theta

Toronto Health Economics and
Technology Assessment Collaborative

Cost-Effectiveness of Epidermal Growth Factor Receptor Gene Mutation Testing for Patients with Advanced Non-Small Cell Lung Cancer

Wendong Chen MD, PhD[1]; Peter Ellis MD, PhD[2];
Leslie Levin MD[3]; Murray Krahn MD, MSc[1]

1. THETA, University of Toronto
2. Department of Medicine, McMaster University
3. Medical Advisory Secretariat, MOHLTC

www.theta.utoronto.ca

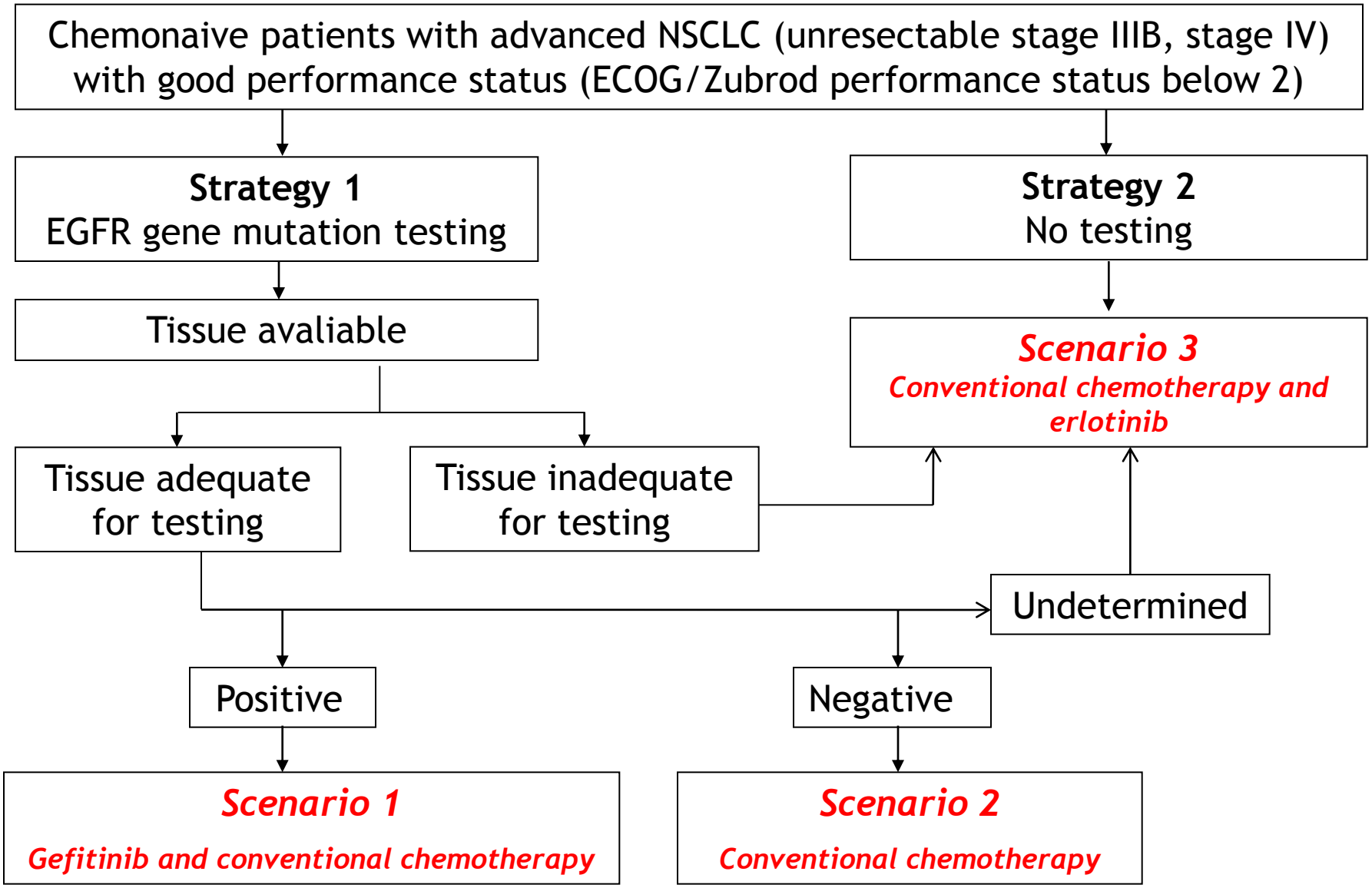
Background

- Systemic cytotoxic treatment for advanced NSCLC has reached a plateau
- New approaches for NSCLC: targeting EGFR pathway
  - Monoclonal antibody
  - EGFR tyrosin kinase inhibitors (TKI): erlotinib and gefitinib
- Biomarkers to predict the response of TKI
  - EGFR gene mutation on exons 18-21
  - High EGFR gene copy number
  - EGFR over expression
  - K-ras mutation

Objective

- To conduct a cost-effectiveness analysis to assess the benefits and costs for using EGFR gene mutation testing to guide the selection of ***gefitinib*** as ***first-line*** therapy in patients with advanced NSCLC under the perspective of MOHLTC

Framework


Chemonaive patients with advanced NSCLC (unresectable stage IIIB, stage IV) with good performance status (ECOG/Zubrod performance status below 2)
Strategy 1
EGFR gene mutation testing
Strategy 2
No testing
Tissue avaliable
Scenario 3
Conventional chemotherapy and erlotinib
Tissue adequate for testing
Tissue inadequate for testing
Undetermined
Positive
Negative
Scenario 1
Gefitinib and conventional chemotherapy
Scenario 2
Conventional chemotherapy

