Deterministic, Threshold and Scenario Analyses

Back to Website

Learning Objectives and Outline

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Learning Objectives

- Explain the purpose of deterministic sensitivity analysis and provide examples of one-way versus two-way analyses.
- Detail the advantages/disadvantages of deterministic sensitivity analysis.

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Outline

1. Net Benefit Outcome Measures
2. One-way sensitivity analysis.
3. Two-way sensitivity analysis.
4. Limitations and extensions.
5. Threshold analysis
6. Scenario analysis

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Alternatives to ICERs

- ICERs the most common approach for describing CEA results
  - Good: summarize all aspects of decision problem except WTP (which comes from decision-maker)
  - Bad: algorithms a bit complicated, negative ICERs, ratios can act poorly when denominator uncertain

Back to Website

An Alternative

- If willing to choose a fixed willingness-to-pay threshold (e.g., $\lambda = 100{,}000$ / QALY), can write down an equation for the contribution of health and cost to utility.
  - Net Health Benefit (NHB)
  - Net Monetary Benefit (NMB)
- Objective: Select the strategy with the highest NHB/NMB

Back to Website

Net Health Benefit (NHB)

$$\text{NHB}_s = E_s - \frac{C_s}{\lambda}$$

where E_s is effectiveness of strategy s, C_s is cost of s and λ is WTP threshold.

Back to Website

Net Health Benefit (NHB)

$$\text{NMB}_s = E_s \times \lambda - C_s$$

where E_s is effectiveness of strategy s, C_s is cost of s and λ is WTP threshold.

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Example: NHB

E_1 = 0.07 years

E_2 = 0.10 years

C_1 = 1,500

C_2 = 2,800

λ = 50,000 per year of life saved

$$ICER = \frac{2800 - 1500}{0.10 - 0.07} = 43,333$$

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Example: NHB

$$NHB_1 = 0.07 - 1500/50000 = 0.040$$
$$NHB_2 = 0.10 - 2800/50000 = 0.044$$
$$\text{Incremental } NHB = 0.044 - 0.040 = 0.004$$

Back to Website

VANDERBILT
Center for Health
Economic Modeling

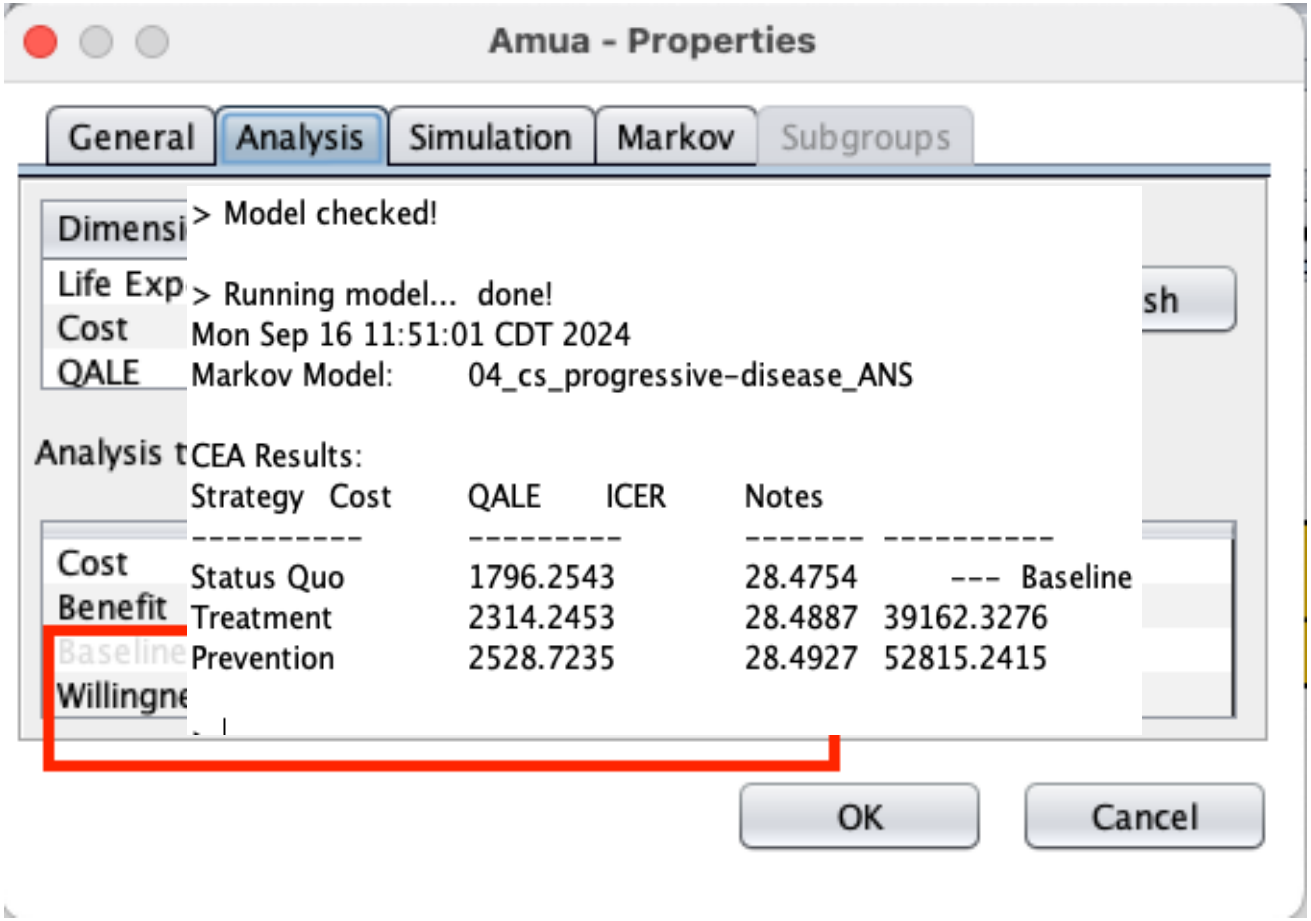
Example: Net Monetary Benefit (NMB)

