Dose escalation with IMRT and/or 3D-CRT
- Hypofractionation
- No randomized trials in US of 3D-CRT vs. IMRT
- Canadian phase III RTC begun 2005, completed in 2014

# Coverage, Reimbursement, Use

- Medicare
- Private insurers
- Reimbursement: 4 x 3D-CRT = IMRT
- 2002-2004: 32%-73% penetration
  - 61% academic and 93% community clinicians using for GU cancer
  - 91% of non-users planned to adopt in near future

# The Evidence

- Previous tech assessments
  - AHRQ, 2007
  - CTAF, 2005-2006
  - NCCHTA, 2003
  - TEC, NICE, CADTH: no review
- Systematic literature review
  - 62 IMRT articles
  - 283 3D-CRT articles

# Key Findings

- Disease-free survival
  - Benefits to escalation to 75-81 Gy
  - No data yet on >81 Gy vs. 75-81 Gy
- Potential harms
  - No data on secondary malignancy
- Differential risk of toxicity

<b>3D-CRT</b>	<i>Late GI toxicity <math>\geq 2</math></i>	<i>Late GU toxicity <math>\geq 2</math></i>	<i>Impotence</i>
75-80 Gy	21% (Michalski, 2005) 19% (Shippy, 2007) 16% (Zelefsky, 1999) 16% (Skwarchuk, 2000) 14% (Zelefsky, 2001) 13% (Schultheiss, 1997) 12% (Jani, 2007) 11% (Peeters, 2005) 10% (Zelefsky, 2000) 10% (Kirichenko, 2007) 0% (D'Amico, 2006)	23% (Jani, 2007) 13% (Zelefsky, 2001) 13% (Shippy, 2007) 8% (Kirichenko, 2007)	39% (NCCHTA, 2003) 28% (D'Amico, 2004)
<b>IMRT</b>	<i>Late GI toxicity <math>\geq 2</math></i>	<i>Late GU toxicity <math>\geq 2</math></i>	<i>Impotence</i>
75-81 Gy	6% (Kirichenko, 2007) 6% (Jani, 2007) 4% (Zelefsky, 2002) 3% (Shippy, 2007) 2% (Zelefsky, 2006)	23% (Jani, 2007) 19% (Shippy, 2007) 15% (Zelefsky, 2002) 6% (Kirichenko, 2007)	49% (Zelefsky, 2006) 48% (Zelefsky, 2002)

