Introduction to Decision Modeling

Janssen Decision Modeling in R Workshop

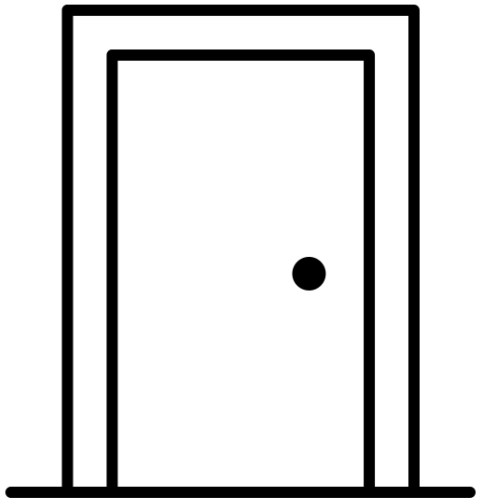
April 2021

Decision Analysis

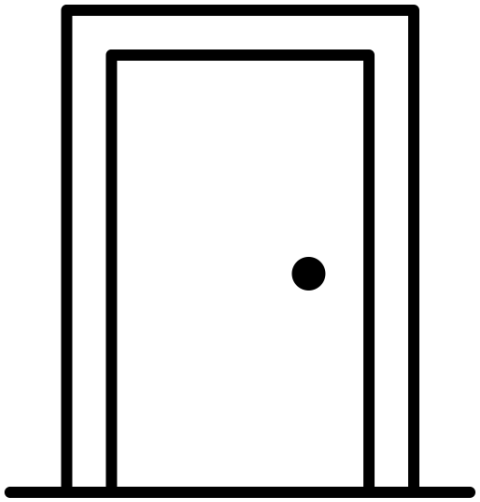
- Explicit, quantitative and systematic approach to decision making under *uncertainty*
- Identify, measure, and value the consequences of decisions as well as the uncertainty that exists when the decision needs to be made
- Help structure the analysts' thinking and facilitate the communication of assumptions
- Provide a structural framework for synthesizing data from disparate sources and allows for *extrapolation*
- Elements are incorporated into a *model* to structure the decision problem over time, and used to compare the outcomes of different options or interventions

Decision Analysis

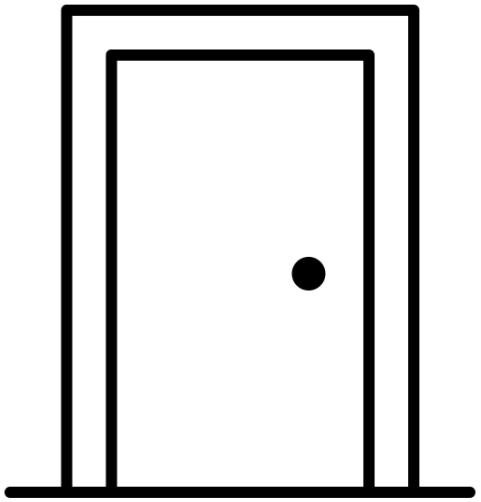
Option 1



Option 2



Option 3



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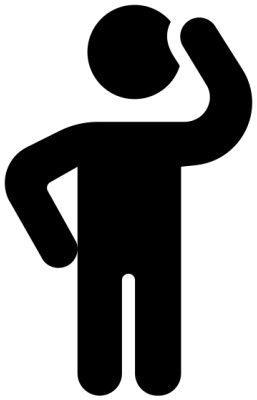
Benefits?



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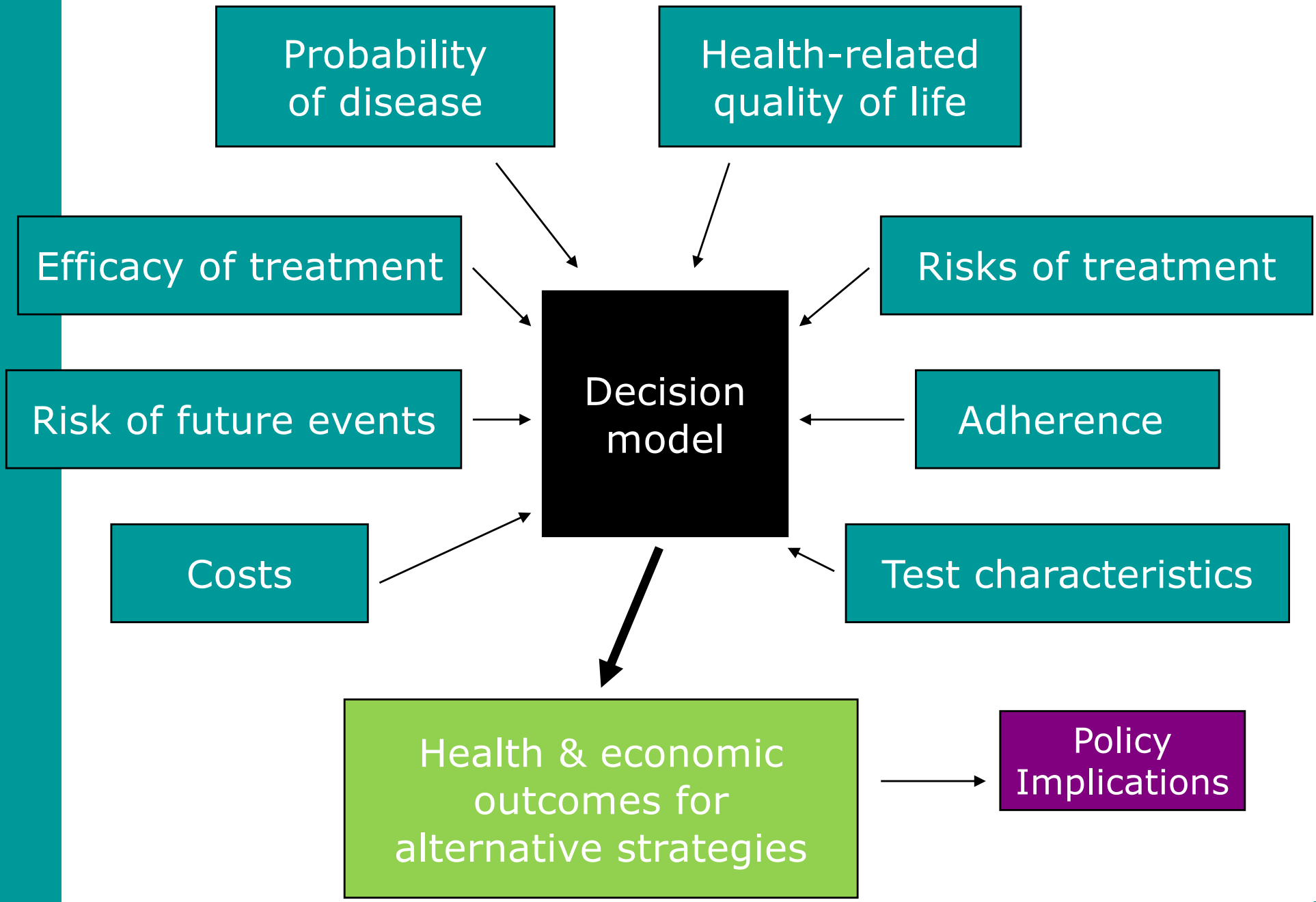
Harms?

Cost?


Probability of disease
Health-related quality of life
Efficacy of treatment
Risks of treatment
Risk of future events
Decision model
Adherence
Costs
Test characteristics
Health & economic outcomes for alternative strategies
Policy Implications