$$NHB_1 = 0.07 \times 50000 - 1500 = 2000$$
$$NHB_2 = 0.10 \times 50000 - 2800 = 2200$$
$$\text{Incremental } NHB = 2200 - 2000 = 200$$

Back to Website

VANDERBILT Center for Health Economic Modeling

Calculating NMB in Amua



Back to Website

VANDERBILT
Center for Health
Economic Modeling

Sensitivity

- ICER for Prevention strategy is just above WTP threshold of $50,000/QALY.
- NMB for treatment only slightly above NMB for prevention.
- How sensitive are these results to changes in specific model inputs?

Back to Website

One-way sensitivity analysis

Back to Website

VANDERBILT Center for Health Economic Modeling

One-way sensitivity analysis

- Usually the starting point for sensitivity analyses
- Sequentially testing one variable at a time (i.e., Age, BMI, QALY, other clinically important parameters), while holding everything else constant
- Determining how this variation impacts the results
- One-way sensitivity analyses are often presented in a **tornado diagram**
  - Used to visually rank the different variables in order of their overall influence on the magnitude of the model outputs

Back to Website

Examples from publications

Back to Website

VANDERBILT Center for Health Economic Modeling

Rotavirus study

Costs (in 2007 rupees)†			
Cost of one dose of RIX4414	285.2 (142.6 to 570.4)	Based on price paid by Brazilian government[25]	Triangular
Cost of administering vaccine (per dose)	20.4 (10.2 to 81.6)	Podewils et al,[28] Isakbaeva et al[29]	Triangular
Hospital treatment of rotavirus infection:			
Direct medical:			
Paid by patient's family	2444.3 (1833.2 to 3055.4)	Mendelsohn et al[47]	Normal
Subsidised by government	189.4 (142.1 to 236.8)	Mendelsohn et al[47]	Normal
Direct non-medical	39.9 (29.9 to 49.9)	Mendelsohn et al[47]	Normal
Indirect	0	Mendelsohn et al[47]	NA
Outpatient treatment of rotavirus infection:			
Direct medical:			
Paid by patient's family	156.2 (117.2 to 195.3)	Mendelsohn et al[47]	Normal
Subsidised by government	52.1 (39.1 to 65.1)	Mendelsohn et al[47]	Normal
Direct non-medical	23.6 (17.7 to 29.5)	Mendelsohn et al[47]	Normal
Indirect	1.8 (1.4 to 2.3)	Mendelsohn et al[47]	Normal
Oral rehydration solution (per course)	15.4 (11.3 to 18.8)	Patel et al[80]	Normal

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Rotavirus study

Table 5 | Base case cost effectiveness results: strategy of no vaccination compared with strategy of vaccination with two doses of RIX4414

	Mean cost (2007 rupees)	Marginal cost	Mean years of life lost	Life years saved (LYS)	ICER* (rupees/LYS)
No vaccination	106.5	—	2.06627	—	—
Vaccination	538.9	432.4	2.01237	0.05390	8023

*Incremental cost effectiveness ratio (ICER) calculated as marginal cost in 2007 rupees divided by life years saved.