Descriptions of Scenarios

Scenario 1

Gefitinib and conventional chemotherapy

Gefitinib as first-line

↓

Cisplatin and gemcitabine as second-line

↓

Docetaxel or pemetrexed as third-line

↓

Best supportive care

Scenario 2

Conventional chemotherapy

Cisplatin and gemcitabine as first-line

↓

Docetaxel or pemetrexed as second-line

↓

Best supportive care

Scenario 3

Conventional chemotherapy and erlotinib

Cisplatin and gemcitabine as first-line

↓

Docetaxel or pemetrexed as second-line

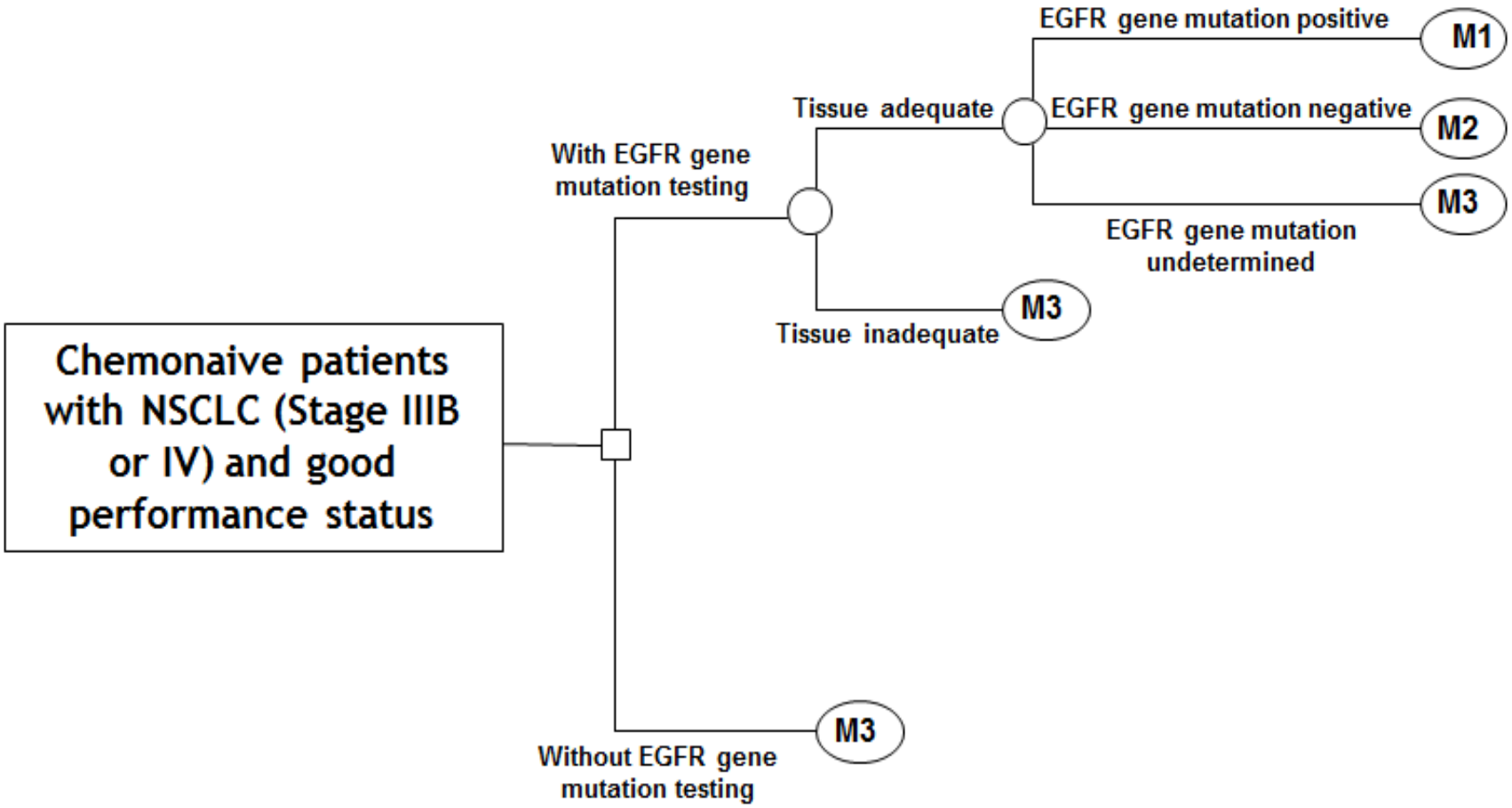
↓

Erlotinib as third-line

↓

Best supportive care

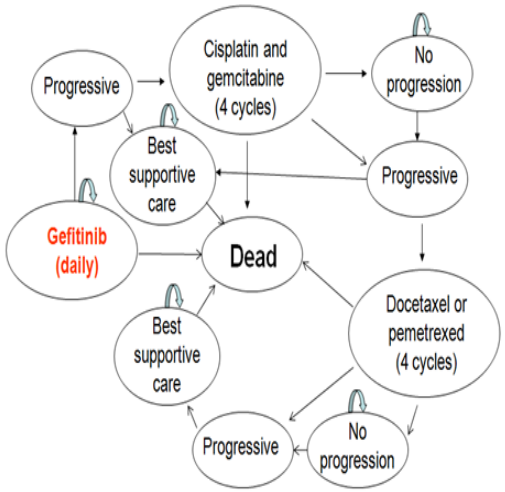
Decision Analytical Model



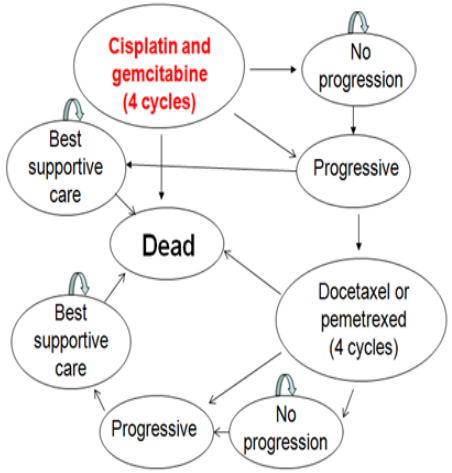
M1: Scenario 1; M2: Scenario 2; M3: Scenario 3

Markov Models for Scenarios

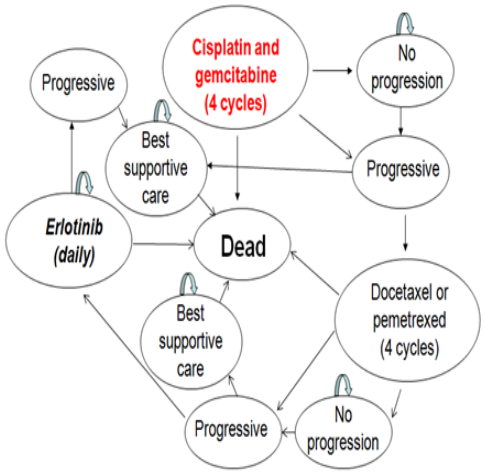
Markov Model for *Scenario 1*



Markov Model for *Scenario 2*



Markov Model for *Scenario 3*



www.theta.utoronto.ca

Model Parameters

- **Time horizon**: lifetime
- **Cycle length**: 3 weeks
- **Perspective**: Ontario Ministry of Health and Long-Term Care
- **Benefits**:
  - Life years
  - Quality adjusted life years (QALY)
- **Costs**: Direct medical costs (2010 CAN$)
- **Discount rate**: 5% per annum for benefits and costs

Data Sources

- **Probability**
  - Distribution of NSCLC: squamous vs. non-squamous
  - Prevalence of EGFR gene mutation
  - Failure rate of EGFR gene mutation testing
  - Efficacy of treatments
- **Utility**
  - Under treatment
  - Post-treatment
  - Best supportive care
- **Cost**
  - EGFR gene mutation testing
  - Drugs
  - Care for treatments
  - Best supportive care

Types of NSCLC
squamous vs. non-squamous

- **Data source**: Canadian Cancer Registry 1992-2007
- **Total cases of squamous type**: 63,199
- **Total cases of NSCLC**: 274,013
- **Proportion of squamous type**:
  - 23.1%, 95% CI: 22.9% to 23.2%

