Cost-effectiveness of Cetuximab and Panitumumab in First-line Treatment for Patients with KRAS Wild-Type Metastatic Colorectal Cancer in Ontario

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Outline

1. Background: Treatment Options
2. Project Aim
3. Methods
4. Results
5. Discussion

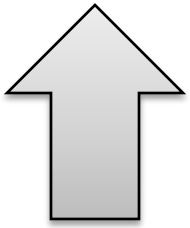
1.

Background: Bevacizumab

Bevacizumab (Avastin®)

- Beva+ FOLFIRI: Used in current clinical practice in 1st line treatment for patients with MCRC in Ontario.

- Bevacizumab + FOLFOX/FOLFIRI:



ORR, PFS, and OS compared to Chemo alone

1.

Background: Cetuximab and Panitumumab

Cetuximab (Erbitux®) and Panitumumab (Vecitibix®)

- Only effective in KRAS-WT patients.
- Currently funded in Ontario:
  - Cetuximab: 2nd line, 3rd line with Irinotecan
  - Panitumumab: 3rd line

- RCTs: Addition to FOLFIRI/FOLFOX in first line ORR, PFS, and OS compared to chemo alone

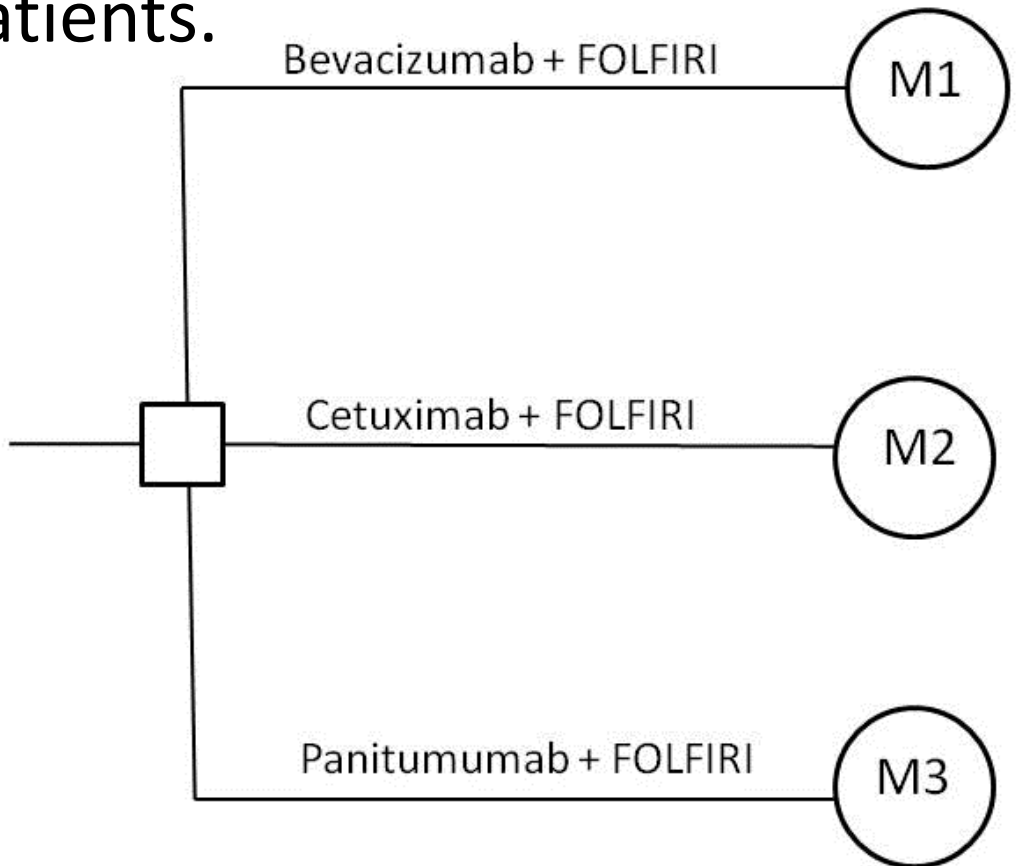
2. Project Aim

- To evaluate the cost-effectiveness of the use of cetuximab or panitumumab plus FOLFIRI compared bevacizumab plus FOLFIRI, as first-line treatment for KRAS wild-type MCRC patients from the perspective of the Ontario Healthcare Payer.

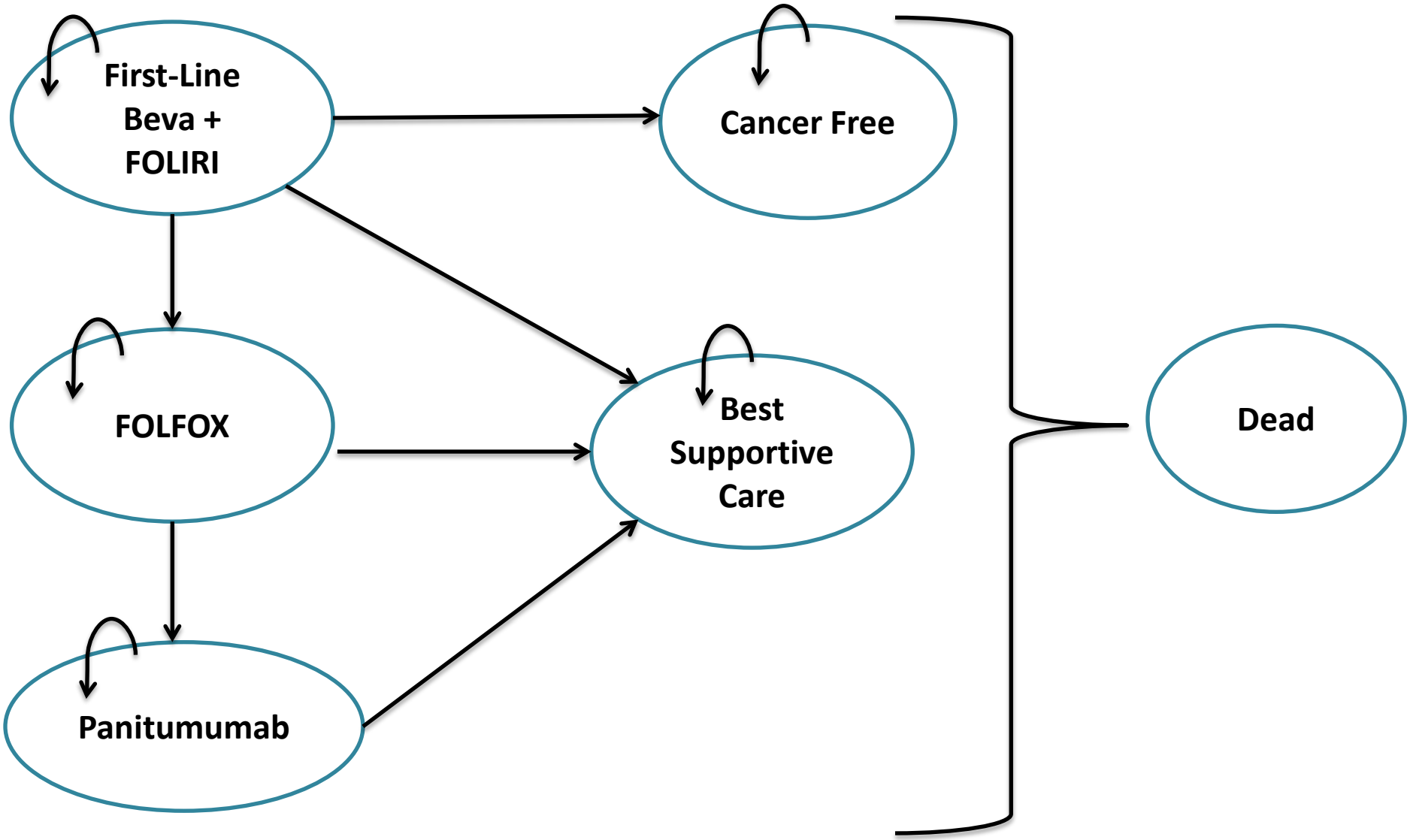
3.