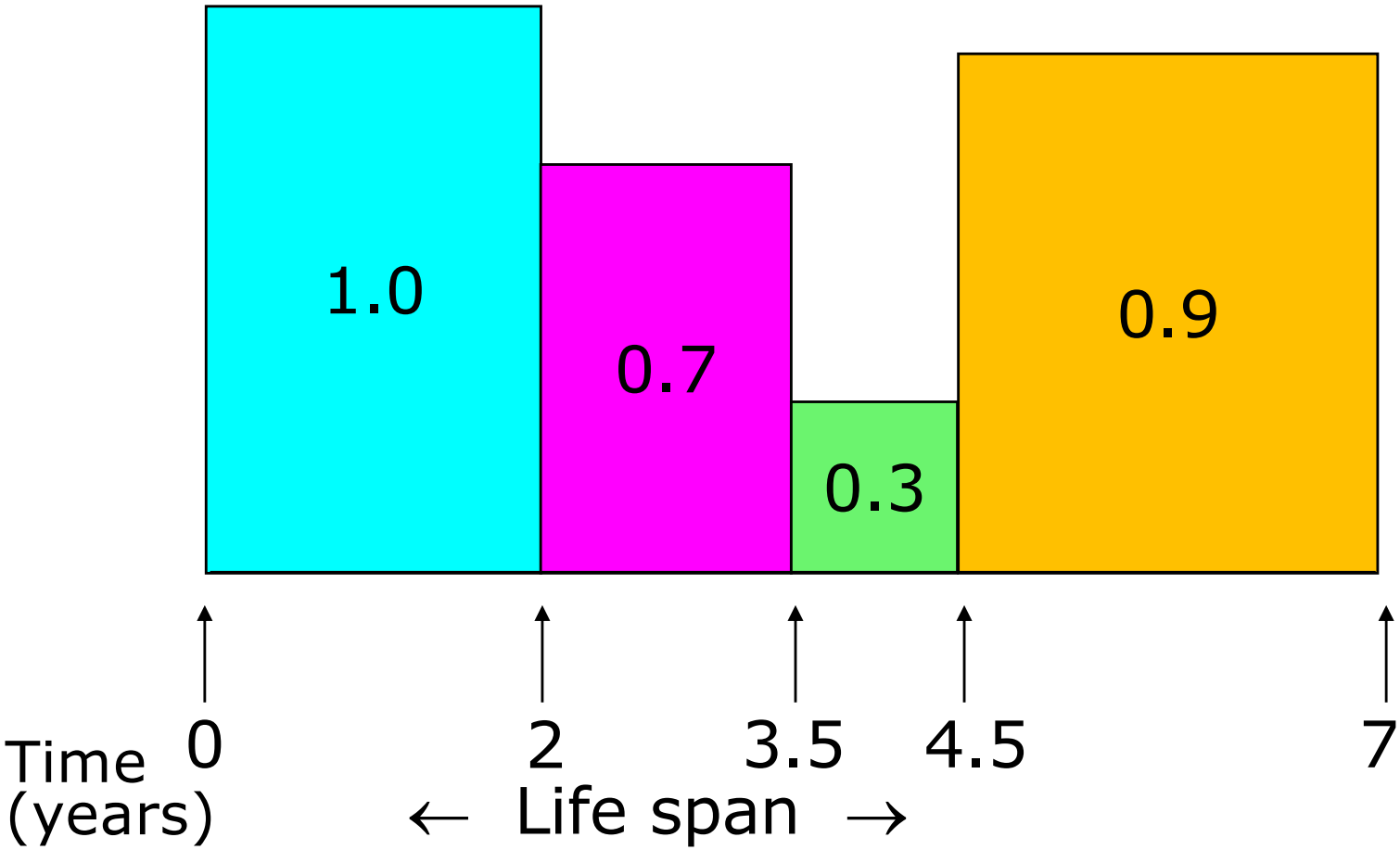
Model Types

- Decision trees
  - Schematic representation of uncertain events/consequences of different alternatives
- Cohort state transition models
  - Dynamic model that captures disease progression and other events
  - Simulates a homogeneous cohort
  - Usually deterministic
- Individual-based models / microsimulation
  - Stochastic dynamic model
  - Simulates individuals
  - Most flexible model type

Health Outcomes

- Disease-specific
  - Intermediate clinical markers
  - Cases averted
  - Events averted
- Generic
  - Lives saved / deaths averted
  - Life-years gained
  - Quality-adjusted life-years (QALYs) gained

Quality-Adjusted Life-Years



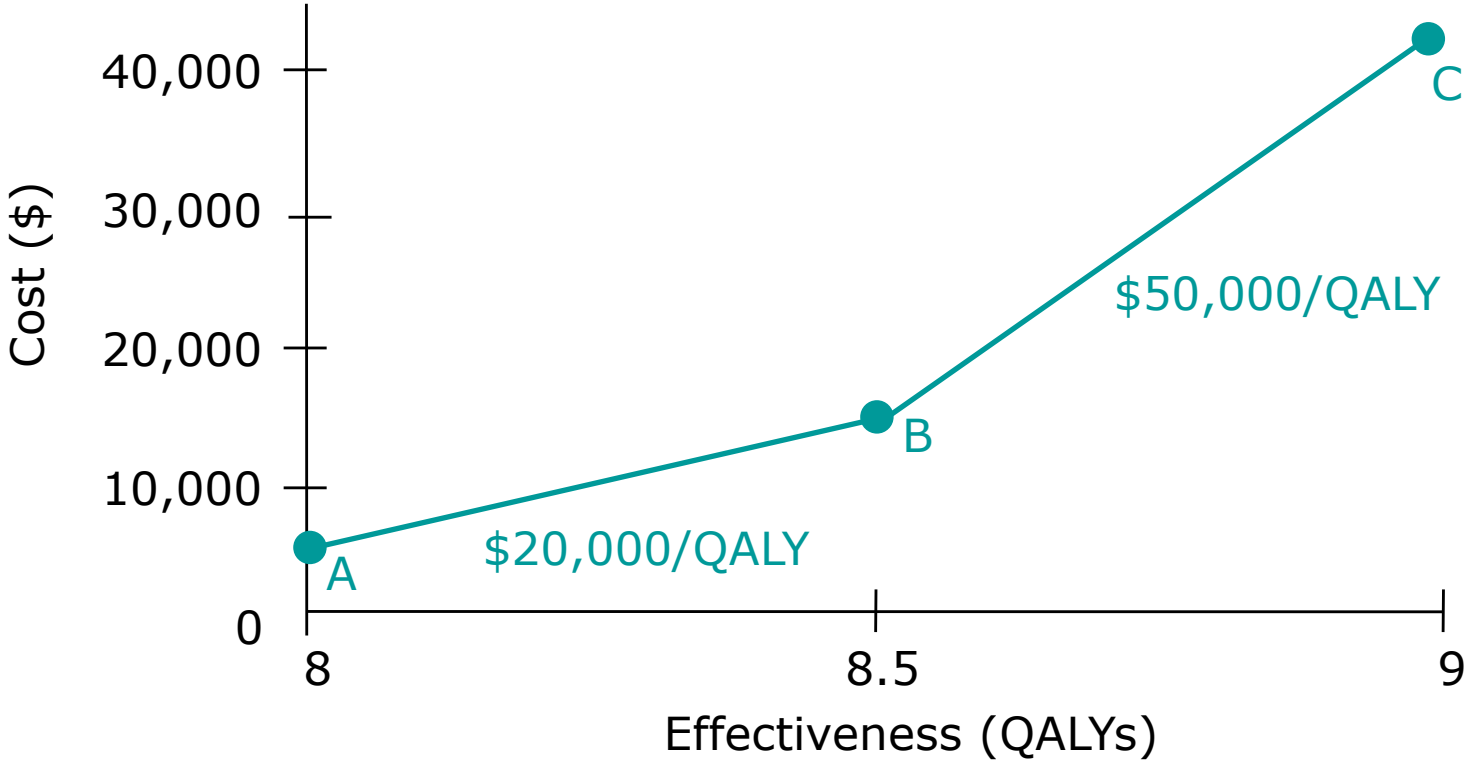
$$QALYs = (2)(1)+(1.5)(.7)+(1)(.3)+(2.5)(.9) = 5.6$$

Costs

- Formal healthcare sector
  - Facilities and resources
  - Drugs and devices
  - Personnel time
- Informal healthcare sector
  - Patient time
  - Unpaid caregiver time
  - Transportation costs
- Non-healthcare sector
  - Legal or criminal justice
  - Education
  - Housing

Cost-Effectiveness Analysis

- Subset of decision analytic questions where the objective is to balance costs and health benefits
- Defined willingness-to-pay per unit of health benefit (also called cost-effectiveness threshold)



Strengths and Challenges of Decision Modeling

Strengths of Modeling

- Clarifies decision-making
- Can use data from different sources
- Allows explicit and systematic characterization of uncertainty
- Extrapolates short-term observations into long-term outcomes
  - Can translate intermediate endpoints into life-years or QALYs gained
- Encourages “what if” analyses

Challenges of Modeling

- Validation issues
  - Model may be incorrectly specified (wrong structure)
  - Data to inform input parameter values may be lacking or of poor quality
- Not all decision considerations lend themselves well to modeling
- Communication issues
  - Transparency
  - Trust

Decision Tree Example

Simple Decision Tree

- Viral encephalitis can be caused by herpes virus (HVE) or other viruses (OVE); Pr(HVE) = 52%.
- Untreated HVE leads to death or severe sequelae in 71%; for OVE the figure is 1%.
- A drug, vidarabine, decreases mortality or severe sequelae due to HVE from 71% down to 36%.
- Side effects cause an increase in mortality among OVE patients treated with vidarabine from 1% to 20%.