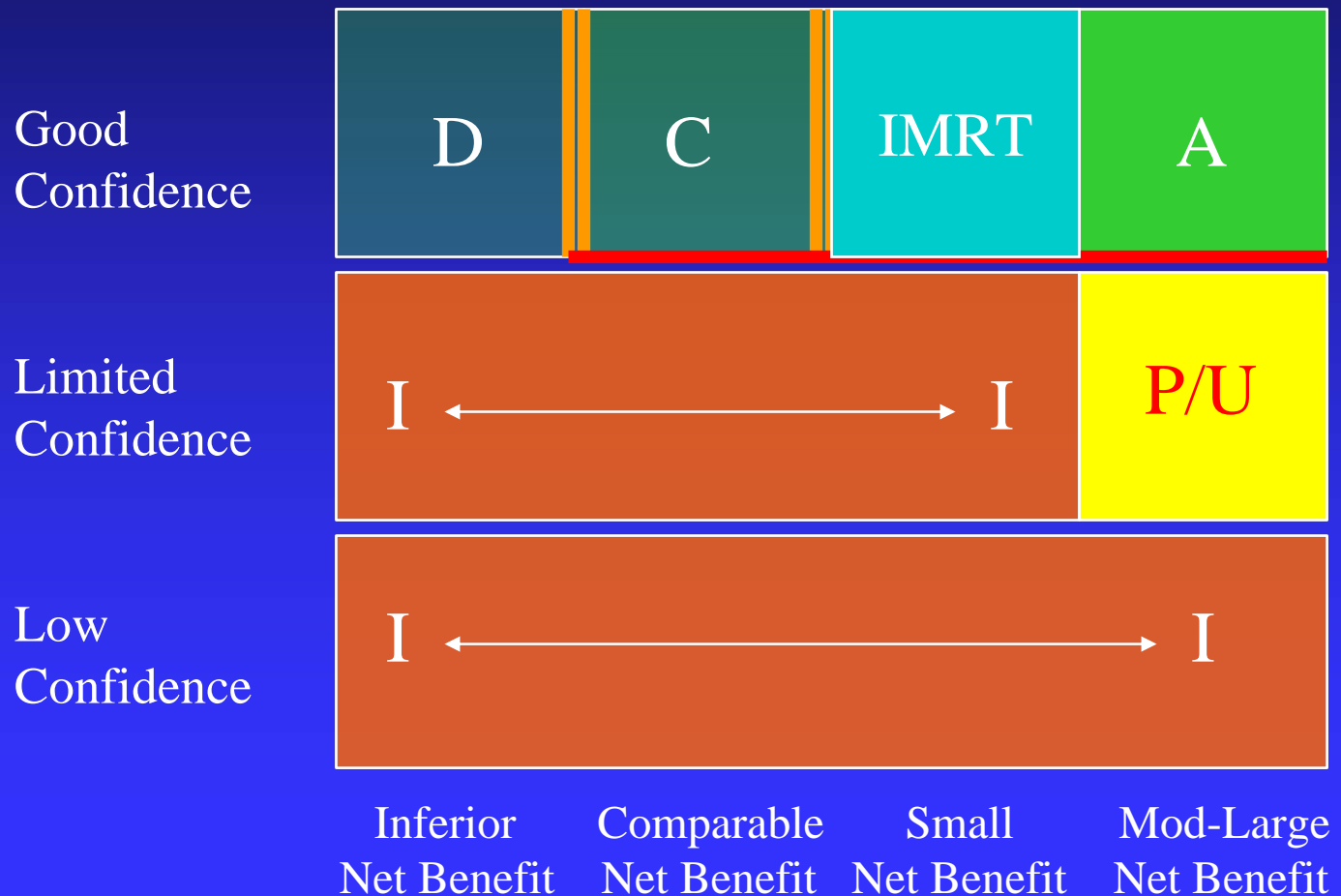
# GI toxicity: proctitis

- 14% for 3D-CRT and 4% for IMRT
- Treat 100 patients with IMRT will have 10 fewer cases of proctitis
- NNT = 10 patients



# Comparative Clinical Effectiveness

## IMRT vs. 3D-CRT for Rx 75-80 Gy



# Draft Integrated Evidence Rating

# Key Findings

- Cost per case of proctitis avoided = \$313,000
- Cost per QALY = \$706,000
- If risk of proctitis =
  - 25%, cost/QALY = \$400,000
  - 75%, cost/QALY = \$130,000
- Threshold analysis for cost of IMRT
  - Cost/QALY = \$100,000 → \$16,900
  - Cost/QALY = \$150,000 → \$19,100

# Integrated Evidence Rating

## IMRT vs. 3D-CRT Rx 75-80 Gy

Comparative Clinical Effectiveness

Superior	A	Aa	Ab	Ac
Incremental	B	Ba	Bb	IMRT
Comparable	C	C	C	C
Pot/Unprov P/U		Pa	Pb	Pc
Inadequate	I	I	I	I

Comparative Value

a  
High

b  
Reasonable/  
Comparable

c  
Low

# Potential Application of ICER Ratings to Medical Policy

# Radiation for low-risk prostate CA

Comparative Clinical Effectiveness

Superior	A	Aa	Ab	Ac
Incremental	B	Brachytherapy	Bb	IMRT
Comparable	C	C	C	C
Pot/Unprov P/U	P/U	Hypofract Rx	Pb	Pc
Inadequate	I	Proton Beam Therapy		

Comparative Value

a	b	c
High	Reasonable/ Comparable	Low

# From Tech Assessment to Medical Policy

Brachytherapy  
Ba

No prior auth  
0% co-pay  
Premium price

Prior auth  
20% co-pay  
Lower reimbursed price

Hypofract Rx  
Pa

Proton Beam  
I

Prior auth/CED

Non-covered

# Outstanding elements

- Budget impact
- Ethical considerations
- Research considerations



# ERG Feedback

- ICER format: useful?
- What information would you have liked?
  - Draft ratings before the meeting?
- What information did you not find useful?
- Process: a vote, consensus, or some blend for rating determination?
- Best role for patients, clinical experts, and manufacturers?
- Other?

# Conclusion and Next Steps

- IMRT vs. 3D-CRT
  - Potential for technology assessment with integrated assessment of comparative value to support innovative medical policy
- Next steps
  - Pegfilgrastim, virtual colonoscopy
  - Complete appraisals of the “family” of EBRT
  - Establish sustainable funding and strategic models

Thank you!