Methods: Model Structure

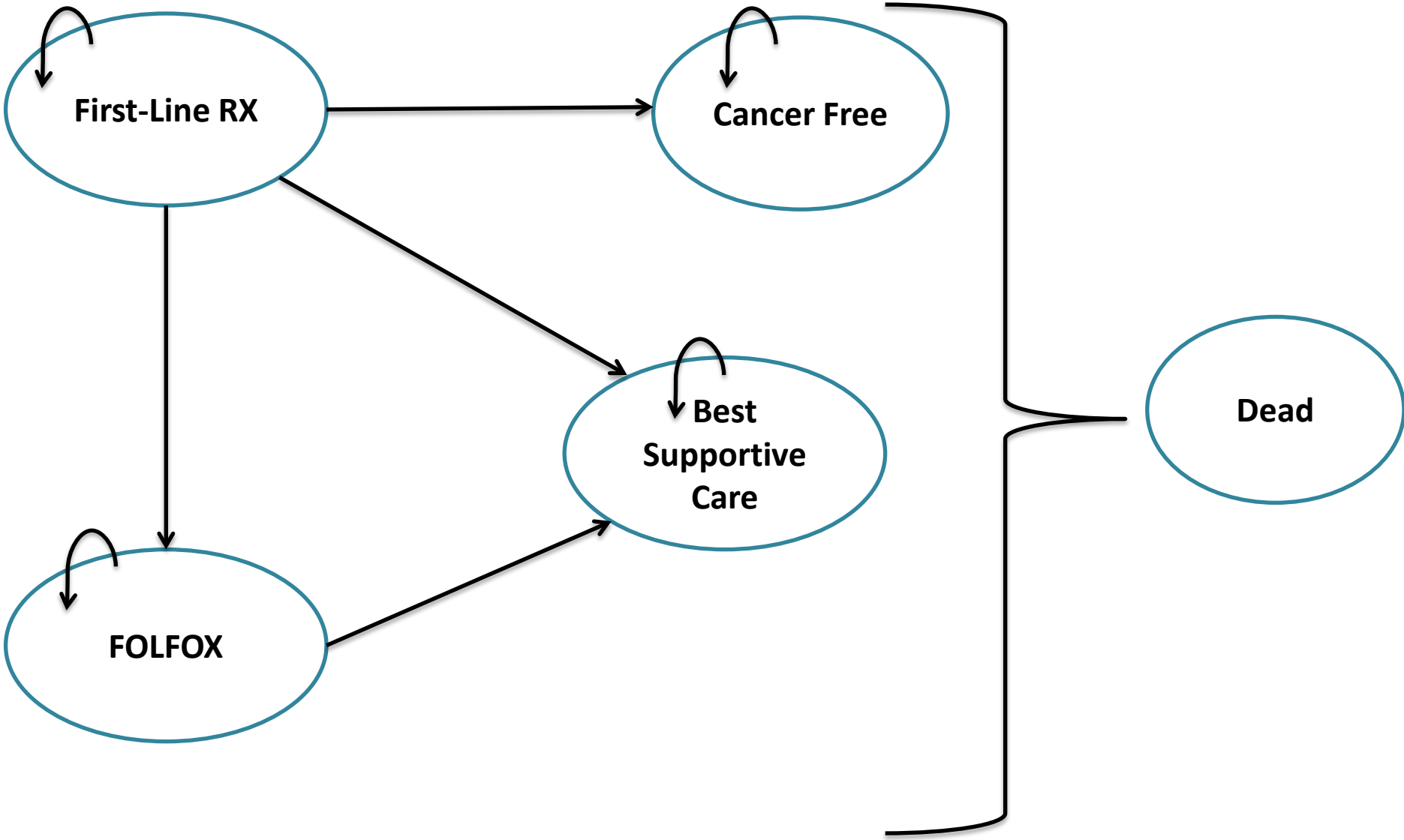
- We developed a decision analytic model to simulate the lifetime clinical and economic consequences of MCRC patients.