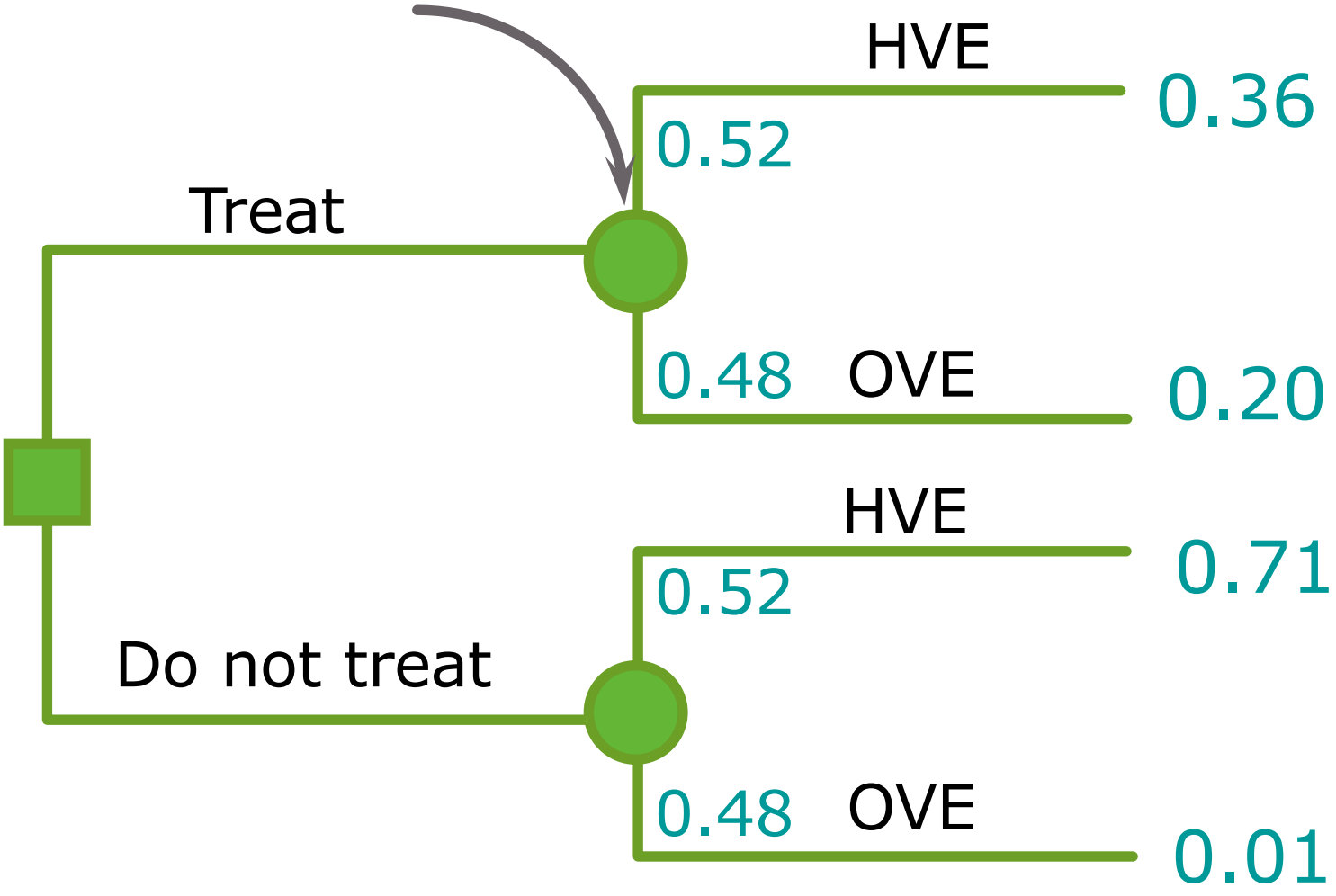
To treat or not to treat

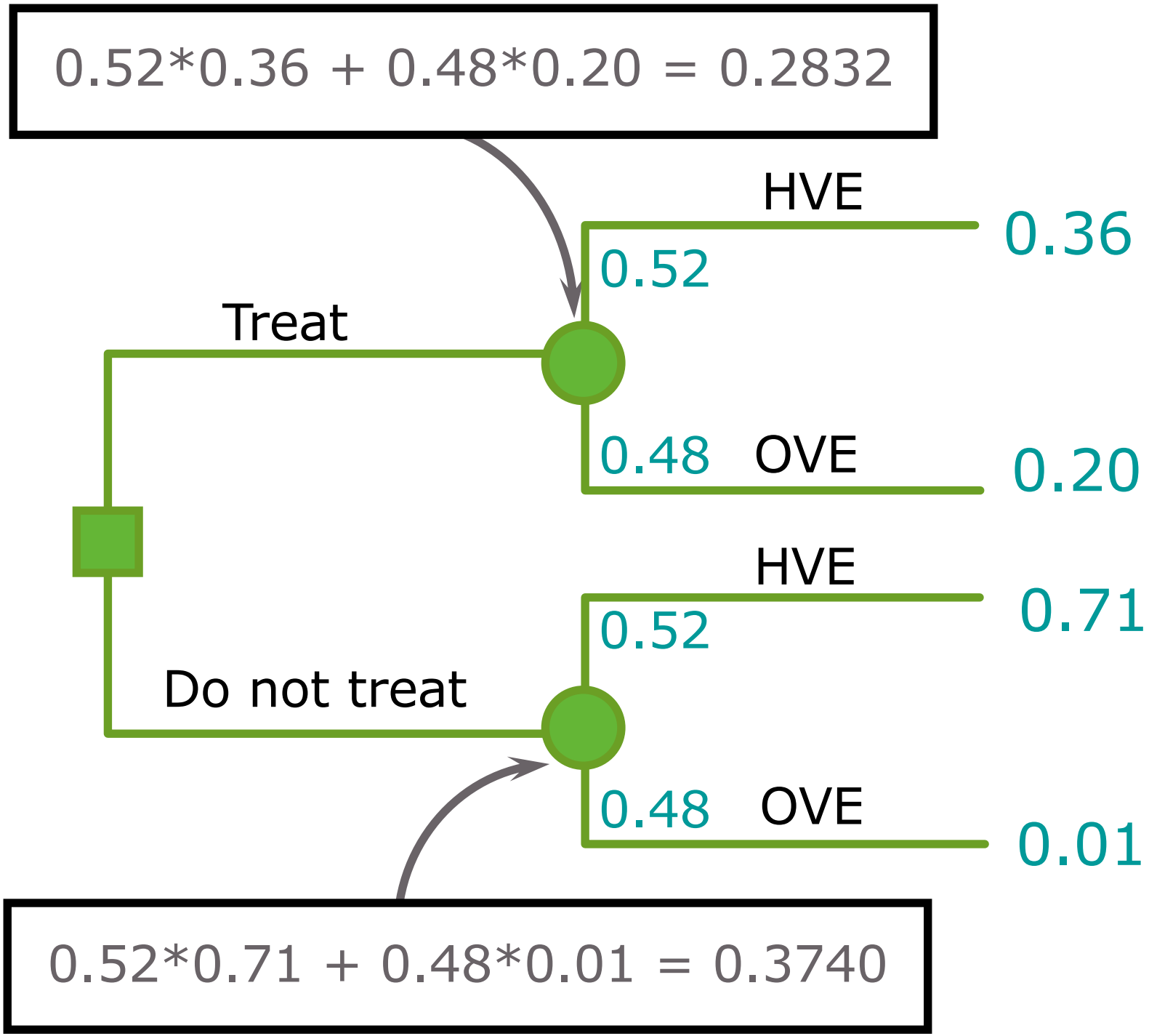
Outcome = Pr(mortality or severe sequelae)

Define Model Parameters

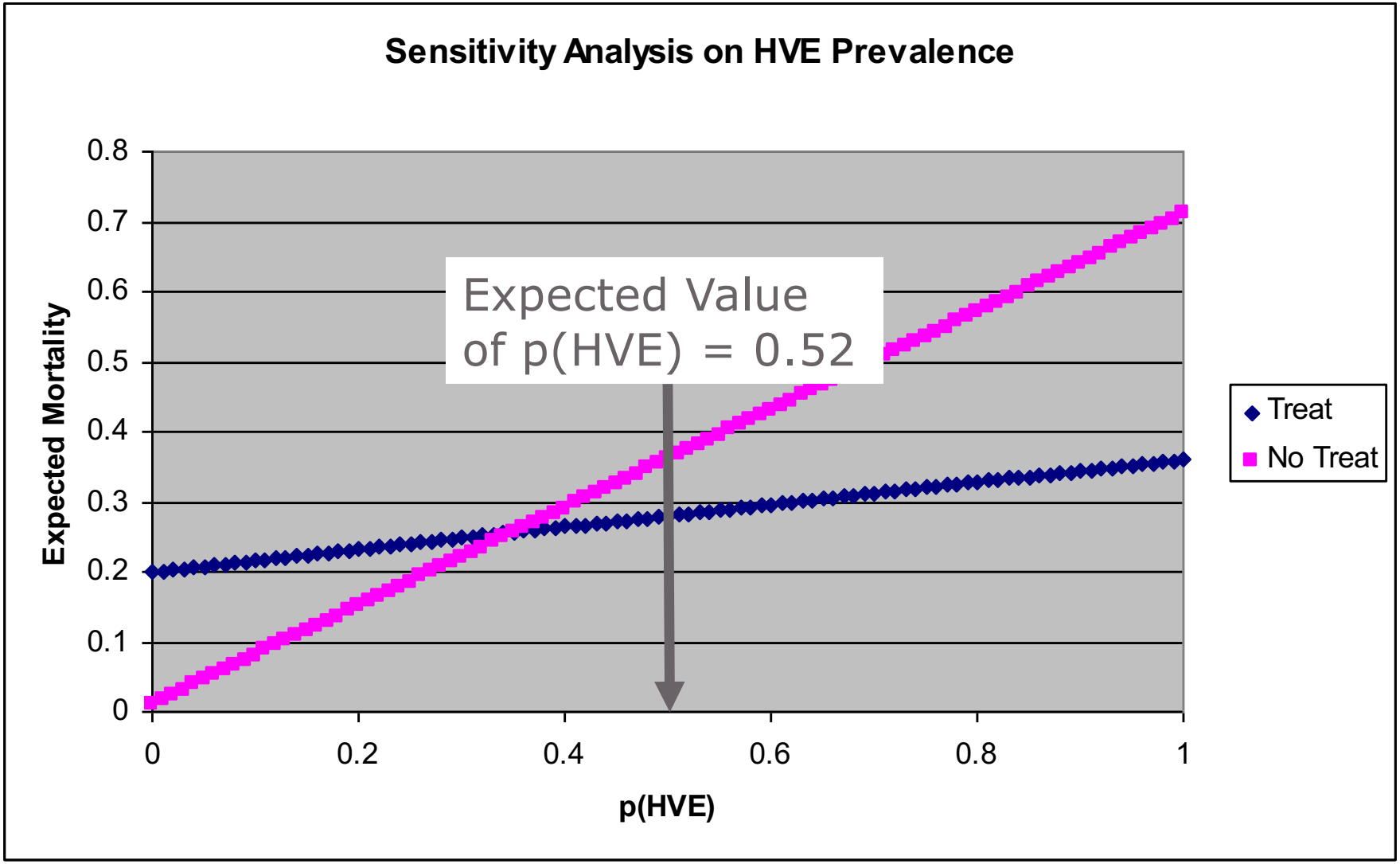
Variable	Variable Name	Value
Prevalence of HVE	p_HVE	0.52
Probability of complications (death or sequelae) without treatment		
HVE	p_HVE_comp	0.71
OVE	p_OVE_comp	0.01
Probability of complications (death or sequelae) with vidarabine treatment		
HVE	p_HVE_comp_tx	0.36
OVE	p_OVE_comp_tx	0.20