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Rotavirus study

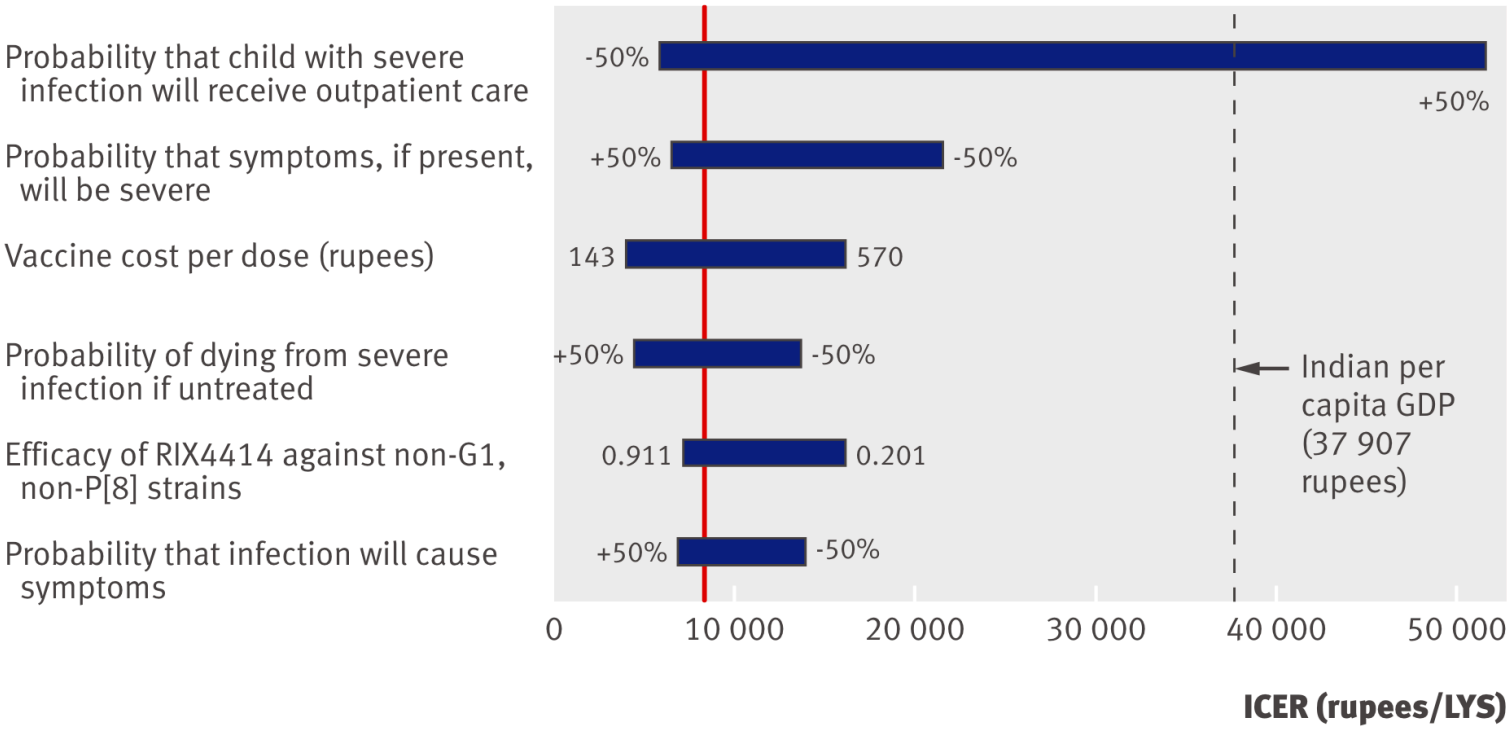


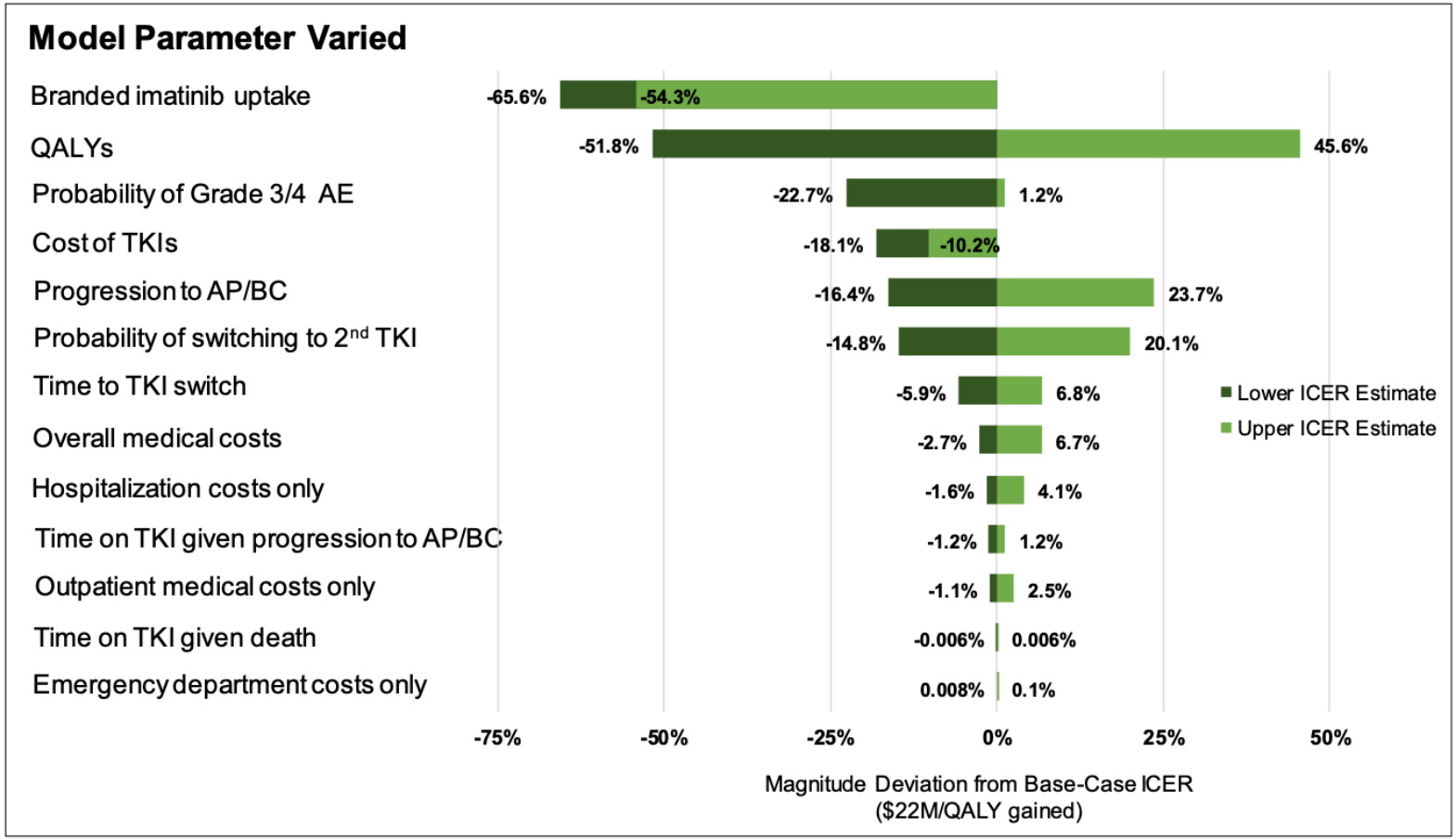
Fig 3 | **Individual parameters with greatest influence on incremental cost effectiveness ratio, expressed in rupees per life year saved (LYS), in univariate sensitivity analysis. Solid vertical line represents base case incremental cost effectiveness ratio of 8023 rupees per life year saved**