3. Methods: Model M1



3. Methods: Models M2 and M3

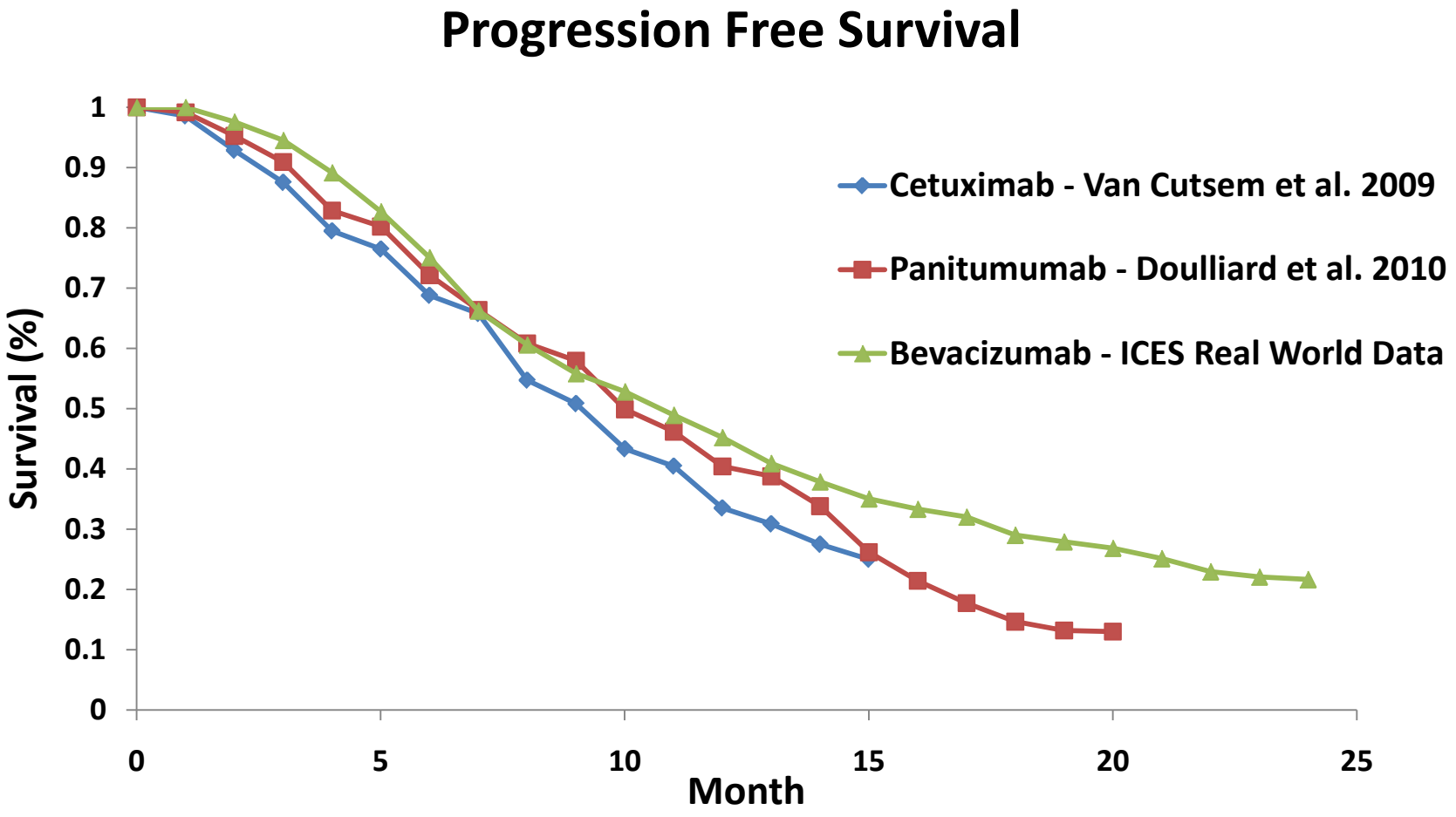


2. Methods: Data Sources

1. Patient-level data: ICES-CD link program.
   - Cohort of interest: 1,216 with MCRC and received Beva+ FOLFIRI as 1st line RX

2. Phase III and IV RCT data

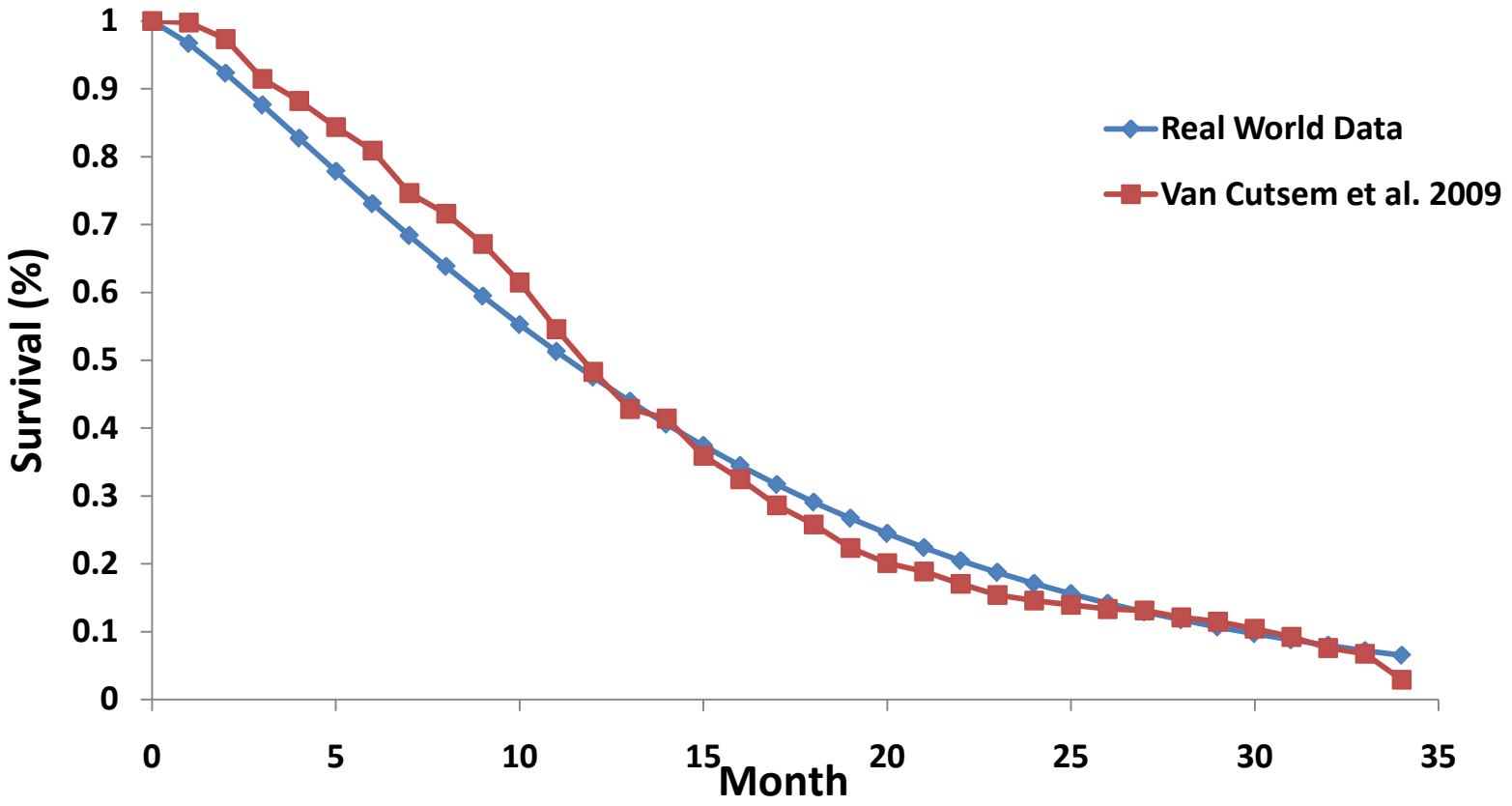
2. Methods: Data Sources - Treatment Efficacy



Cetuximab + FOLFIRI: Van Cutsem et al. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. N Engl J Med. 2009;360(14)
Panitumumab + FOLFIRI: Douillard et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010;28(31)

2. Methods: Data Sources – Real World vs. RCT

Progression Free Survival : Bevacizumab + FOLFIRI



Van Cutsem et al. Safety and efficacy of first-line bevacizumab with FOLFOX, XELOX, FOLFIRI and fluoropyrimidines in metastatic colorectal cancer: the BEAT study. Ann Oncol. 2009;20(11)

3.

