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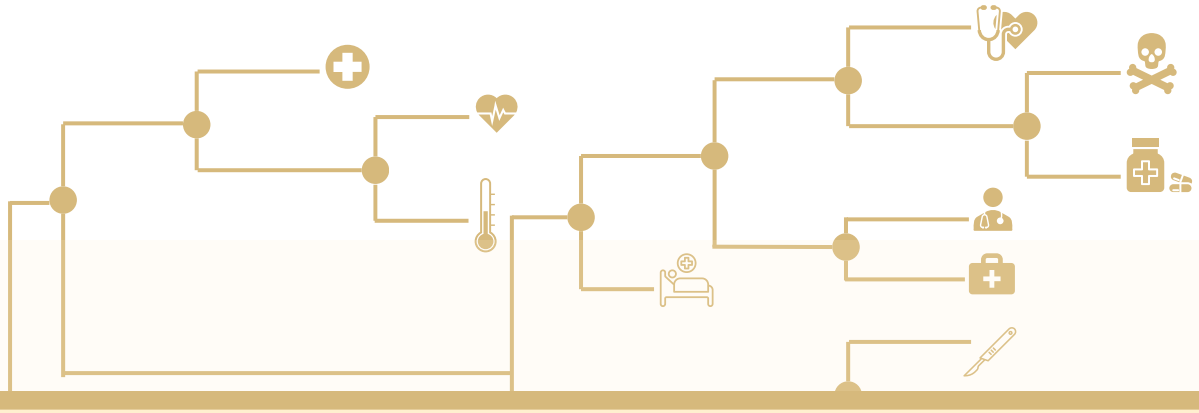

Quick Start Guide to Health Economic Modeling

(Using Decision Trees, Markov Models, and/or Microsimulation)

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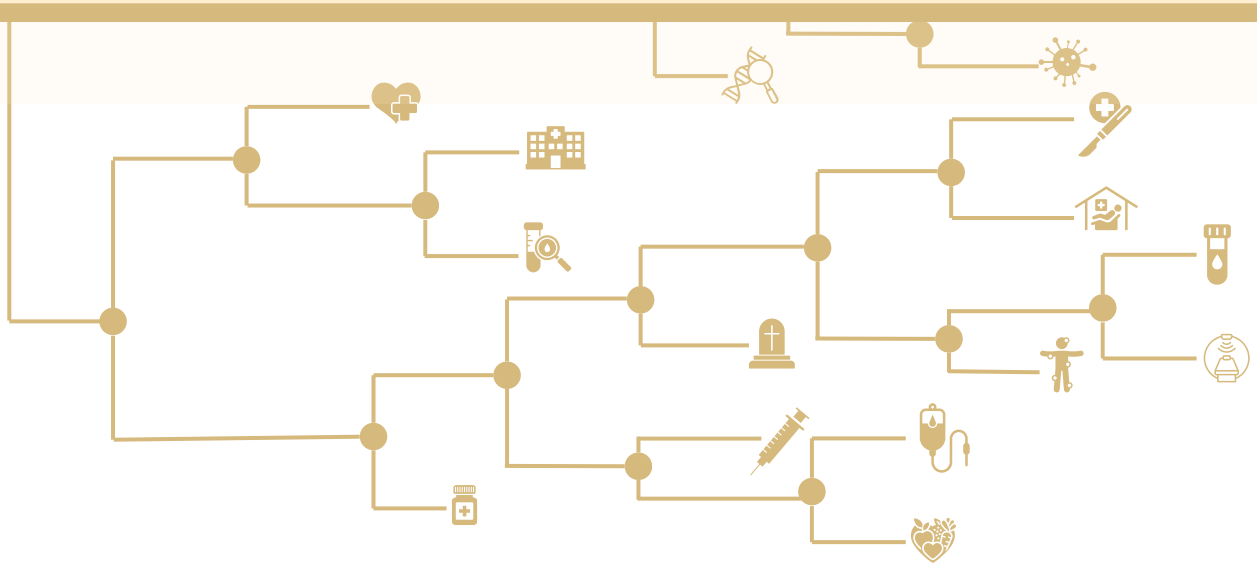

WORKING DOCUMENT

A Note from the Authors:

This is meant to be a tool for understanding the steps to creating a decision trees, Markov models, and/or microsimulation models for health econ omic modeling. Simulation modeling is a technique used to build out the progression of a health condition to analyze the interactions of biology, infrastructure, and finances. These models allow for the ability to test how different strategies of care for a condition would impact the cost, quality of life, and outcomes of the population.