Back to Website

VANDERBILT Center for Health Economic Modeling

Other examples

Dasatinib vs. Imatinib



Back to Website

Other examples

ICER
INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value

Final Evidence Report

Back to Website

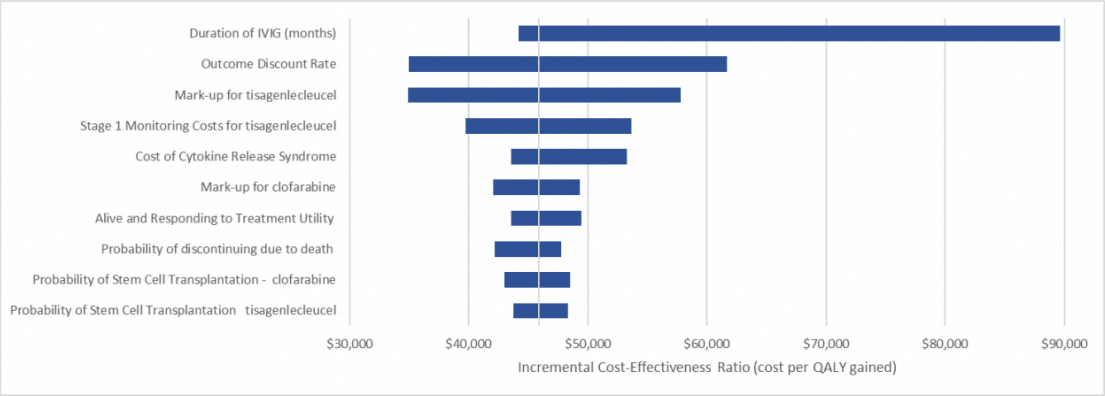
VANDERBILT
Center for Health
Economic Modeling