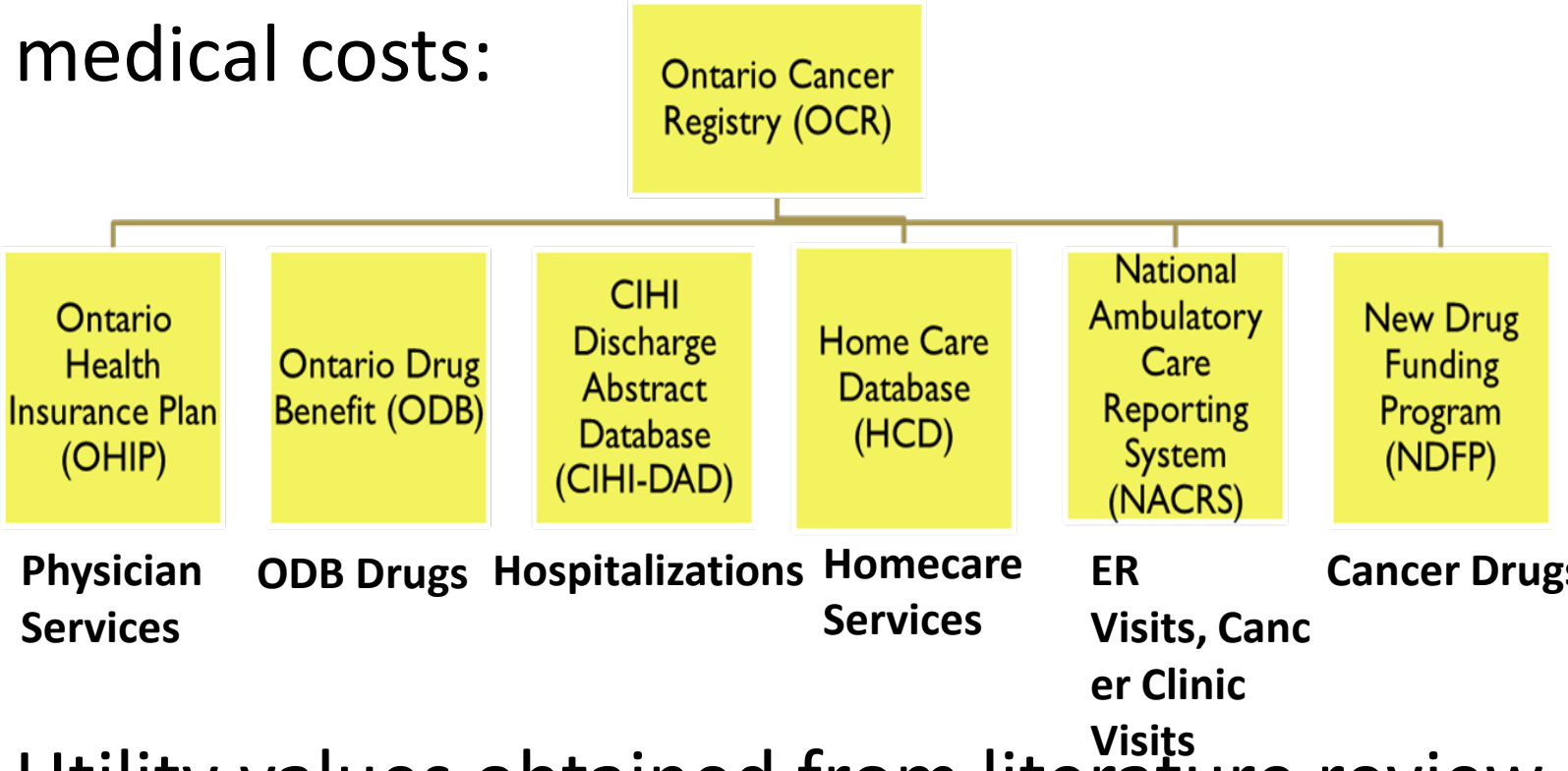
Methods: Transition Probabilities

- Estimated monthly state-dependent transition probabilities from Kaplan-Meier survival estimates.
- Parametric distributions were fit to each curve to extrapolate survival.
  - Monthly probabilities determined using scale and shape parameters
- Mortality unrelated to cancer progression was obtained from Statistics Canada Life Tables for age-dependent mortality

3.

Methods: Health Utility Cost Data

- Average monthly, state-dependent direct medical costs:



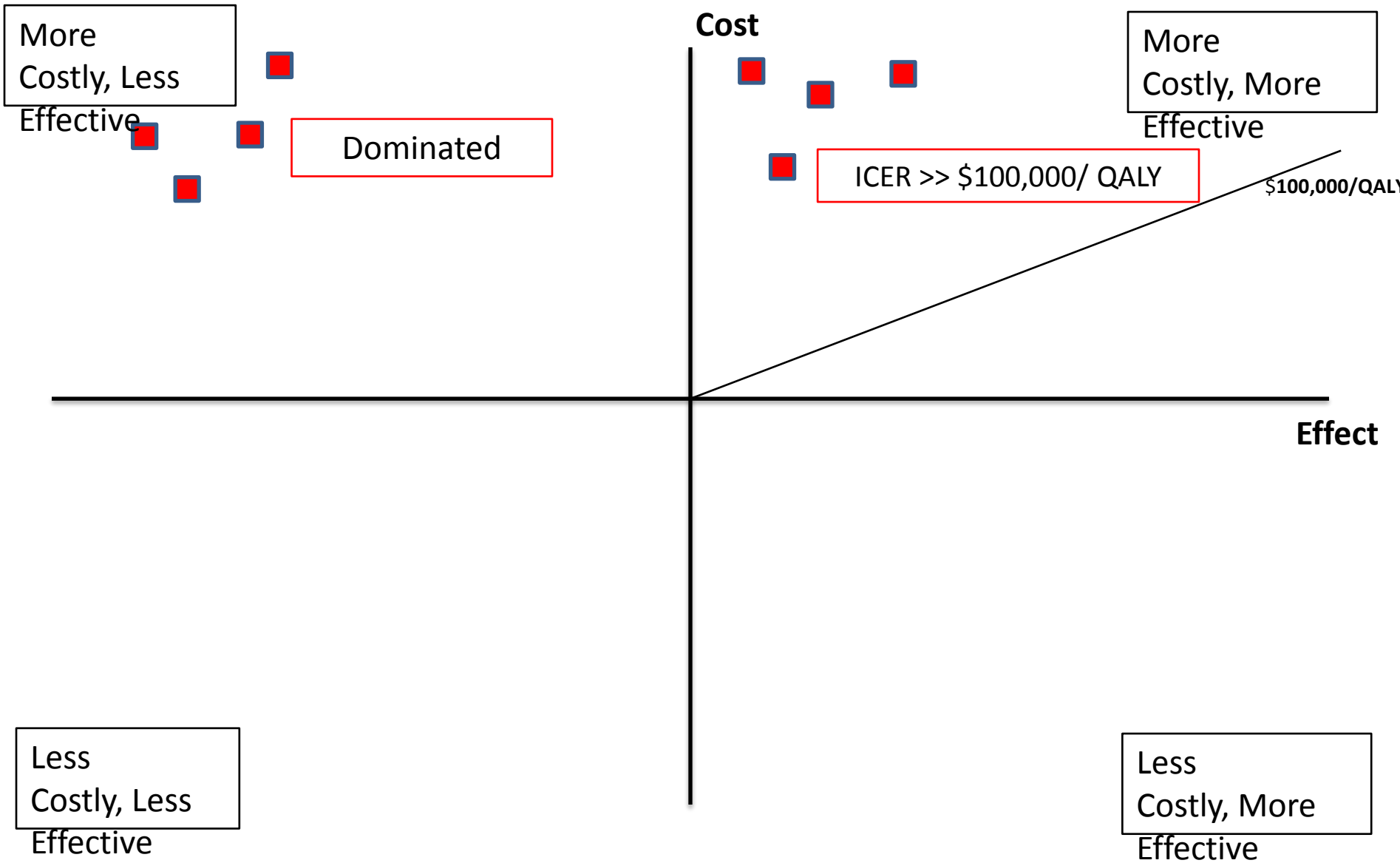
- Utility values obtained from literature review.
- Costs and utilities were discounted at 5%.