0.52*0.36 + 0.48*0.20 = 0.2832

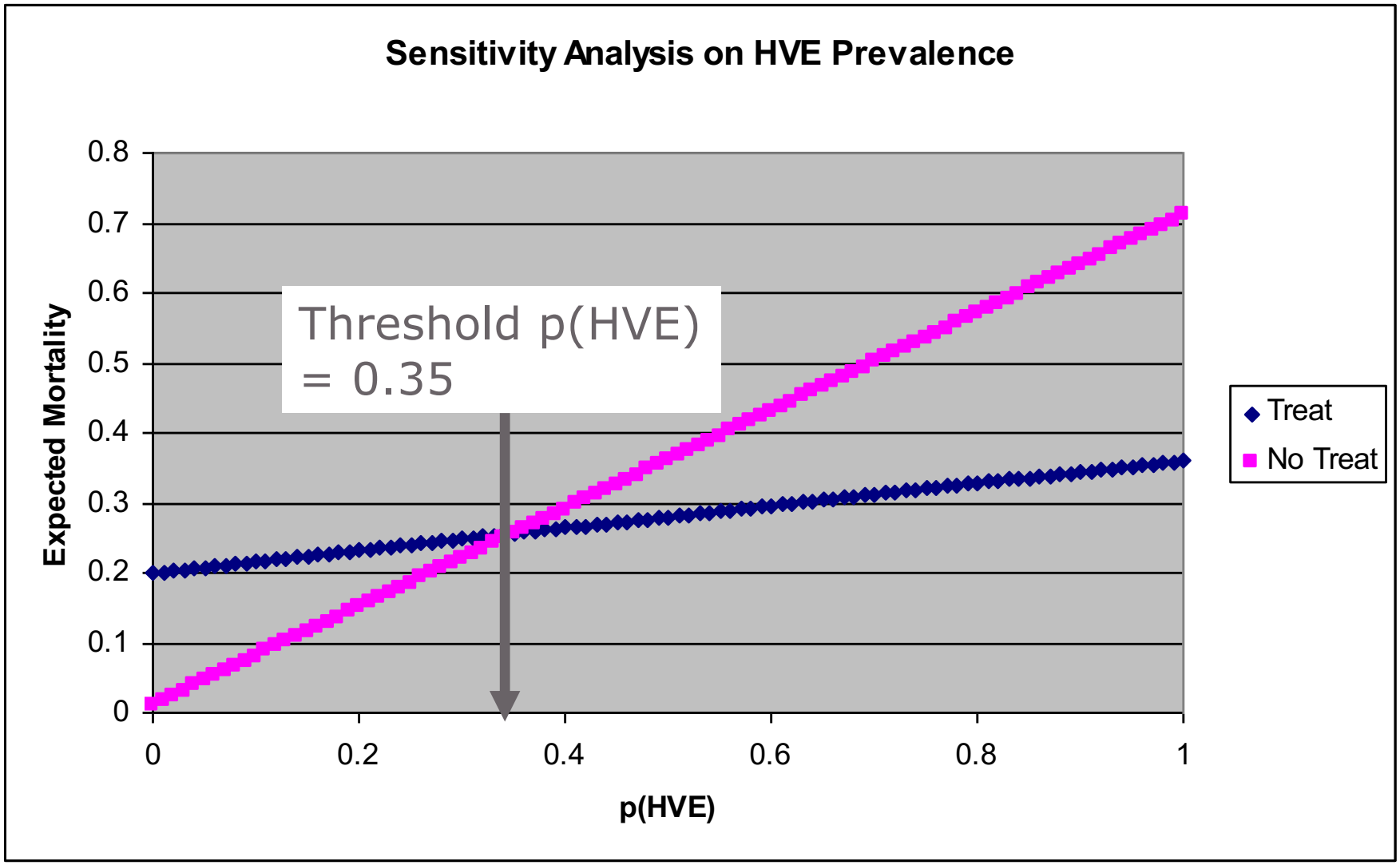



0.52*0.36 + 0.48*0.20 = 0.2832
HVE
0.36
0.52
Treat
0.48
OVE
0.20
HVE
0.71
0.52
Do not treat
0.48
OVE
0.01
0.52*0.71 + 0.48*0.01 = 0.3740

One-Way Sensitivity Analysis



Threshold Analysis

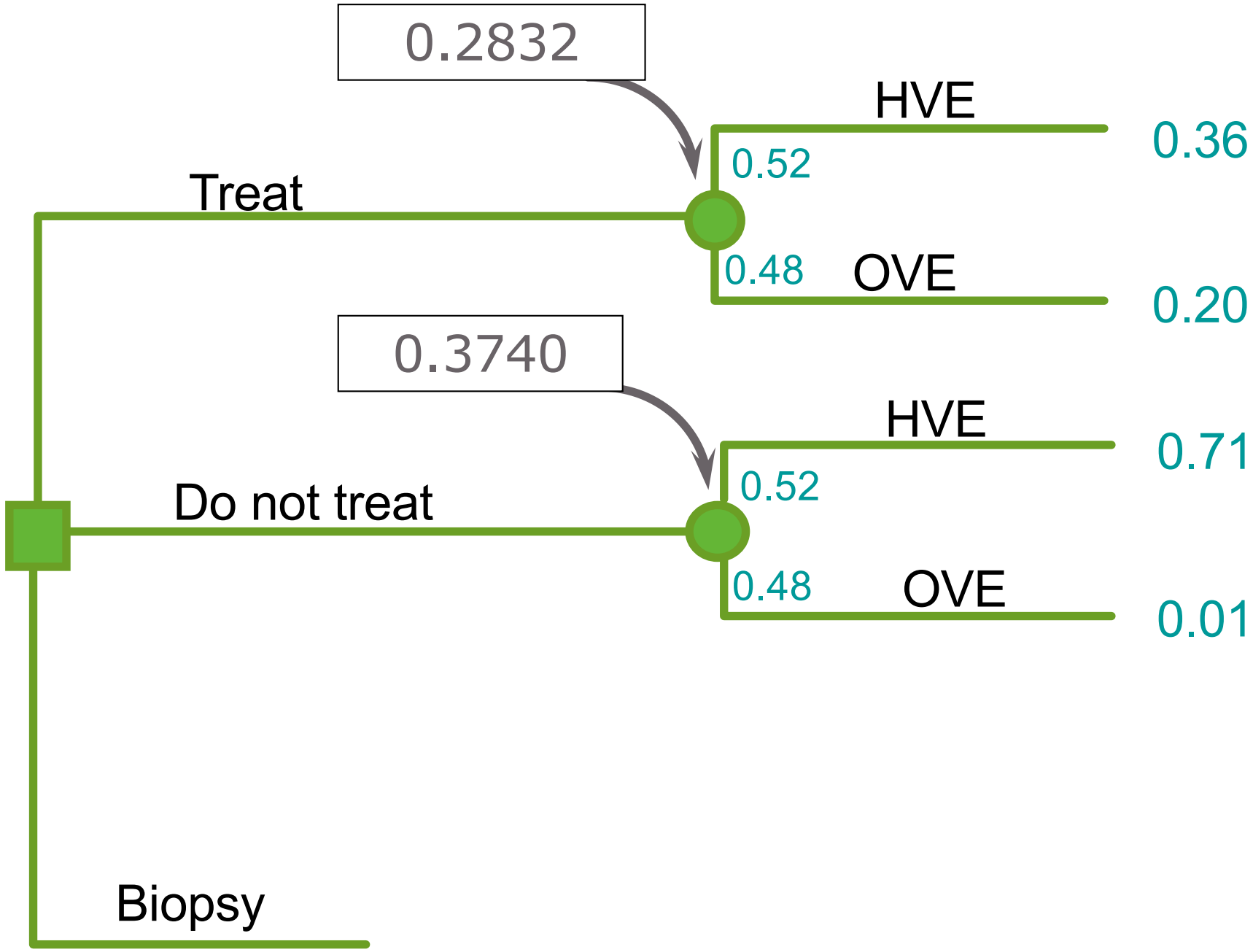


There is a third option

It is possible to obtain a definitive diagnosis by means of brain biopsy, but this procedure itself carries a rate of mortality or severe sequelae of 5%.