# **IMRT Appraisal**

**Economic Model of Side Effects**

**Evidence Review Group**

**June 11, 2007**

# ICER Appraisal Process: Economic Review

- Key economic questions from scoping committee
- Identify existing economic model
- Contract with developers of existing model or create model to run scenarios that reflect key questions
- Technical review of model: Model Review Group
- Presentation of results to Evidence Review Group
- Final Report

# IMRT

- Key Questions from Scoping Committee:  
reduced side effects
- No existing model that specifically modeled individual side effects
- Commissioned development of simple economic model focusing on side effects
- Technical review
- Evidence review group – clinical and economic evidence
- Recommendations

# Overview of Presentation

- Model structure and key assumptions
- Data inputs
  - Transition probabilities
  - Costs
  - Quality adjustments
- Results
- Summary of feedback from Model Review Group

# IMRT Economic Model: Key Assumptions (i)

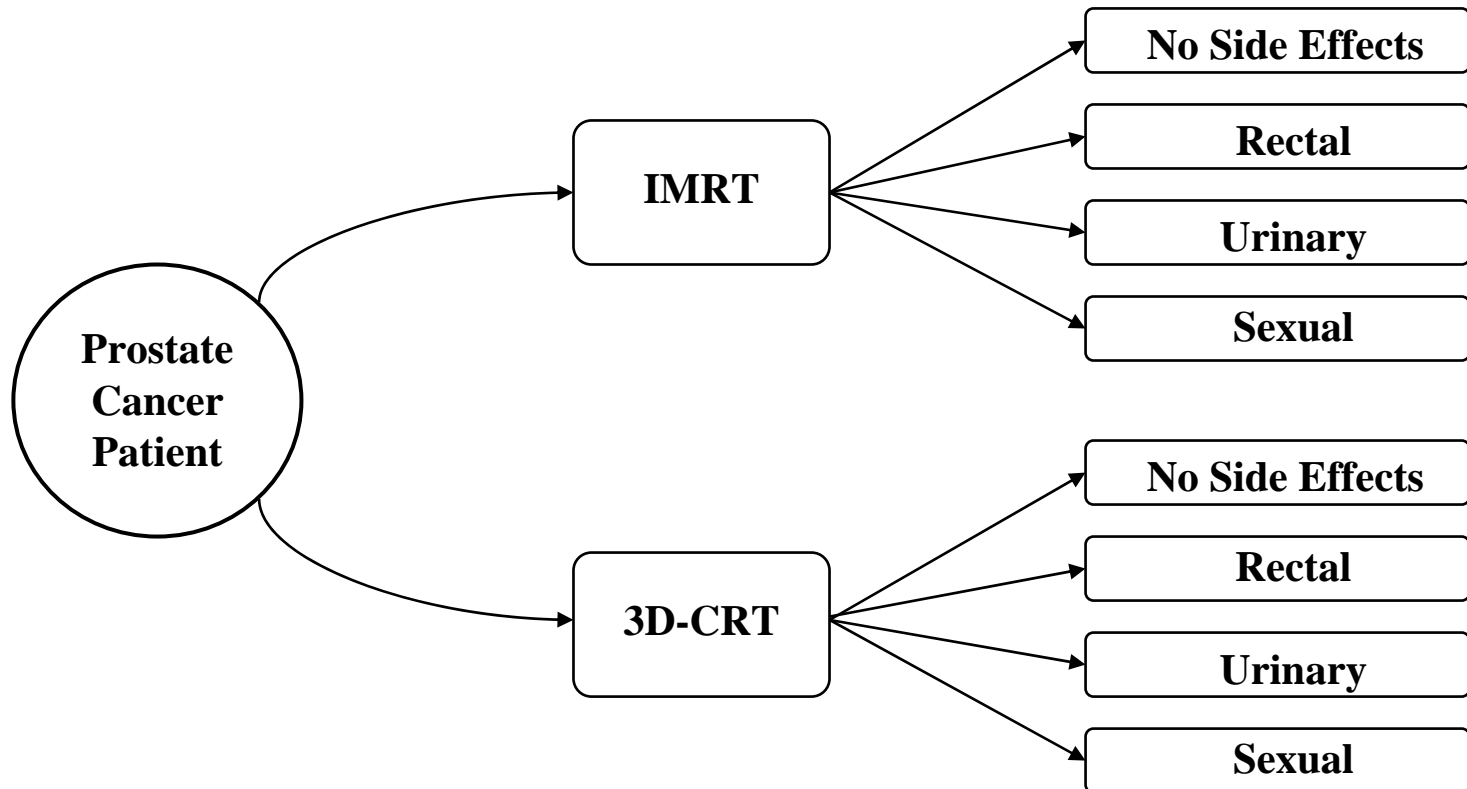
- Cost-effectiveness analysis of IMRT compared with 3D-CRT
- Treatment dose of 75 to 81 Gy for both therapies
- Limited to incidence of treatment-related adverse effects (long-term survival does not differ between treatments)