4. Results: Base Case

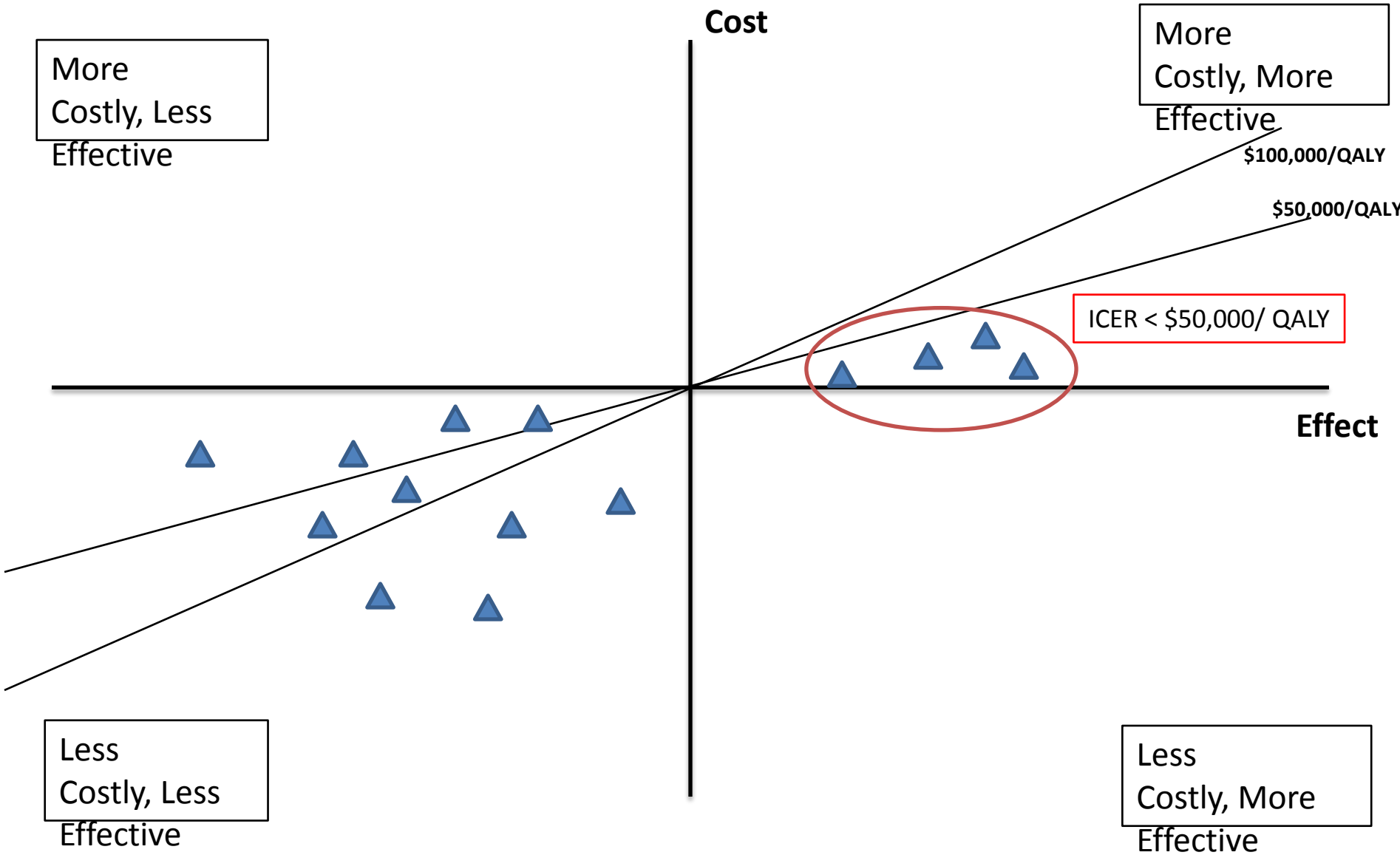
Treatment Strategy	Cost	QALY	ICER
Bevacizumab + FOLFIRI	$150,573	1.749	
Cetuximab + FOLFIRI	$153,731	1.741	Dominated
Panitumumab + FOLFIRI	$173,931	1.716	Dominated

Incremental Cost Effectiveness Ratio (ICER) = Incremental Cost / Incremental Effect

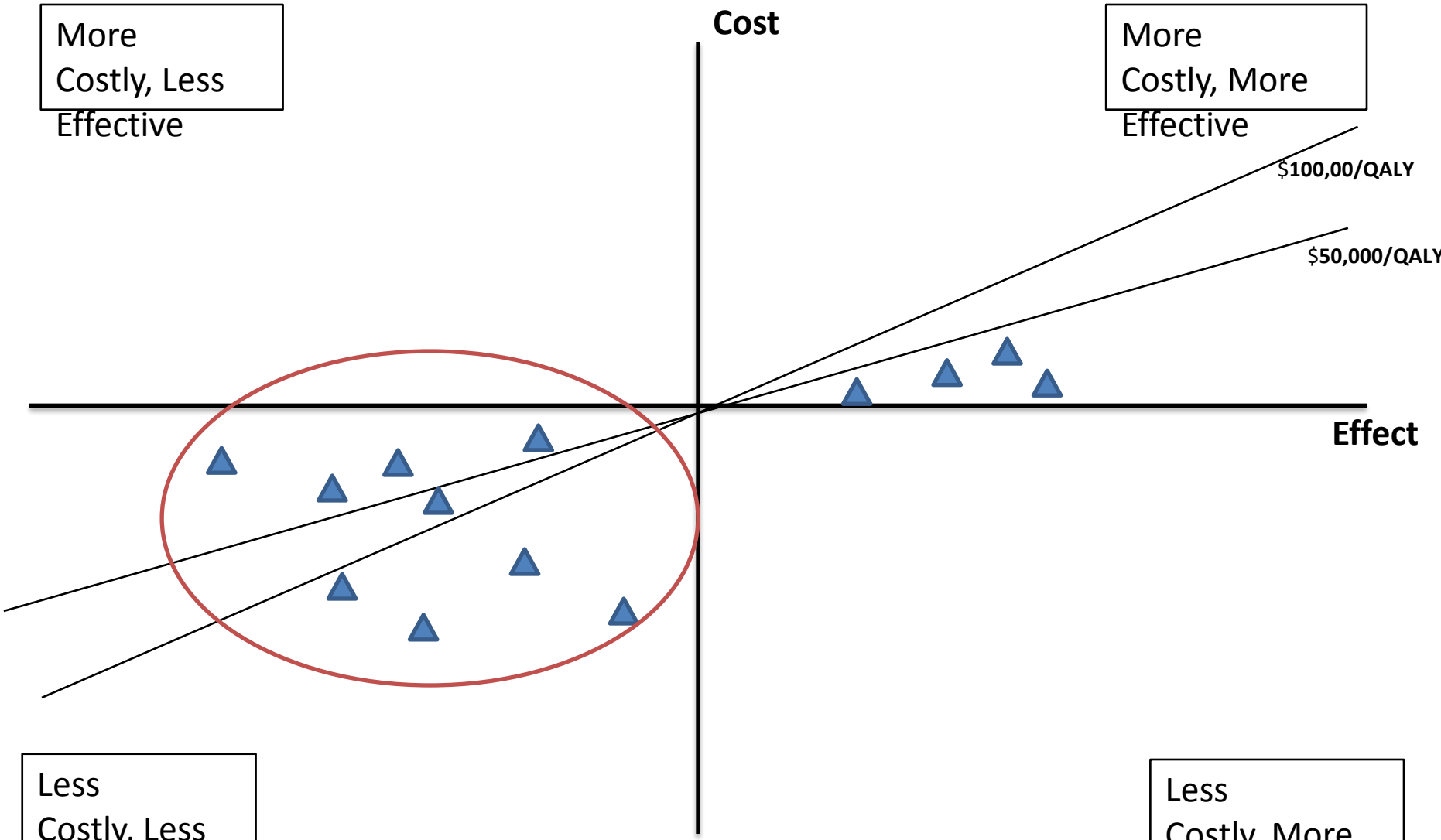
4. Results: Deterministic Sensitivity Analysis: Panitumumab vs. Bevacizumab