Add one more parameter

Variable	Variable Name	Value
Prevalence of HVE	p_HVE	0.52
Probability of complications (death or sequelae) without treatment		
HVE	p_HVE_comp	0.71
OVE	p_OVE_comp	0.01
Probability of complications (death or sequelae) with vidarabine treatment		
HVE	p_HVE_comp_tx	0.36
OVE	p_OVE_comp_tx	0.20
Probability of complications due to brain biopsy	p_biopsy_comp	0.05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Do not treat
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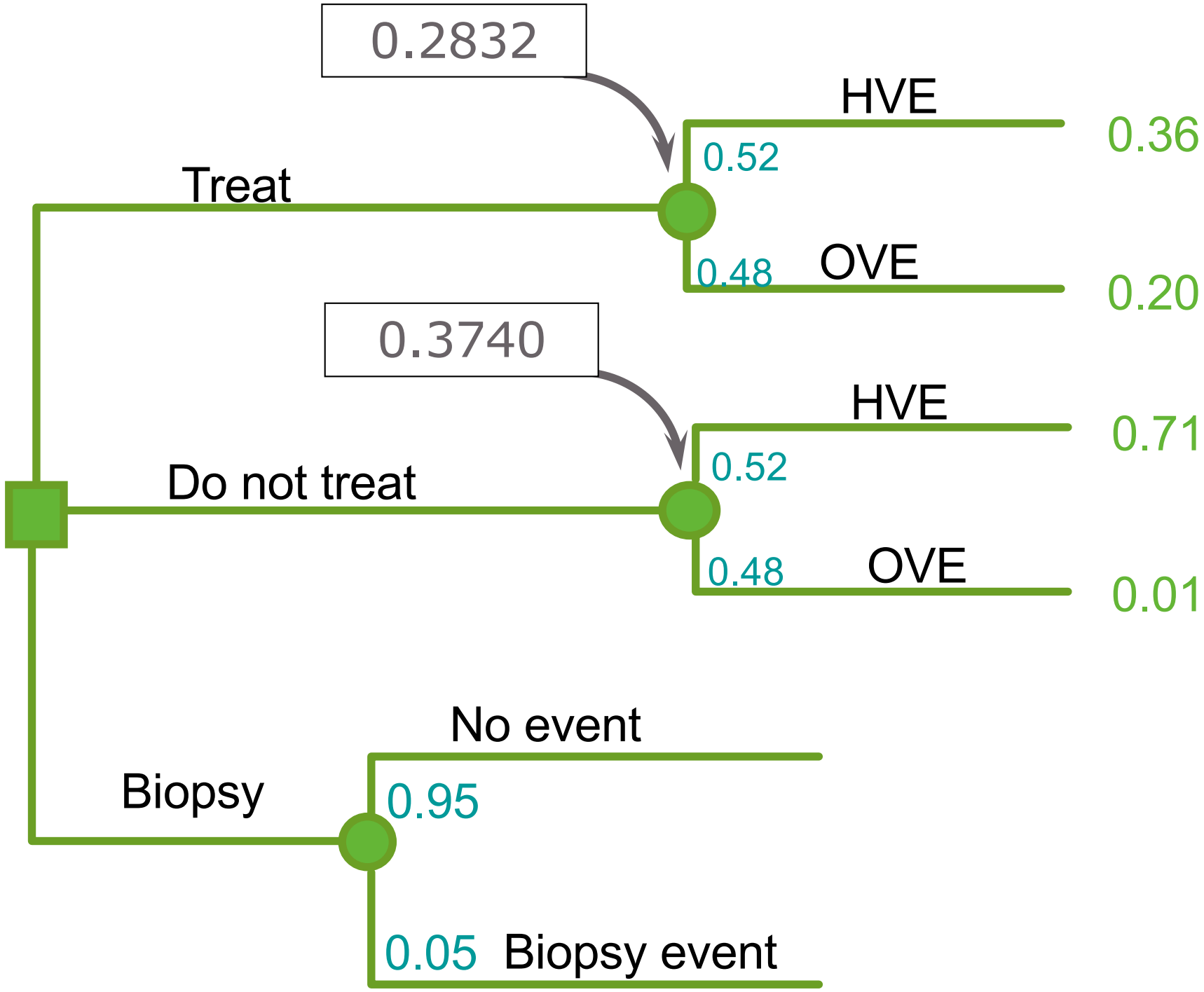
OVE
0.01
Biopsy