This is meant to be a guide for individuals who are attempting to create a beginner model. It cannot replace the valuable insights from trainings, mentorship, and collaborations. This guide does not provide all the information needed to create a model but is intended to be a supplement to formal training and methods papers.

Models can be used to analyze diseases, disorders, injuries, or more. To encompass all of these, the term "Condition" is used throughout this guide.

Below are a few textbook recommendations to help you build a deeper understanding:

- Hunink MGM, Weinstein MC, Wittenberg E, Drummond MF, Pliskin JS, Wong JB, and Glasziou PP, eds. 2014. Decision Making in Health and Medicine 2nd edition. Cambridge, UK: Cambridge University Press. DOI: https://doi.org/10.1017/CBO9781139506779

- US Second CEA panel book: Neumann PJ, Sanders GD, Russell LB, Siegel JE, and Ganiats TG, eds. 2017. Cost-Effectiveness in Health and Medicine 2nd edition. New York: Oxford University Press. ISBN: 9780190492939

- Briggs, A., Sculpher, M. and Claxton, K., 2006. Decision modelling for health economic evaluation. Oup Oxford. DOI: https://doi.org/10.1093/ije/dym062

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Creating a Health Economic Decision Model

1 Understand Your Condition

It is important to fully understand the condition being modeled. Consider seeking clinical assistance to understand treatments, costs, progression, and typical side effects.

2 Complete a Literature Review

Spending time now to understand how other models were created on your specific condition will help save time on future steps. It also will help you understand common assumptions and where research on the topic is missing.

3 Determine Model Factors

To create a model you need to determine a population to model on, which perspective to take (typically healthcare or societal), and the strategies. Map out how the variables differ by strategy type.

4 Determine Model Type

Based on your literature review and your research question, determine which model is the best fit. Some options include: decision trees, Markov models, Microsimulation.

5 Build Out Model Framework

For many models, a bubble diagram is a great starting place. Determine how long each cycle should be and how long the model should run. Create a framework that illustrates the various condition states that the cohort/person moves through.

6 Data Collection

Prepare to find and collect the data needed for the model (probabilities, costs, and utility) but expect to collect more as you see what you are missing. Keep clear records of data sources, data points, and key assumptions.

7 Add Probabilities

Start adding probabilities to your model for each decision arm or branch of the model. Each decision node should have probabilities that add to 1 on the decision arms.

8 Add All Parameters

Add remaining output parameters, discounting, and cycle correction. When adding costs, ensure that all parameters are converted to one currency and year (example: 2024 USD). If using software, it is easiest to complete the status quo then copy it for all strategies and edit where strategies vary.

9 Validate The Model

Complete an internal validation to ensure that the model is matching expected outputs. If you can, complete an external validation to further prove the validity of your findings.

10 Run a Cost-Effectiveness Analysis

This can be run throughout the process for testing but this should be the point where you have a cost-effectiveness analysis that is accurate to your model and validation.

*Please note that there is often a need to revisit and refine earlier steps while building a model.

11 Additional Analyses

Run a one-way sensitivity analysis to determine uncertainty in the model. Depending on your research question you may also need other analyses like two-way sensitivity, probabilistic sensitivity, or value of information.

12 Formalize Results

Compile all your results, assumptions, and parameter list to present findings as a policy brief or publication. Consider the CHEERS checklist for publication to ensure all information is included.