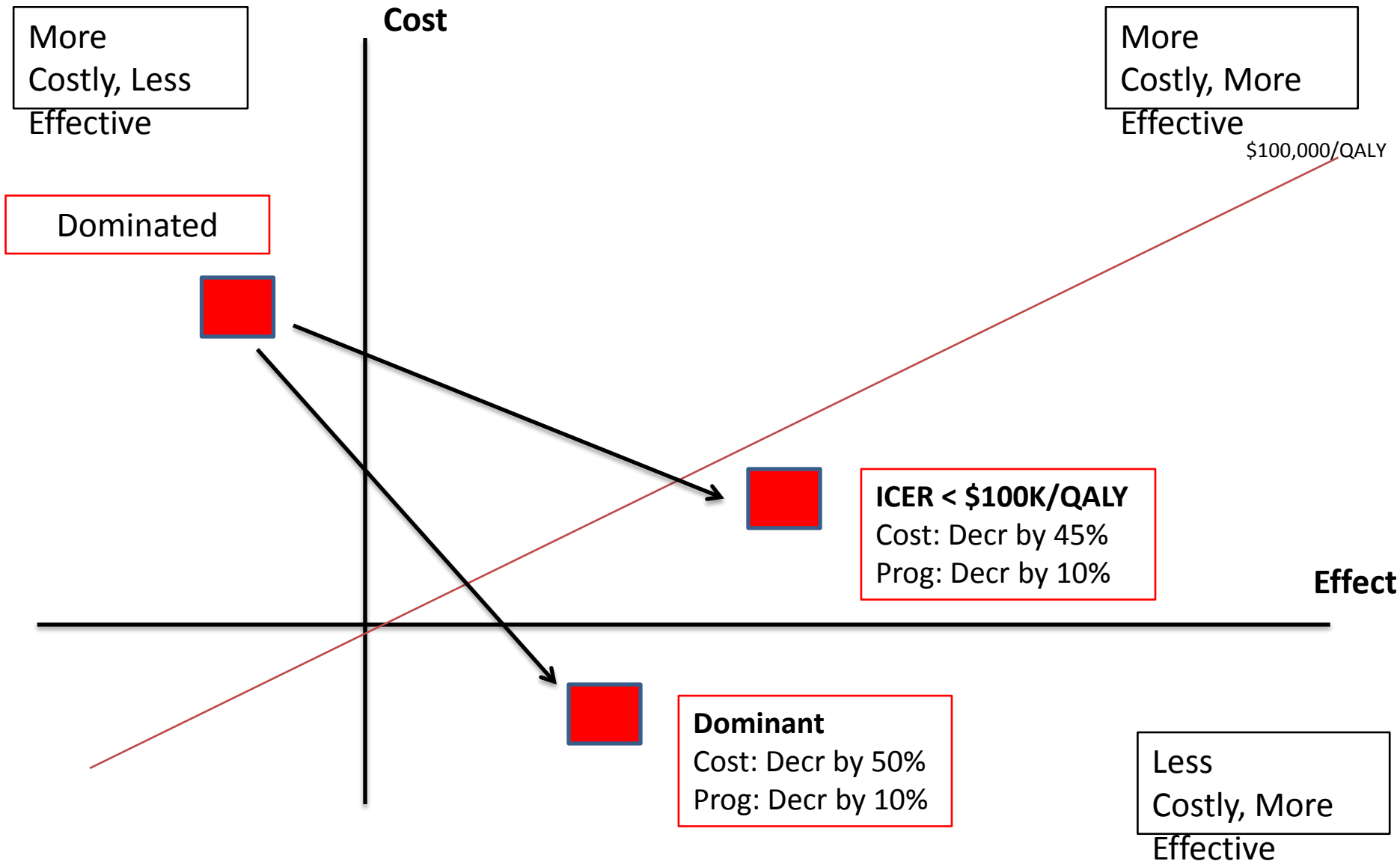
4. Results: Deterministic Sensitivity Analysis: Cetuximab vs. Bevacizumab - Utility