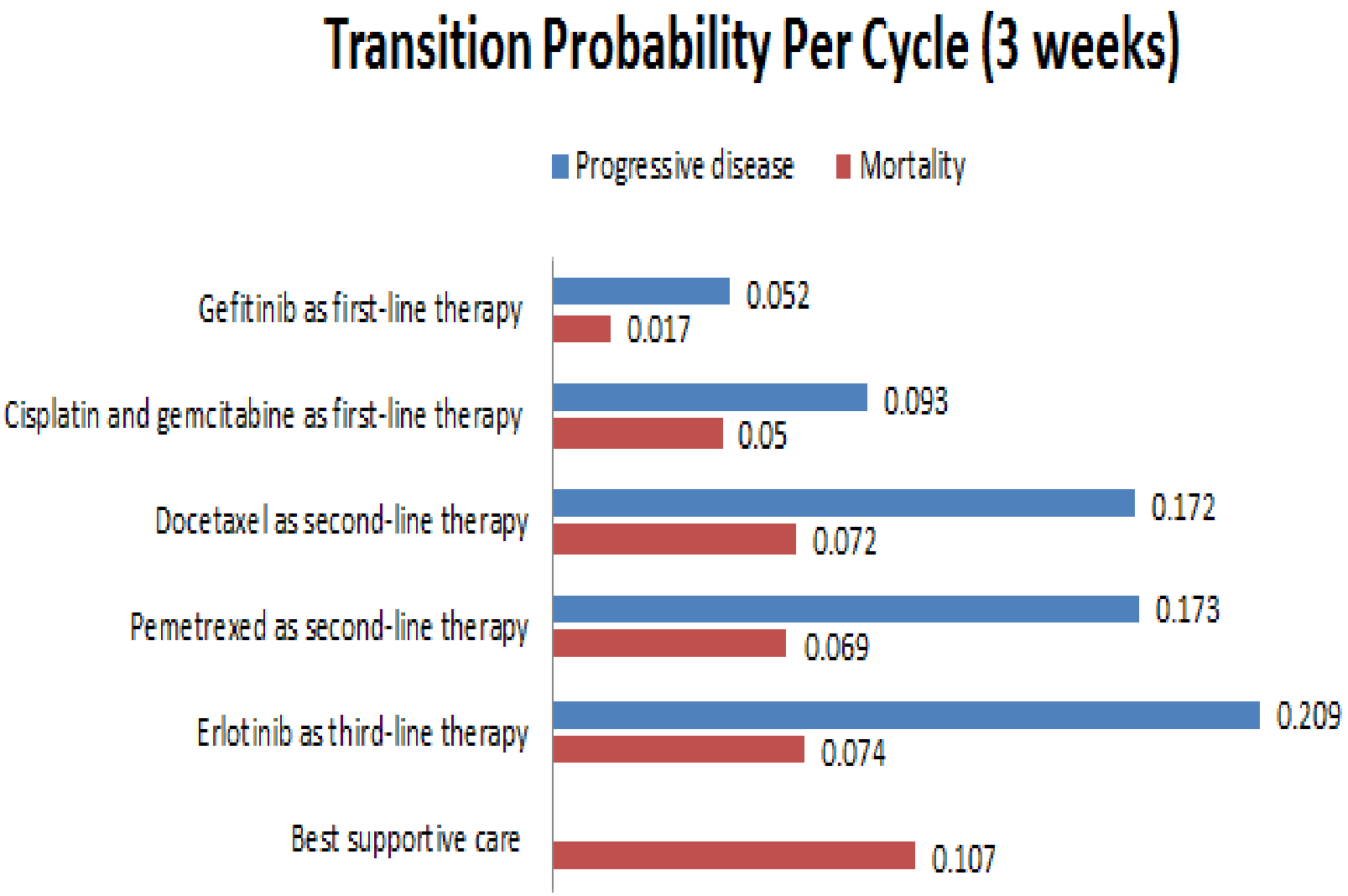
EGFR Mutation Prevalence

- **Data bases**: MEDLINE and EMBASE
- **Search strategy**: Any population based studies screening EGFR gene mutation among patients with NSCLC
- **Search result**: 1 study (Rosell 2009)
- **Prevalence**: 16.6%, 95% CI: 15.0% to 18.2%