0.2832
HVE
0.36
0.52
Treat
0.48
OVE
0.20
0.3740
HVE
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Do not treat
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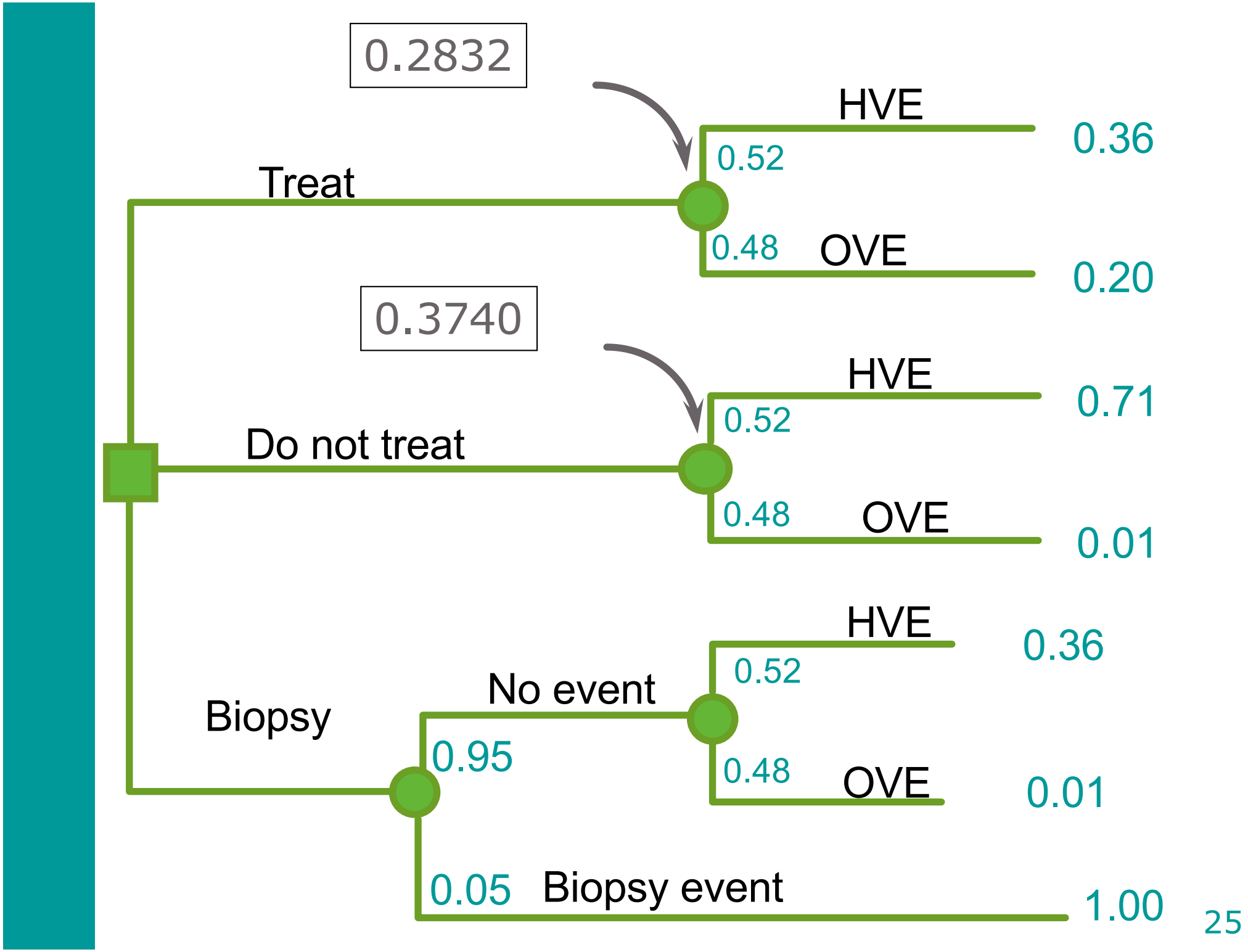
OVE
0.01
No event
Biopsy
0.95
0.05
Biopsy event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Do not treat
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OVE
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No event
Biopsy
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0.48
OVE
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Biopsy event
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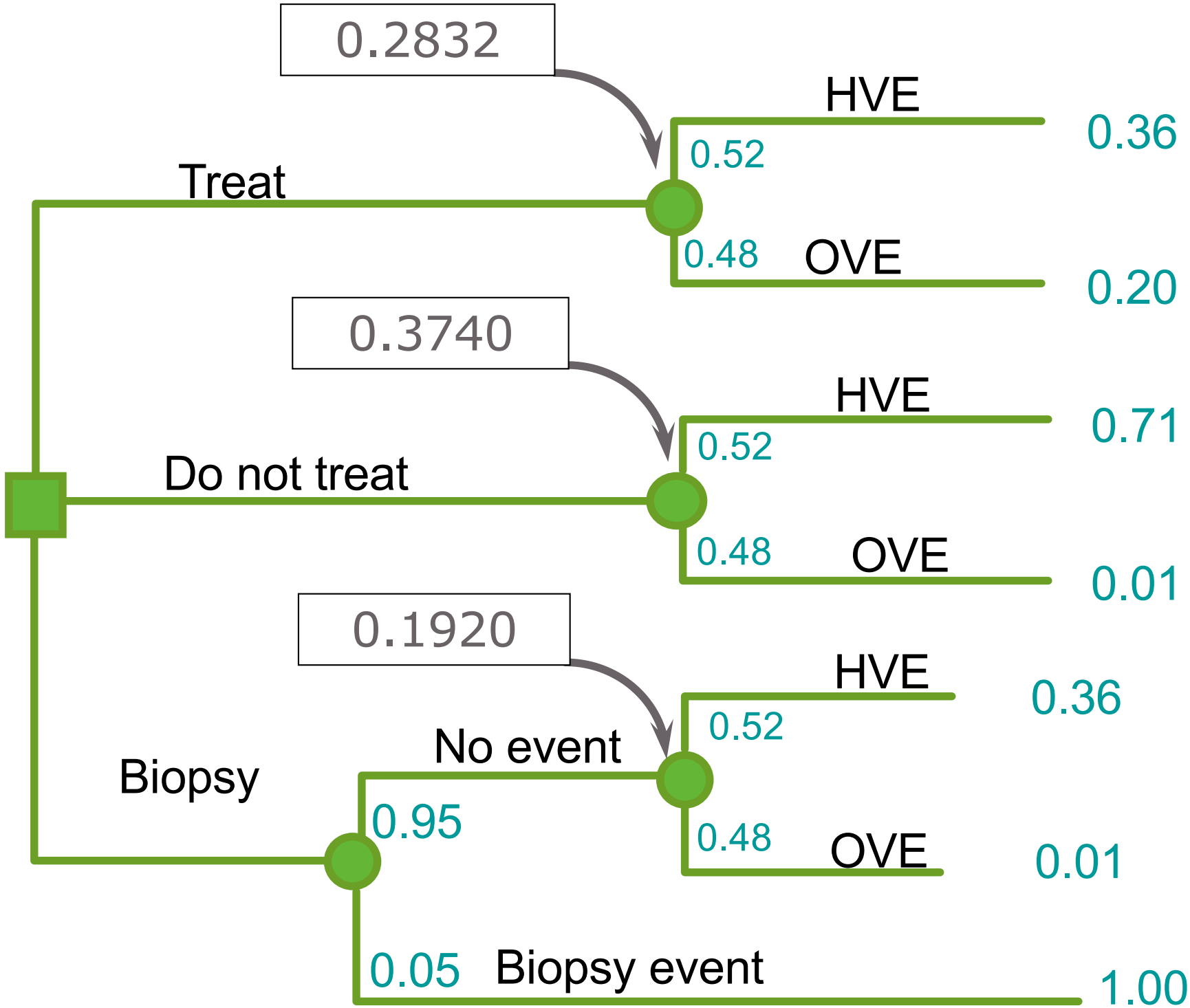
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Biopsy event
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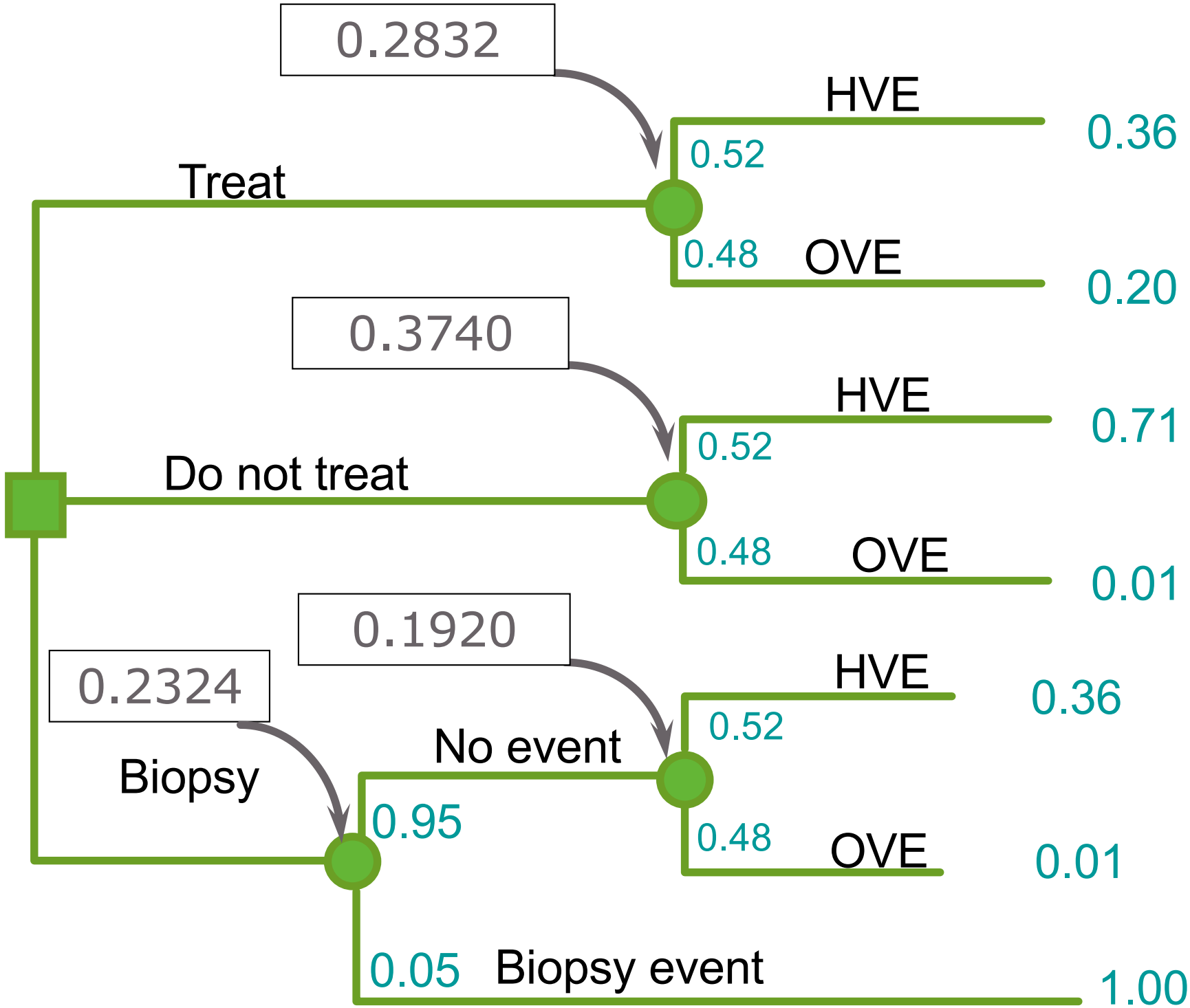
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HVE
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No event
Biopsy
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OVE
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Biopsy event
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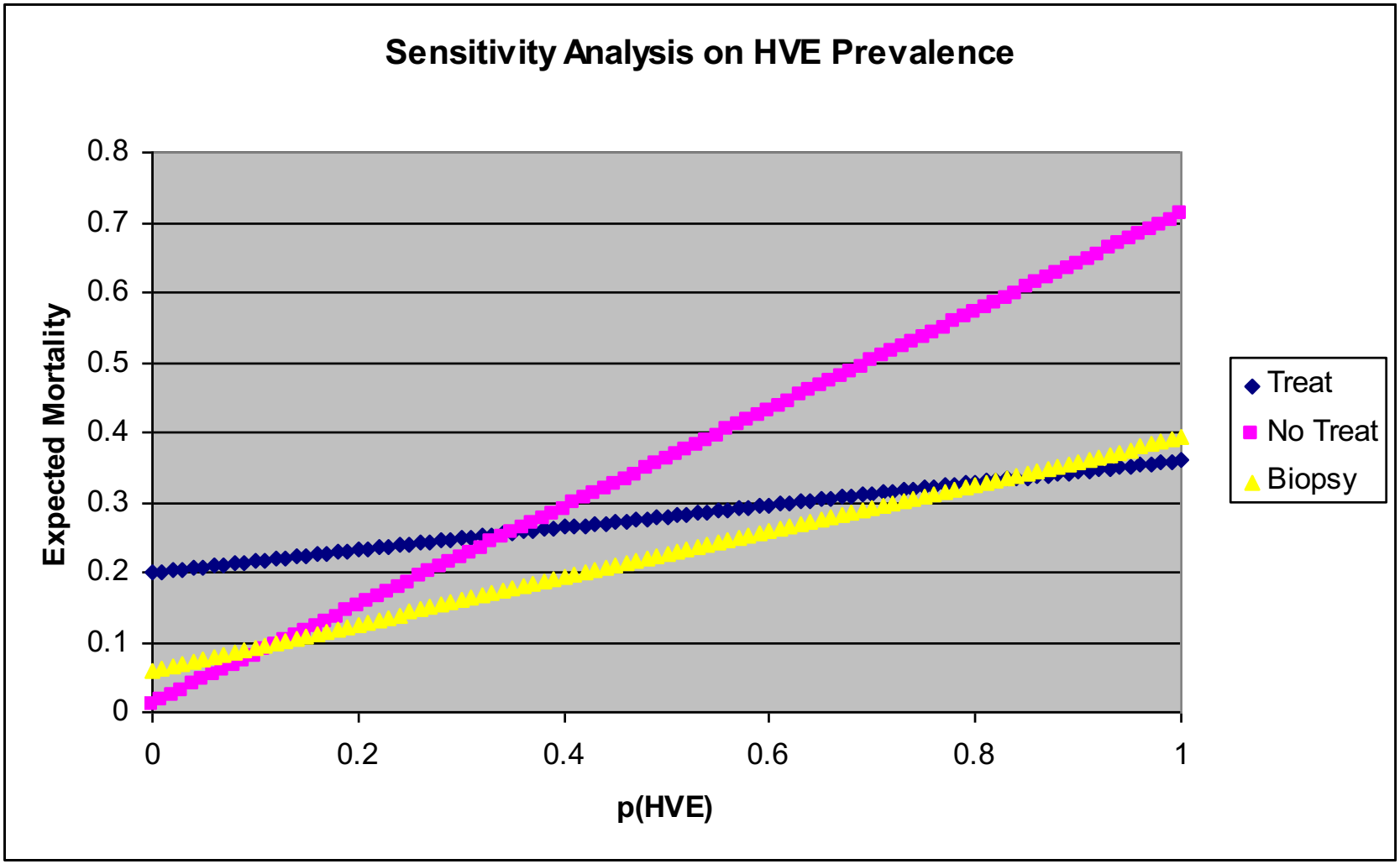
One-Way Sensitivity Analysis