Questions that Selected Models* Excel at Answering

Simulation modeling is a technique used to build out the progression of a health condition to analyze the interactions of biology, infrastructure, and finances. These models allow for the ability to test how different strategies of care for the condition would impact the cost, quality of life, and outcomes of the population.

Note: The models covered in this guide are meant to make population-level decisions and not for individual decision-making.

There are different factors that can help determine if modeling is right for your question. Note that even if you have some negatives, a model may still be possible.

- Modeling based on a clinical trial
- Other models for disease exist
- Modeling strategies that would be expensive or unethical to test in the real world
- Multiple data sources are needed to answer a question
- Future predictions beyond existing data

- Minimal Data Exists
- Want an answer that can easily be solved without all the computation of a model
- Contagious Diseases (Dynamic modeling is a better options for these diseases)

*Decision Trees, Markov Models, & Microsimulation Models

Understanding your Condition

It is best practice to build out a model based on the condition and research question instead of the data. Here are some questions to help you get started researching.

How does it progress?	How long does the condition take to progress?	What does a standard of care treatment look like?
How long does treatment take?	What are common side effects (short or long term)?	What other treatments are available?
Are there screening or diagnostic tests ?	Which parts of treatment have costs?	How does it effect the length and quality of life?

If you do not have a clinical background, it can be helpful to talk with clinicians to understand more about the condition and how treatment functions in practice. It may also bring to light common issues within treatment.

Initial Literature Review

Before you start building your model, it is important to start with a literature review. This process of reviewing papers and data will continue throughout the entirety of your project but the initial search can help set you up for more success.

An initial literature review helps in a few key areas:

1. Find similar models to your question to ensure feasibility
2. Find common gaps in research that might be worth investigating
   - Look at recent high profile clinical studies to see if a model has been built yet
3. Learn common assumptions used to model your condition

If you have a very specific research question that is a direct response to a policy, an initial literature review will still provide you an understanding of how other researchers have modeled the condition. For some conditions, there are standardized models that can be used.

If you are researching without a strict question about the condition in mind, an initial review will provide a lot of insight into where research is missing and how your objectives offer an opportunity to advance previous research findings.

Just remember to always have a clear listing of the papers you review!

Search Terms to get you started*:

- Cost Effectiveness Analysis (CEA)
- Markov Model
- Microsimulation (model)

*try searching these plus your condition or strategy

Tufts Registry:

Created to help find papers on methods, and parameters for CEA models.

cearegistry.org

Tips For Reviewing Health Economic Modeling Literature

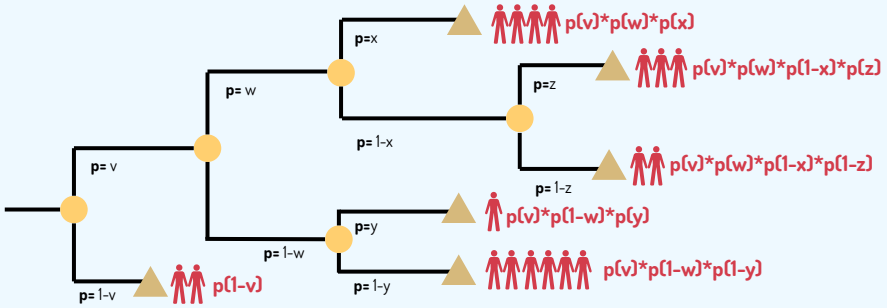
1. Methods sections provide a lot of information about how the model was built
   a. Take notes on model features: model horizon, population, model type, etc.
2. Check to see that the researchers have clear listing of their data sources
3. Look at the internal and external verification of the model
4. Look at the limitations and assumptions
5. Take note of the strategies compared in each model

Model Types

	Decision Tree	Markov Model	Microsimulation
	One Cycle	Multiple Cycles	Multiple Cycles
	Cohort	Cohort	Individual
	Single Events	Repeatable Events	Repeatable Events
	Cohort has same risk	Cohort has same risk	Individual risk factors
	Low Computation	Low to Medium Computation	Heavy Computation