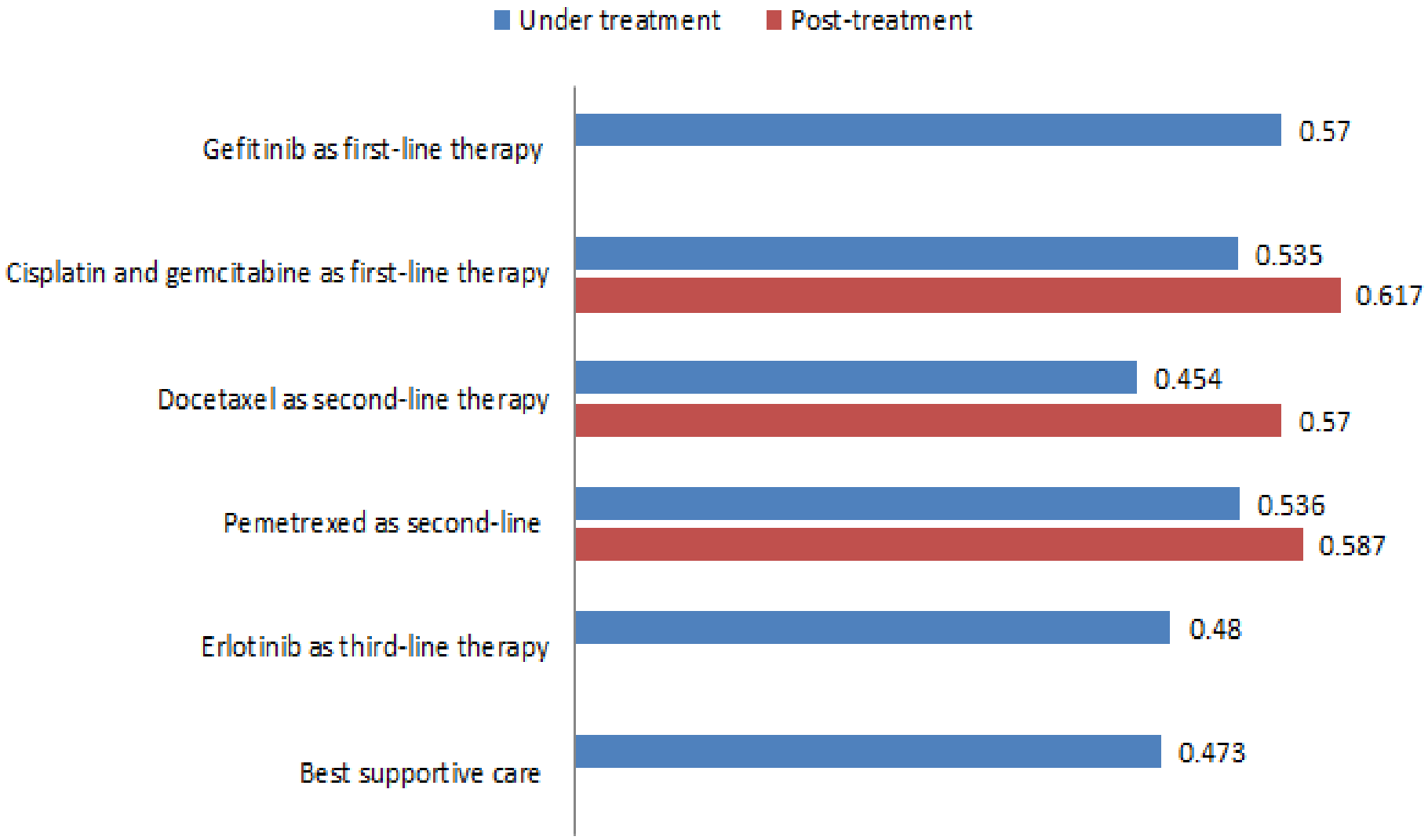
EGFR Mutation Testing

- **Mutation site**: exon 19 and 21 of EGFR gene
- **Data source**: Tsao 2005
- **Failure due to inadequate tissues**
  - 32.3%, 95% CI: 27.1% to 37.5%
- **Failure due to other reasons**
  - 1.8%, 95% CI: 0% to 3.9%