Other examples

Sensitivity Analyses

To demonstrate effects of uncertainty on both costs and health outcomes, we varied input parameters using available measures of parameter uncertainty (i.e. standard errors or plausible parameter ranges). Figure ES3 presents the tornado diagram resulting from the one-way sensitivity analysis for tisagenlecleucel versus clofarabine in B-ALL. Key drivers of the model included the duration of IVIG therapy for B-cell aplasia, "outcome discount rate" (i.e., the discount percentage applied to future clinical benefits), and hospital mark-up percentage for tisagenlecleucel. The incremental cost-effectiveness ratio assuming no hospital mark-up for tisagenlecleucel was approximately $35,000 per QALY gained. Across broad ranges in influential model inputs when varied one-by-one, the incremental cost-effectiveness ratio remained within acceptable cost-effectiveness thresholds.

Figure ES3. Tornado Diagram for One-Way Sensitivity Analyses of Tisagenlecleucel versus Clofarabine



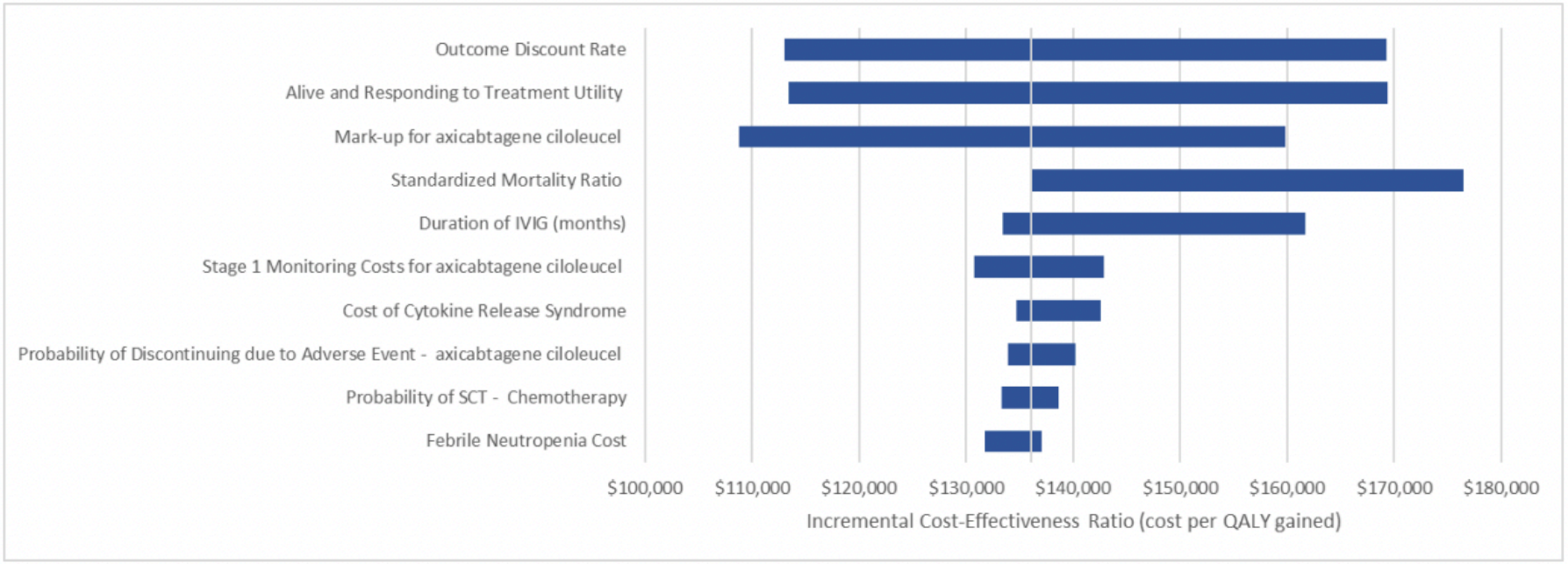
Base-case incremental cost-effectiveness ratio: $45,871 per QALY gained

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Other examples

Figure ES4. Tornado Diagram for One-Way Sensitivity Analyses of Axicabtagene Ciloleucel versus Chemotherapy



Base-case incremental cost-effectiveness ratio: $136,078 per QALY gained

Back to Website

Interactive Amua Session

Back to Website

VANDERBILT Center for Health Economic Modeling

Primary Results: Progressive Disease

Strategy	ICER
Status Quo	-
Treatment	49,513
Prevention	139,630

- Treatment is cost-effective at WTP=$50,000/QALY—but *barely.*
- How sensitive is this result to the input parameter values used?