# IMRT Economic Model: Key Assumptions (ii)

- Target population: 69 year old men with clinically localized prostate cancer and low/intermediate recurrence risk
- Payer perspective
  - Did not consider opportunity cost of time, etc.
- Time horizon – lifetime

# IMRT Economic Model\*



\*Model also allows for the occurrence of multiple side effects in a single patient 7

# IMRT Economic Model: Data inputs

- Data from primary and secondary sources
  - Probabilities: Literature review, expert opinion
  - Utilities: Primary data
  - Costs: Literature review, cost interviews
- Direct medical costs of treating toxicities include costs of:
  - physician visits
  - diagnostic tests
  - procedures
  - prescription medications

# Model Inputs: Probabilities

	IMRT	3D-CRT	Time to onset (mo)	Time to resolution (mo)
Rectal	0.04 <sup>1</sup>	0.14 <sup>2</sup>	12 <sup>3</sup>	12 <sup>3</sup>
Urinary	0.15 <sup>1</sup>	0.15 <sup>2,4</sup>	12 <sup>3</sup>	12 <sup>3</sup>
Sexual	0.50 <sup>4</sup>	0.50 <sup>4</sup>	12 <sup>3</sup>	Lifetime

<sup>1</sup>Zelevsky 2002 (772 patients)

<sup>2</sup>Zelevsky 2001 (810 patients)

<sup>3</sup>Zelevsky 1999 (743 patients)

<sup>4</sup>Clinician-expert guidance secondary to limited data

# Clinical Vignette for Patients with GI Toxicity\*

- Treatment with 6 month course of anti-inflammatory enemas
- Effective in controlling bleeding in 70% of patients
- Remainder undergo an average of three sigmoidoscopy procedures with ablation, followed by an additional 6 month course of enemas

# Model Inputs: Costs and Quality of Life

	Cost per case	Utility weight <sup>2,3</sup> (0 to 1 scale)
IMRT	\$42,450 <sup>1</sup>	-
3D-CRT	\$10,900 <sup>1</sup>	-
Rectal	\$2,346	0.612
Urinary	\$954	0.685
Sexual	\$2,113	0.729

<sup>1</sup>Konski 2006, CPT codes

<sup>2</sup>Personal communication with Dr. Basu, Univ. of Chicago (207 patients, time trade-off method)

<sup>3</sup>Used to estimate quality-adjusted life-years (QALYs)

# Results (i)

- Base case
  - Cost per case averted =

# Results (i)

- Base case
  - Cost per case averted = \$313,000



# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio =

# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio = \$706,000/QALY

# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio = \$706,000/QALY
  
- Sensitivity analysis
  - C/E Ratio = \$150K/QALY → IMRT cost =

# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio = \$706,000/QALY
  
- Sensitivity analysis
  - C/E Ratio = \$150K/QALY → IMRT cost = \$19,100

# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio = \$706,000/QALY
  
- Sensitivity analysis
  - C/E Ratio = \$150K/QALY → IMRT cost = \$19,100
  - C/E Ratio = \$100K/QALY → IMRT cost =

# Results (i)

- Base case
  - Cost per case averted = \$313,000
  - Incremental C/E Ratio = \$706,000/QALY
  
- Sensitivity analysis
  - C/E Ratio = \$150K/QALY → IMRT cost = \$19,100
  - C/E Ratio = \$100K/QALY → IMRT cost = \$16,900

# Results (ii)

Risk of Rectal Toxicity (IMRT)	Risk of Rectal Toxicity (3D-CRT)	Cost-effectiveness
7%	25%	\$400,000/QALY
14%	50%	\$198,000/QALY
21%	75%	\$130,000/QALY