Cohort State-Transition Model Example

CDX2 Biomarker Testing

- Adjuvant chemotherapy is not recommended for patients with average-risk stage II colon cancer (T3N0)
  - Thus, these patients are usually treated with surgery alone
- Lacking CDX2 biomarker expression (CDX2-negative) predicts responsiveness to adjuvant chemotherapy
- In the absence of chemotherapy, CDX2-negative patients had poorer 5-year disease-free survival compared with CDX2-positive patients
  - Survival was improved and recurrence reduced in CDX2-negative patients who received adjuvant chemotherapy

Question

What is the **cost-effectiveness** of testing for the absence of CDX2 biomarker expression followed by adjuvant chemotherapy for average risk stage II colon cancer patients from the healthcare sector perspective?

Decision model

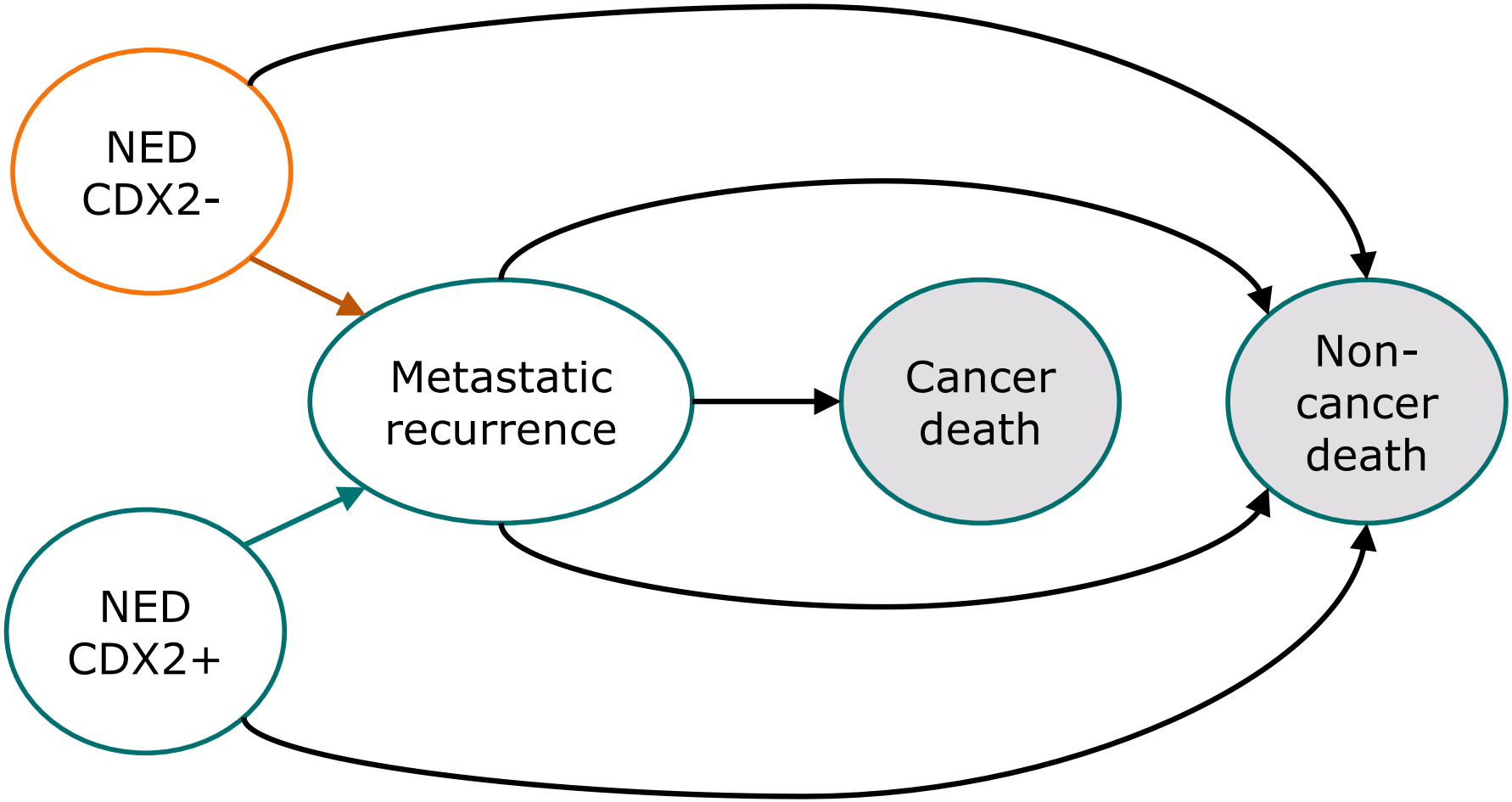
- **State-transition model** to simulate a hypothetical **cohort** of 65-year-old patients with newly-diagnosed average-risk stage II colon cancer patients over a lifetime under two interventions:

1. Test for CDX2 biomarker followed by adjuvant chemotherapy for CDX2-negative patients
2. No CDX2 testing and no adjuvant chemotherapy for any patient

Decision model

- All stage II colon cancer patients start the simulation with no evidence of disease (NED) following surgery
- A proportion of these patients (7.2%) are CDX2-negative and would be identified if tested
- Each month, simulated patients face a risk of developing recurrence and a risk of dying from non-cancer-related causes

State-transition Diagram



Model Parameters

Parameter	Value
Proportion CDX2-negative	0.072
Monthly rate of recurrence in CDX2-positive patients	0.004
Recurrence rate in CDX2-negative compared to CDX2-positive patients – hazard ratio	2.96
Recurrence rate in CDX2-negative patients receiving chemotherapy compared to no chemotherapy – hazard ratio	0.86
Monthly risk of metastatic disease mortality	0.047
Monthly risk of non-cancer mortality	Life Table

Utilities

Health State	Utility
NED no chemotherapy	0.74
NED with chemotherapy	0.67
Metastatic recurrence	0.25
Dead	0