Back to Website

Two-way sensitivity analysis

Back to Website

Two-way sensitivity analysis

- A way to map the interaction effects between two parameters in a decision analysis model
- Varies 2 parameters at a time
- Explores the robustness of results in more depth

Back to Website

Examples from publications

Back to Website

VANDERBILT Center for Health Economic Modeling

HIV prevention

Cost-Effectiveness of Pre-Exposure Prophylaxis for HIV Prevention for Conception in the United States

Ashley A. Leech, PhD, MS[1,2], James F. Burgess Jr., PhD[3,2,*], Meg Sullivan, MD[4,6], Wendy Kuohung, MD[5], Michal Horný, Ph.D., MSc.[2,8,9], Mari-Lynn Drainoni, PhD[2,3,6], Cindy L. Christiansen, PhD[10], Benjamin P. Linas, MD, MPH[4,6]

Back to Website

VANDERBILT Center for Health Economic Modeling

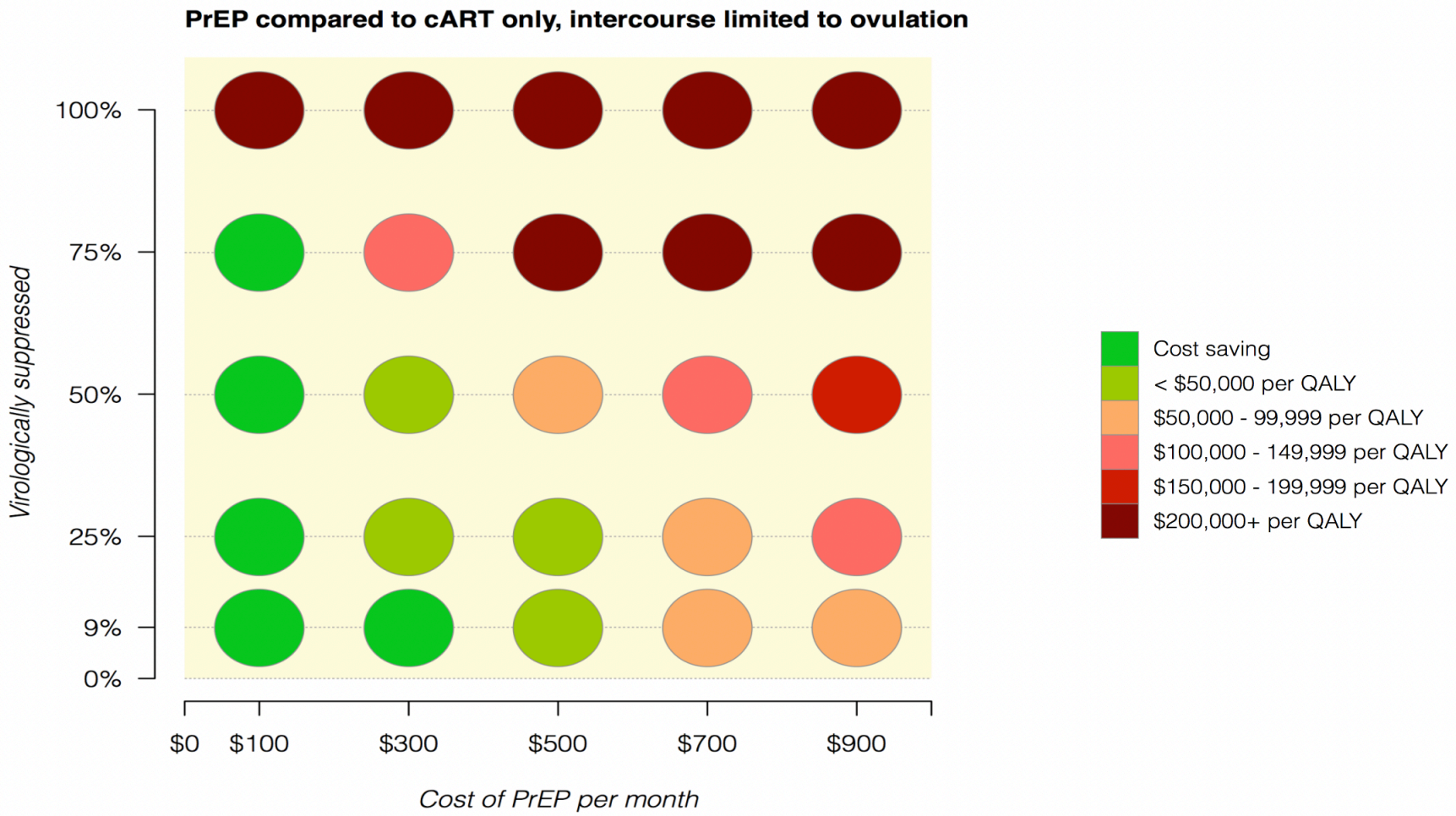
HIV prevention

- Markov model examining strategies for HIV prevention among serodiscordant couples seeking conception (woman does not have HIV and male has HIV)
- We know that if the **male partner is consistently on medication for HIV** (i.e., resulting in virologic suppression), then the risk of transmission is small regardless of the woman taking PrEP (pre-exposure prophylaxis)
- And we also know that PrEP has traditionally been really **costly**