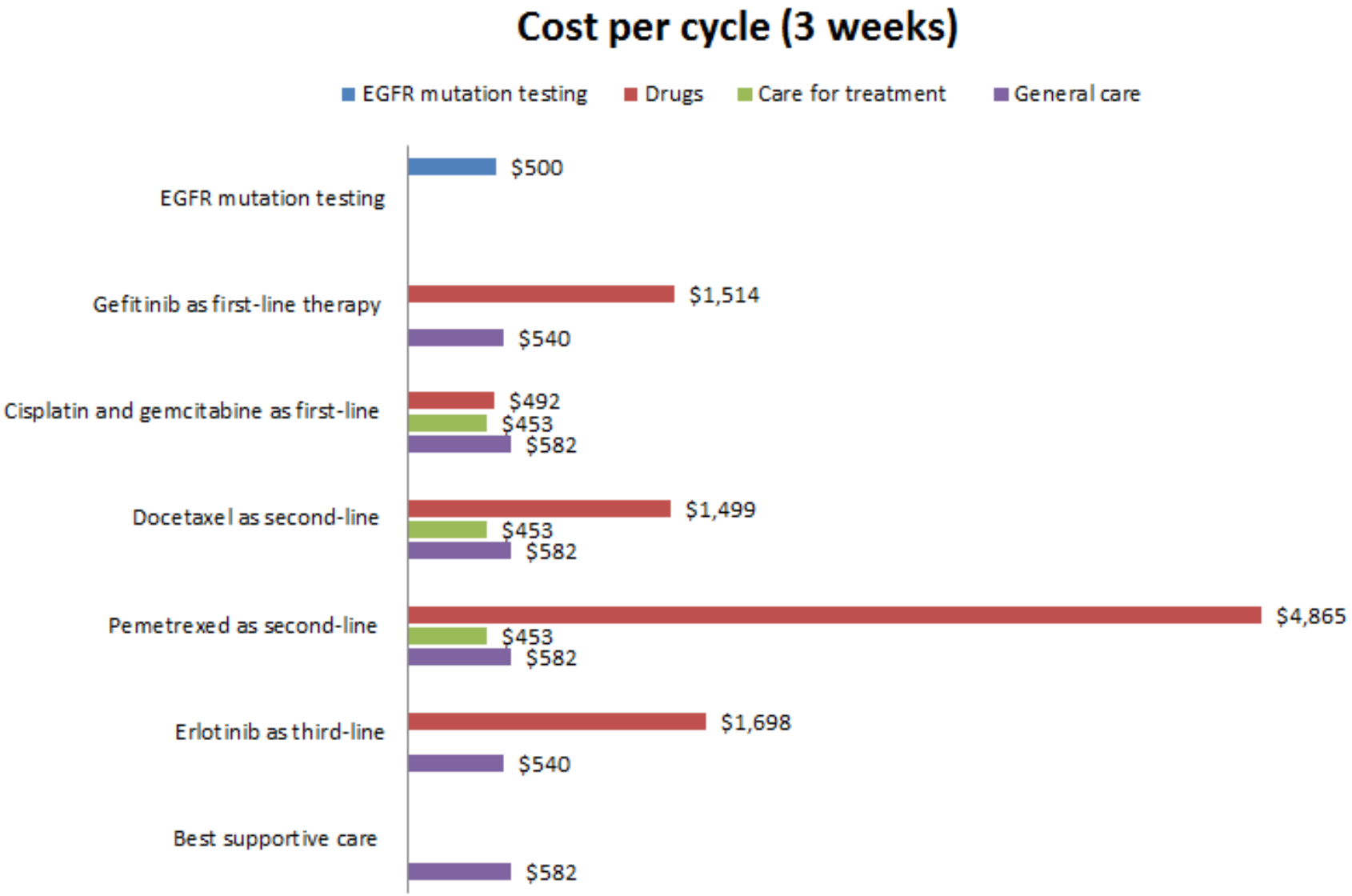
Efficacy of Treatments



Utility Estimation



Direct Medical Costs



Base Case Analysis

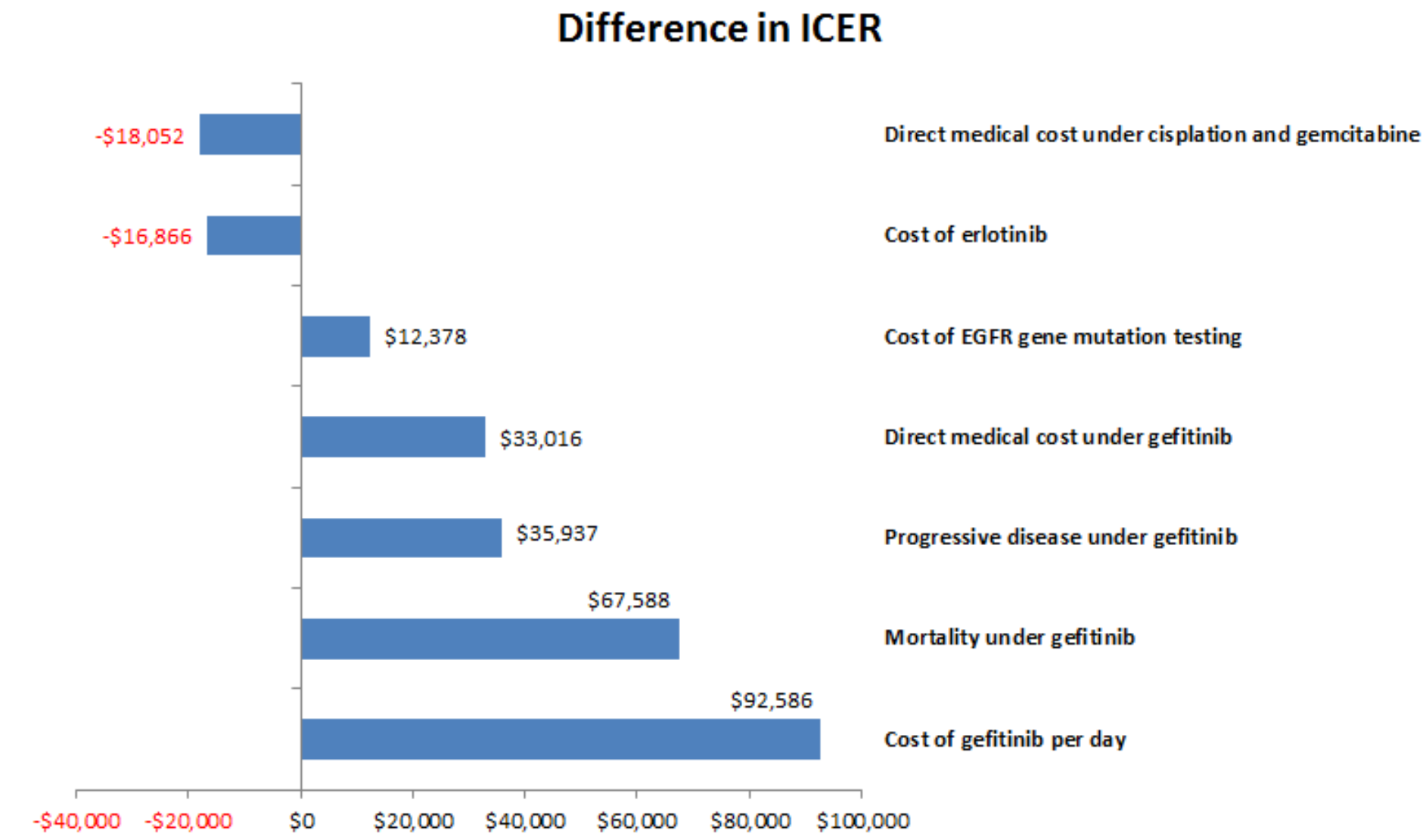
1. Cost-utility analysis

Strategy	Cost	Incr Cost	QALY	Incr QALY	C/E	ICER
No testing	$14,368		0.2881		$49,864	