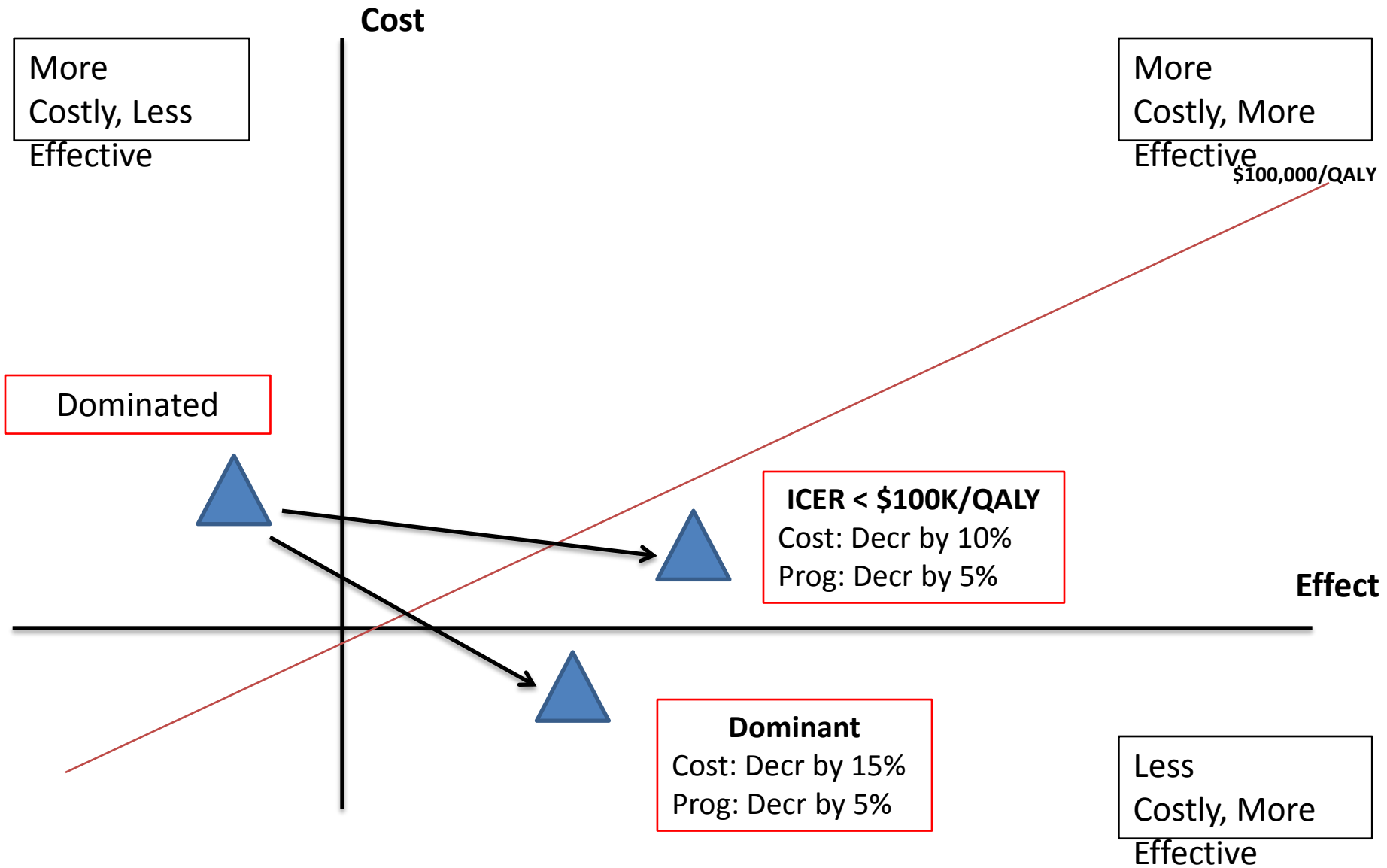
4. Results: Deterministic Sensitivity Analysis: Cetuximab vs. Bevacizumab – Progression and Cost