Back to Website

VANDERBILT Center for Health Economic Modeling

HIV prevention



Back to Website

VANDERBILT
Center for Health
Economic Modeling

Financial incentives for acute stroke care

Can Pay-for Performance Incentive Levels be Determined Using a Cost-Effectiveness Framework?

Ankur Pandya, PhD, Djøra I. Soeteman, PhD, Ajay Gupta, MD, Hooman Kamel, MD, Alvin I. Mushlin, MD, ScM, and Meredith B. Rosenthal, PhD

Back to Website

Financial incentives for acute stroke care

- Under pay for performance policies in the US, **physicians or hospitals are paid more for meeting evidence-based quality targets**
- Study objective: Illustrate how pay-for-performance incentives can be quantitatively bounded using cost-effectiveness modeling, through the **application of reimbursement to hospitals for faster time-to-tPA for acute ischemic stroke**

Back to Website

Financial incentives for acute stroke care

> When administered quickly after stroke onset (within three hours, as approved by the FDA), tPA helps to restore blood flow to brain regions affected by a stroke, thereby limiting the risk of damage and functional impairment

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Financial incentives for acute stroke care

Figure 2. Two-way sensitivity analysis showing the difference in population-level incremental net monetary benefit (pay-for-performance scenarios compared with the status quo) for different combinations of the levels of door-to-needle time reductions and tPA (tissue-type plasminogen activator) payment increases.

The green regions show combinations of values that resulted in positive incremental net monetary benefit (iNMB) compared with status quo acute stroke treatment (population-level incremental cost-effectiveness ratio [ICER]<$50 000/quality-adjusted life year [QALY]); yellow indicates similar iNMB (population-level ICER around $100 000/QALY); and red indicates negative iNMB (population-level ICER>$150 000/QALY).

Back to Website

Interactive Amua Session

Back to Website

Limitations of deterministic sensitivity analyses

Back to Website

Caution: Limitations!

- Limited by the subjectivity of the choice of parameters to analyze
- That's why we also run PSAs!, i.e., varying ALL input parameters at the same time, using priors to play a distribution around each value

Back to Website

Scenario analysis

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Motivation

- Suppose we wanted to model the impact of these interventions under a “lower cost” scenario.
- One option is to
- It may be more efficient to define different scenarios rather than add additional strategies to the model structure itself.

Back to Website

Scenario analysis

- Focuses more on model **assumptions** rather than parameter uncertainty
- Could include separate analysis on:

> Subgroups/sub-populations, including different age cohorts & risk levels

> Different perspectives (societal; modified societal; etc)

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Scenario analysis

> Hypothetical scenarios (“optimistic” and “conservative” scenarios; for example, if we have little evidence of long-term survival associated with medication X, we might have an optimistic versus conservative scenario)

> Time horizons

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value

Final Evidence Report

Back to Website

Examples

Alternative Survival Assumption

In the base-case analysis, we introduced a knot in the survival curve fit once the curve flattened (slope equaled zero). In this scenario analysis, we removed the knot. This scenario should be interpreted as a lower bound for survival. Using this standard parametric modeling practice, tisagenlecleucel resulted in 5.15 life years (4.49 QALYs), clofarabine resulted in 0.66 life years (0.49 QALYs), axicabtagene ciloleucel resulted in 3.17 life years (2.19 QALYs), and chemotherapy resulted in 0.94 life years (0.55 QALYs). The incremental cost-effectiveness ratios increased to $77,511 per QALY gained for tisagenlecleucel as compared to clofarabine and $259,378 per QALY gained for axicabtagene ciloleucel as compared to chemotherapy (Table 4.18).