EGFR mutation testing	$16,857	$2,488	0.3188	0.0307	$52,869	**$81,071**

2. Cost-effectiveness analysis

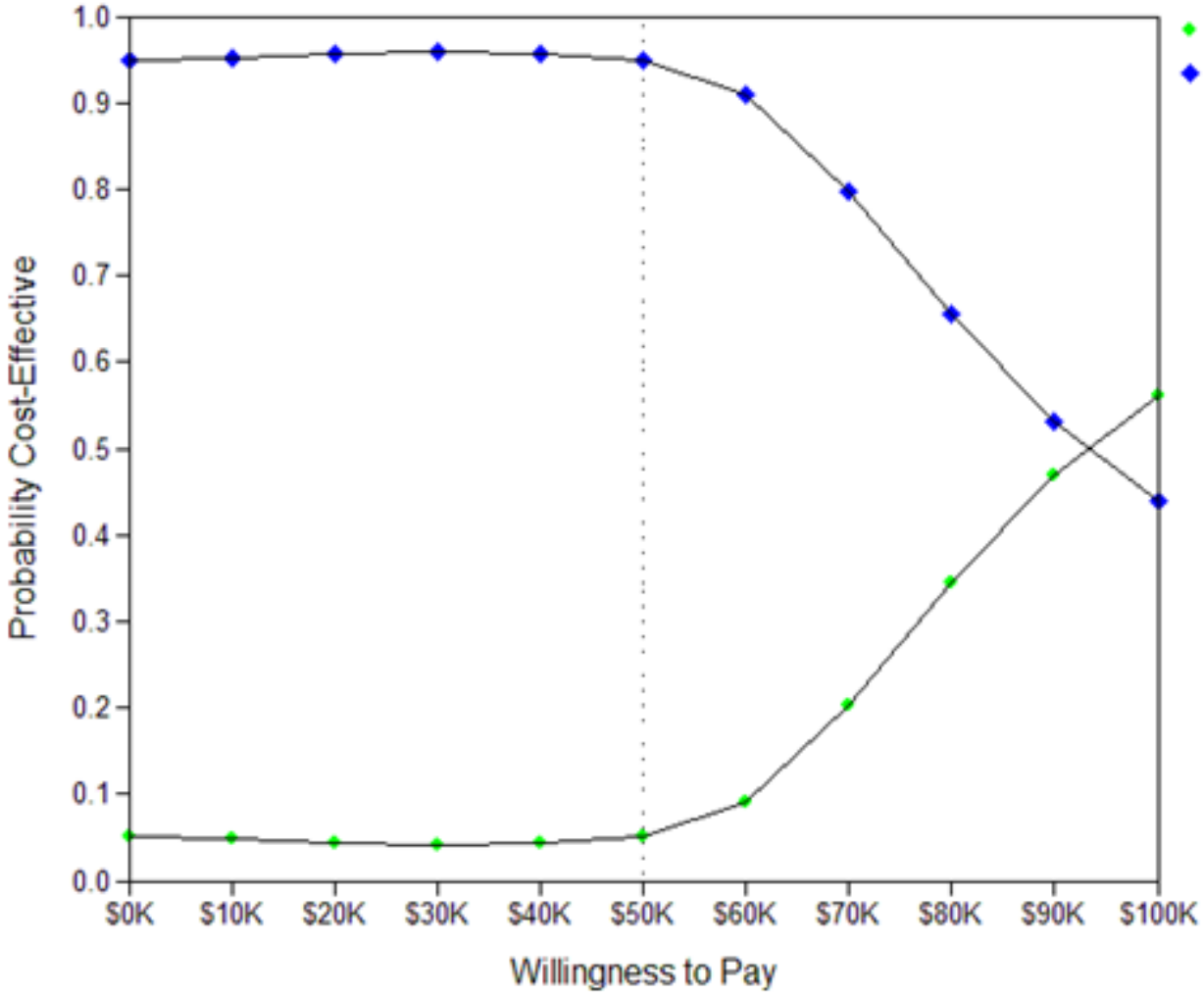
Strategy	Cost	Incr Cost	Life years	Incr life years	C/E	ICER
No testing	$14,369		0.4842		$29,675	
EGFR mutation testing	$16,857	$2,488	0.5383	0.0541	$31,317	**$46,021**