4. Results: Scenario Analysis - Panitumumab

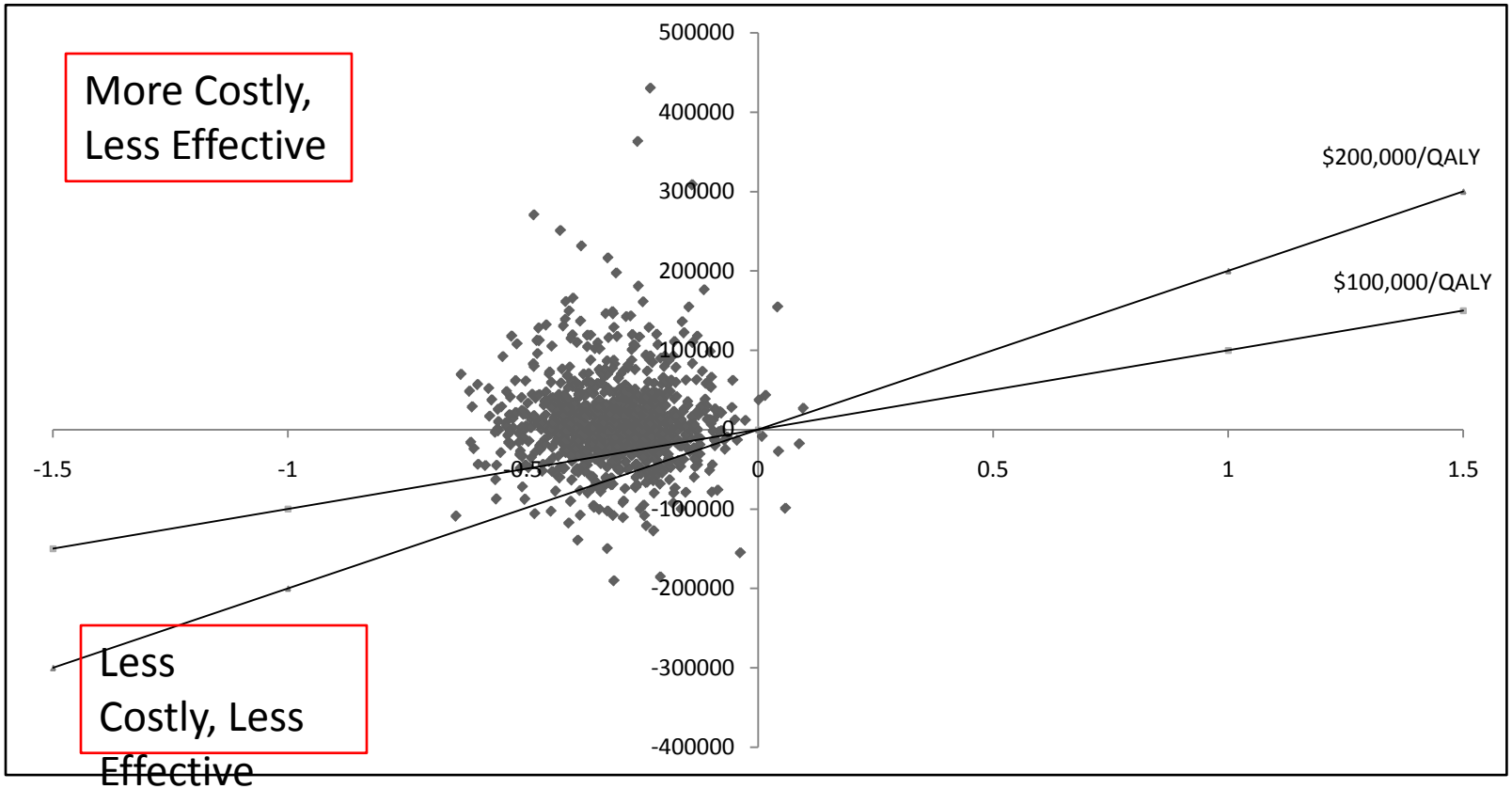


4. Results: Scenario Analysis - Cetuximab



4. Results: Probabilistic Sensitivity Analysis

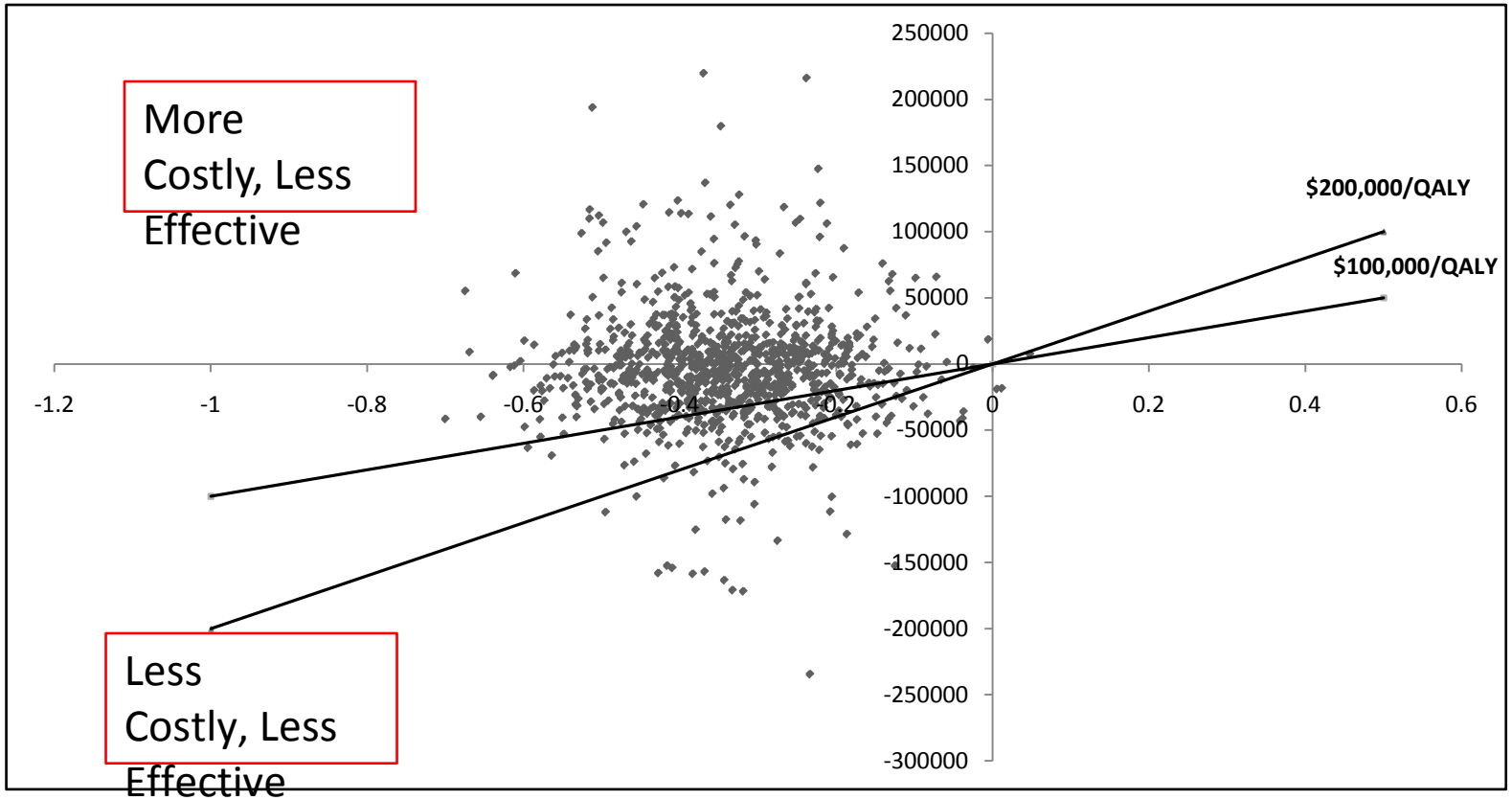
Scatter Plot: Cetuximab vs. Bevacizumab



Dominant → 0.4 % ICER< $100,000/QALY → 0% ICER< $200,000/QALY → 0%

4. Results: Probabilistic Sensitivity Analysis

Scatter Plot: Panitumumab vs. Bevacizumab



Dominant → 0.2 % ICER< $100,000/QALY → 0% ICER< $200,000/QALY → 0.1%

5. Discussion

- For KRAS-WT patients current clinical practice of Bevacizumab + FOLFIRI represents the most cost-effective treatment option.

- Panitumumab should not be considered for use in first line.
  - Dominated or ICER >> $100,000/QALY

- Cetuximab + FOLFIRI: similar to Beva + FOLFIRI in terms of cost and effect.
  - Scenarios where ICER < $50,000/QALY.

5.

Discussion: Limitations

- No head-to-head study comparing all three treatment options.
  - Indirect comparisons with real world and RCT data
- Unable to find cetuximab specific utility value → implications on ICER
- Surrogate marker developed to determine the beginning of BSC state →State costs may not be accurate

5. Discussion: Conclusion

- We were able to investigate cost-effectiveness using survival estimates from real world data in alongside as data from published RCTs.

- It is important to validate survival estimates derived from “real world” data with RCT data
  - as observational studies may tend to overestimate survival compared to RCT

- CD-Link data can be utilized to conduct Ontario-specific CEAs.

Acknowledgments:

Dr. Sisira Sarma and Dr. Greg Zaric, Western University

Department of Epidemiology and Biostatistics, Western University

Ontario Institute for Cancer Research.

Thank You

2. Methods: Data Sources: Clinical Trials

- Cetuximab + FOLFIRI:
  - Van Cutsem E, Kohne CH, Hitre E, Zaluski J, Chang Chien CR, Makhson A, et al. Cetuximab and chemotherapy as initial treatment for metastatic colorectal cancer. N Engl J Med. 2009;360(14):1408-17. doi: 10.1056/NEJMoa0805019.
  - Van Cutsem E, Kohne CH, Lang I, Folprecht G, Nowacki MP, Cascinu S, et al. Cetuximab plus irinotecan, fluorouracil, and leucovorin as first-line treatment for metastatic colorectal cancer: updated analysis of overall survival according to tumor KRAS and BRAF mutation status. J Clin Oncol. 2011;29(15):2011-9. doi: 10.1200/JCO.2010.33.5091.

- Panitumumab + FOLFIRI:
  - Douillard JY, Siena S, Cassidy J, Tabernero J, Burkes R, Barugel M, et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: the PRIME study. J Clin Oncol. 2010;28(31):4697-705. doi: 10.1200/JCO.2009.27.4860

- FOLFOX:
  - Colucci G, Gebbia V, Paoletti G, Giuliani F, Caruso M, Gebbia N, et al. Phase III randomized trial of FOLFIRI versus FOLFOX4 in the treatment of advanced colorectal cancer: a multicenter study of the Gruppo Oncologico Dell'Italia Meridionale. J Clin Oncol. 2005;23(22):4866-75. doi: 10.1200/JCO.2005.07.113.

- 3rd line Panitumumab and BSC
  - Van Cutsem E, Peeters M, Siena S, Humblet Y, Hendlisz A, Neyns B, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol. 2007;25(13):1658-64. doi: 10.1200/JCO.2006.08.1620.

4. Results: One Way Deterministic Sensitivity Analysis

Variables	Treatment Strategy	Parameter -20%	-10%	+10%	+20%
Bevacizumab + FOLFIRI	Cetuximab + FOLFIRI	Less costly, less effective	Less costly, less effective	$167,676	$129,778
Cetuximab + FOLFIRI	Cetuximab + FOLFIRI	$115,448	$164,127	Less costly, less effective	Less costly, less effective
Utility of Bevacizumab	Cetuximab + FOLFIRI	$40,194	$19,037	Dominated	Dominated
Utility of Cetuximab	Cetuximab + FOLFIRI	Dominated	Dominated	$38,676	$18,373
Cost of Bevacizumab	Cetuximab + FOLFIRI	Dominated	Dominated	Less costly, less effective	Less costly, less effective
Cost of Cetuximab	Cetuximab + FOLFIRI	Less costly, less effective	Less costly, less effective	Dominated	Dominated

4. Results: Probabilistic Sensitivity Analysis

Probability of being cost-effective compared to Bevacizumab + FOLFIRI