Table 4.18. Scenario Analysis with Alternate Survival Assumption (Standard Parametric Modeling)

Incremental Comparison	Base-Case Survival Extrapolation ($/QALY)	Scenario Survival Extrapolation ($/QALY)
Tisagenlecleucel vs. Clofarabine (B-ALL)	$45,871	$77,511
Axicabtagene Ciloleucel vs. Chemotherapy (B-cell Lymphoma)	$136,078	$259,378

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

Table 4.17. Cost-Effectiveness by Time Horizon: Incremental Results

	Tisagenlecleucel vs. Clofarabine		Axicabtagene Ciloleucel vs. Chemotherapy	
Time Horizon	Incremental CE Ratio: $/QALY gained	Incremental CE Ratio: $/LY gained	Incremental CE Ratio: $/QALY gained	Incremental CE Ratio: $/LY gained
1 Year	$928,685	$851,384	$4,021,598	$3,259,368
5 Years	$170,358	$189,318	$466,024	$376,570
10 Years	$97,279	$107,571	$207,689	$253,803
Lifetime	$41,642	$45,871	$136,078	$112,168

CE: cost-effectiveness, LY: life year, QALY: quality-adjusted life year

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

Table 4.16. Other Payment Strategies: Incremental Results for B-cell Lymphoma

Axicabtagene Ciloleucel vs. Chemotherapy	Incremental Costs	Incremental LYs	Incremental QALYs	Incremental CE Ratio per LY	Incremental CE Ratio per QALY Gained
Payment at Infusion*	$462,043	4.12	3.40	$112,168	$136,078
Payment for Responders at One Month	$399,831	4.12	3.40	$97,065	$117,756
Payment for Responders at One Year	$322,112	4.12	3.40	$78,198	$94,866

*Base case

CE: cost-effectiveness, LY: life year, QALY: quality-adjusted life year

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

Modelling the cost-effectiveness of pay-for-performance in primary care in the UK

Ankur Pandya[1,3*], Tim Doran[2], Jinyi Zhu[3], Simon Walker[4], Emily Arntson[5] and Andrew M. Ryan[5]

Abstract

Background: Introduced in 2004, the United Kingdom's (UK) Quality and Outcomes Framework (QOF) is the world's largest primary-care pay-for-performance programme. Given some evidence of the benefits and the substantial costs associated with the QOF, it remains unclear whether the programme is cost-effective. Therefore, we assessed the cost-effectiveness of continuing versus stopping the QOF.

Back to Website

VANDERBILT
Center for Health
Economic Modeling

Examples

Table 3 Cost-effectiveness ratios (£/QALY) for continuing the QOF versus stopping the QOF under various model scenarios

QOF effects beyond mortality		How long QOF mortality benefit is sustained if QOF discontinued**				
Non-fatal outcomes	Increased drug costs	No waning	1-year waning	3-year waning	5-year waning	10-year waning
Included	Included	49,362*	51,970	57,616	63,765	81,428
Included	Not included	48,768	51,347	56,931	63,011	80,478
Not included	Included	80,515	84,323	92,565	101,535	127,281
Not included	Not included	79,657	83,424	91,575	100,446	125,907

QOF Quality and Outcomes Framework, *QALY* quality-adjusted life year
*Base-case scenario: non-fatal outcomes and increased drug costs included and instant changes in the QOF mortality benefit if the QOF is discontinued
**In waning scenarios, we assumed linear declines in the QOF mortality benefit from the first year in the model to a time in the future (1, 3, 5 or 10 years from the model start), at which point the mortality benefit from the QOF would equal zero

Back to Website

Threshold analysis

Back to Website

VANDERBILT Center for Health Economic Modeling

Threshold analysis

- Answers the question: What the input parameter need be to meet the country thresholds of:
  - $50,000/QALY gained
  - $100,000/QALY gained
  - $150,000/QALY gained
  - $200,000/QALY gained

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value

Final Evidence Report

Back to Website

VANDERBILT Center for Health Economic Modeling

Examples

A threshold analysis was also conducted to determine the treatment acquisition cost needed to achieve thresholds of $50,000, $100,000, and $150,000 per QALY gained. Table ES16 presents the unit price needed for each therapy to reach these commonly cited cost-effectiveness thresholds. The price needed to achieve the thresholds presented in Table ES15 includes both the manufacturer price and associated mark-up.

Table ES16. Threshold Analysis Results

	Price	Net Price (with Mark-Up)	Price* to Achieve $50,000 per QALY	Price* to Achieve $100,000 per QALY	Price* to Achieve $150,000 per QALY
Tisagenlecleucel (B-ALL)	$475,000	$575,000	$636,894	$1,162,563	$1,688,232
Axicabtagene Ciloleucel (B-cell Lymphoma)	$373,000	$473,000	$157,578	$340,797	$524,015

Payment assumed for tisagenlecleucel was payment for responders at one month. Payment assumed for axicabtagene ciloleucel was payment at infusion.

*Price needed to achieve the thresholds includes both the acquisition cost and associated mark-up.

QALY: quality-adjusted life year, WAC: wholesale acquisition cost

Back to Website

Thank you!

Back to Website