One-Way Sensitivity Analysis



Probabilistic Sensitivity Analysis

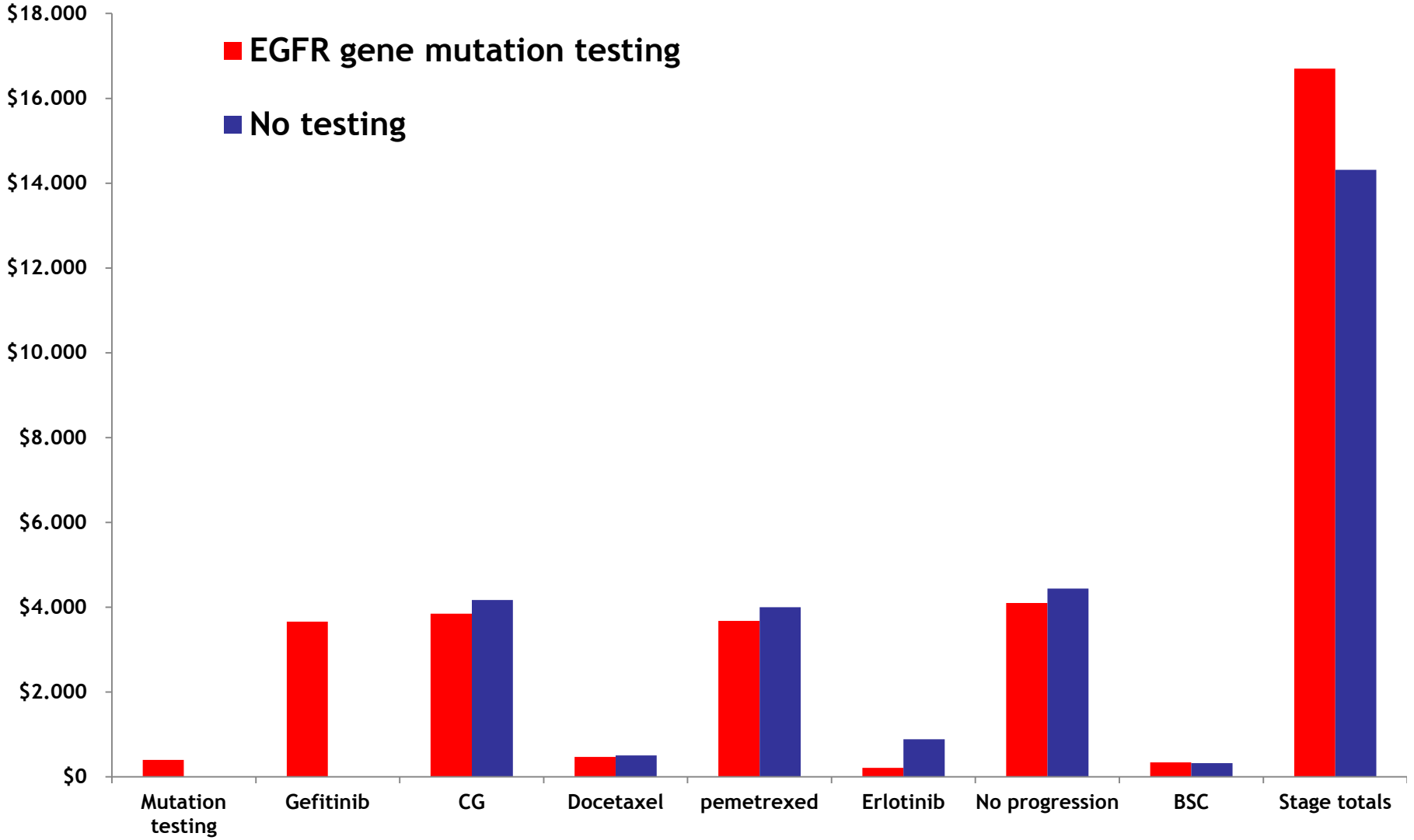
Acceptability Curve



- Proportion of cost-effectiveness for EGFR gene mutation testing under $50K: **5.2%**