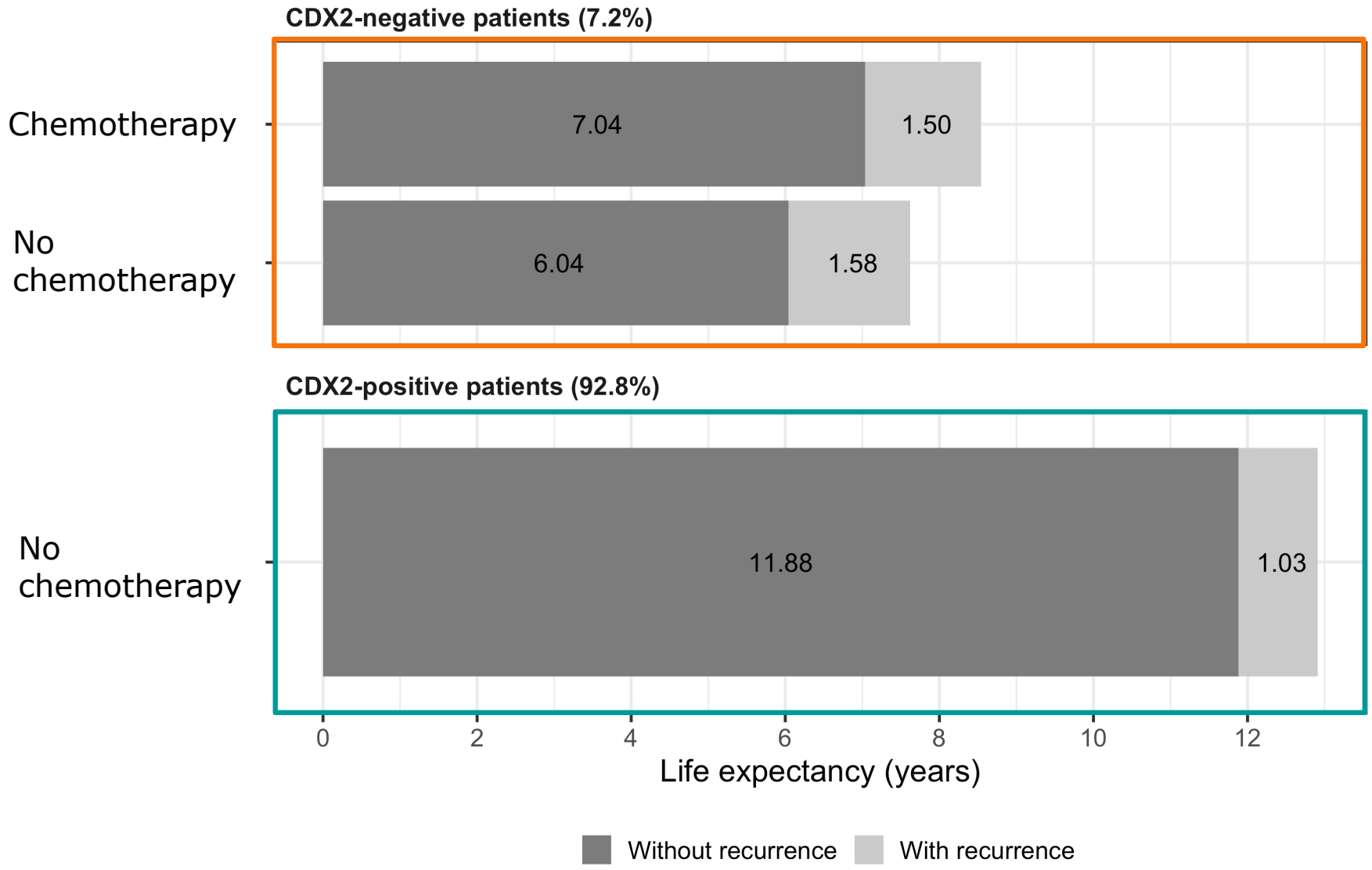
Costs (2020 USD)

Item	Cost ($)
CDX2 biomarker test	116
Adjuvant chemotherapy	1,443
Chemotherapy administration costs	326
Annual cancer care with no evidence of disease	
Initial phase (first year)	40,353
Continuing phase (second year onward)	2,291
Annual cancer care with metastatic recurrence	10,149
Terminal, by cause of death from colon cancer	55,209
Terminal, by cause of death from other causes	11,932

Analysis

- Lifetime (remaining) time horizon
- Health impact: life-expectancy
- Cost-effectiveness analysis
  - health care sector perspective
  - Costs and QALYs discounted at 3% per year

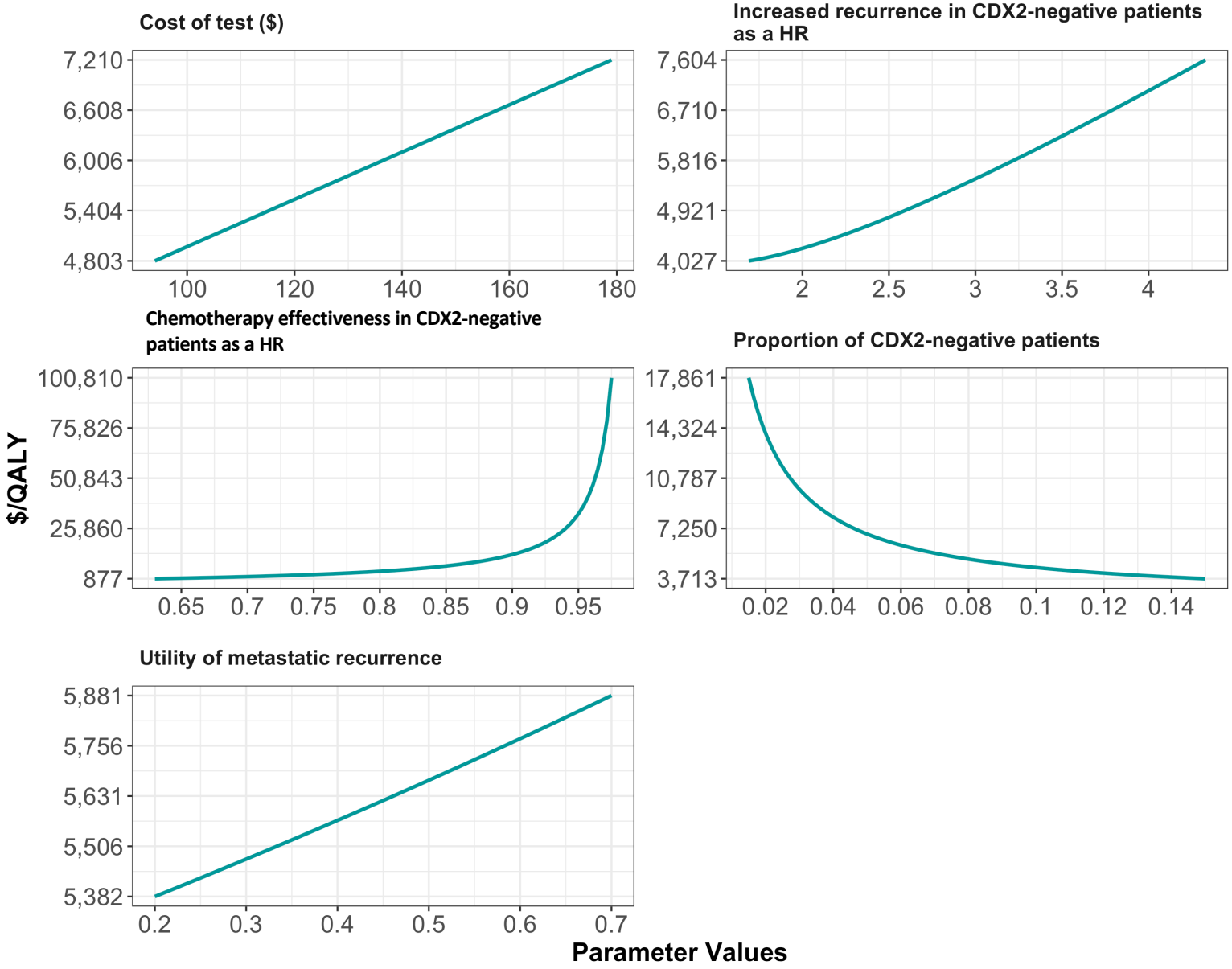
Health Impact



Cost-Effectiveness Results

Strategy	Costs	QALYs	ICER
No testing and no adjuvant treatment	$ 89,797	6.838	-
Test all & treat CDX2-negative patients	$ 89,991	6.874	$ 5,469

One-way Sensitivity Analysis



Choosing your model type

Decision Trees

- Advantages:
  - Simple
  - Intuitive, clear visual representation
- Best for decisions made over a short time horizon
  - Clinical decisions (test, treat, etc.) for acute illness
  - Lifetime consequences can be quantified by using (pre-computed) life-expectancy as terminal value
- Not as appropriate in applications where there are repeated decisions or events
- Can be used to represent upfront strategy decisions, followed by a dynamic model for longer-term outcomes

Cohort State-Transition Models

- Advantages:
  - Represents dynamic processes
  - Still relatively simple
  - Computationally efficient
- Best for dynamic processes that
  - Can be represented with a reasonable number of states
  - Don’t dependent too much on individual heterogeneity (e.g., homogeneous cohort is a good approximation)
  - Minimal dependence on clinical history or time-in-state
- Usually deterministic (generate mean outcomes), but can be simulated stochastically

Quick Note: Compartmental Models

- Dynamic models similar to state-transition models, with key differences:
- Open population (not a cohort)
- Transition probabilities or rates can depend on population state → ***infectious processes***
  - e.g., risk of infection depends on prevalence of infection in the population

Stochastic Individual-Based Models

- Includes: microsimulation models, agent-based models
- Advantages:
  - Represents ***stochastic*** dynamic processes
  - Most flexible model type
  - Can capture ***complex dependencies*** on individual features, clinical history, time-since-event
  - Can capture interactions (agent-based model, network model)
- Best when a state-transition model is not sufficient
- Disadvantages
  - Computationally intensive
  - Data intensive

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