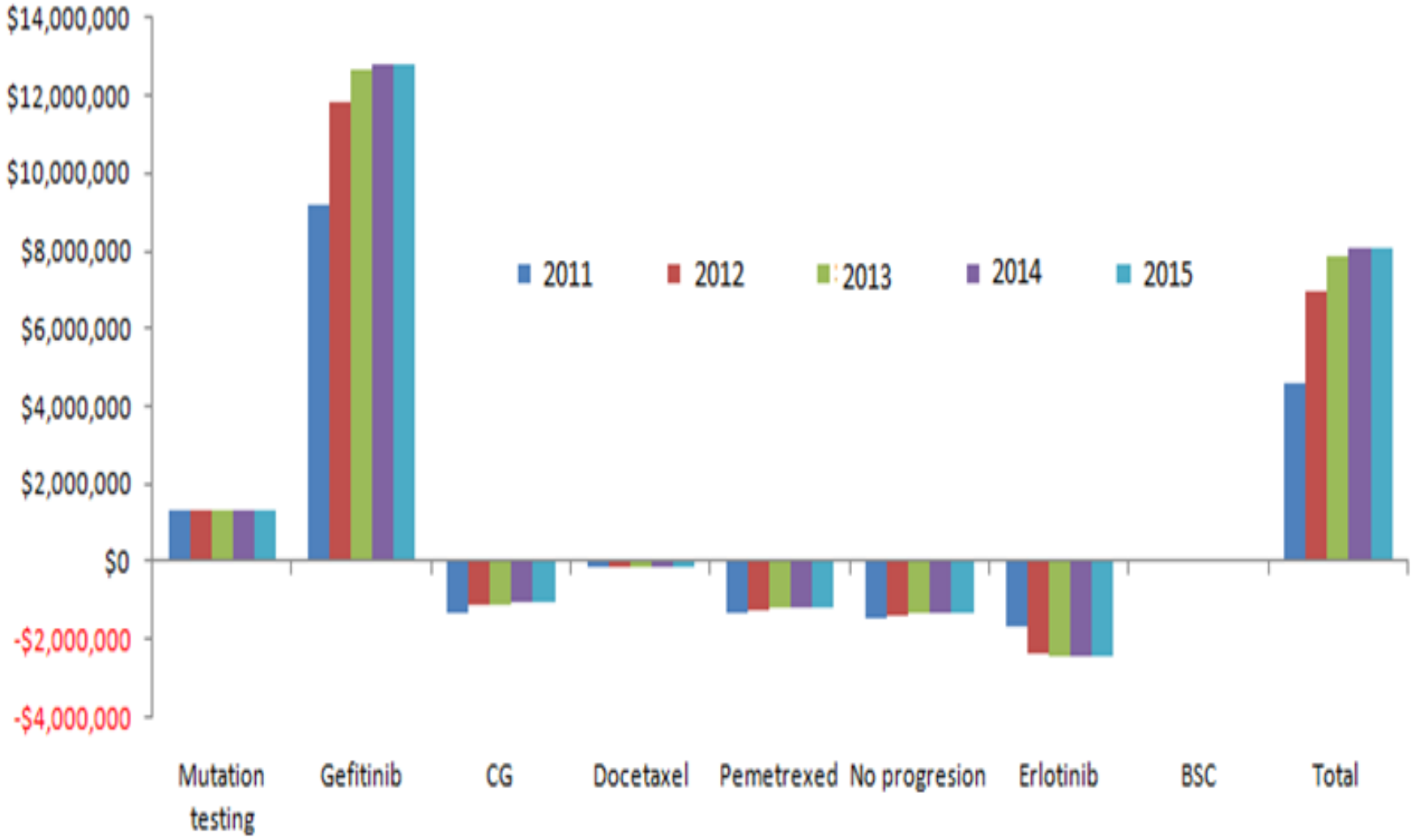
- Proportion of cost-effectiveness for EGFR gene mutation testing under $100K: **56.1%**

Lifetime Direct Medical Costs



Budget Impact Analysis

Differences between the two strategies from 2011 to 2015



Main Limitations

- The efficacy of conventional chemotherapy was assumed unchanged in patients who failed with gefitinib as first-line therapy
- Lack of population based data for the patterns of care and health resources utilization in Ontario
- The approach of utility estimation needs validation

Conclusion

- The cost-effectiveness of using EGFR gene mutation testing for patients with advanced NSCLC is considered attractive when WTP is over $81,000 per QALY
- The cost-effectiveness of EGFR gene mutation testing is highly sensitive to the efficacy and cost of gefitinib
- More research is needed to clarify the existing uncertainty

Acknowledgements

- Dr. Suzanne Kamel-Reid
- Dr. Jeremy Squire
- Dr. Natasha Leighl
- Dr. Richard Gregg
- Dr. Hamid Reza Nakhai-Pour
- Ms. Michelle Bornstein