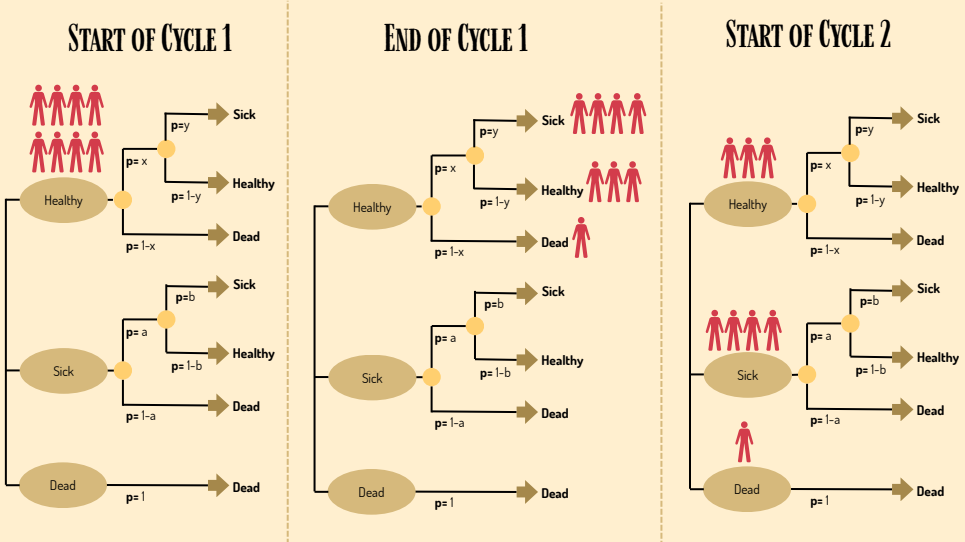
Decision Tree

The decision tree is run and the cohort outcomes are determined by the end node likelihood. Repeat events must be modeled for each time they occur. The model is repeated for each strategy and adjusted as needed.



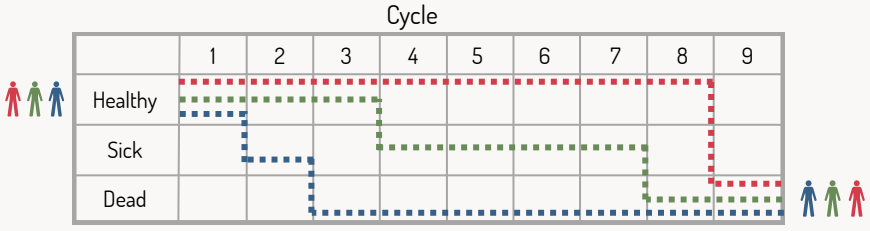
Markov Model

Markov models run on cohort probabilities but easily capture repeat events. The model is repeated for each strategy and adjusted as needed.



Microsim

Built as a Markov model but the population is run through the model one person at a time. This allows for individual risk to be included.



Model Perspectives

It is important to determine the perspective of your model. This will help determine which costs to include in the model. Common perspectives are healthcare and societal. However, it could be something else like payer perspective. For any perspective it is important to be able to explain why you included and excluded different metrics. If you are unable to find data for a societal perspective, a healthcare perspective can be run with the policy brief or academic paper mentioning the societal impacts. This can help provide context of the additional impacts from the condition.

Healthcare

This includes all costs that a healthcare system would incur like:

- Additional Training
- Treatments
- Tests

It is commonly used as the data tends to be more available. It is typically easier to capture all the healthcare costs from a procedure.

Societal

This includes all costs that a society would incur like:

- Loss of productivity
- Transportation
- Unpaid caregiving

This data is typically harder to acquire and the total societal impact is impossible to fully capture so a modeler must be able to explain why the particular selection of metrics were used.

Government

Although you may be asked to complete a model from the government's perspective, it would be best practice to choose either the societal perspective (when the government cares about all costs) or the healthcare perspective (if they are interested in the cost to an insurance program).

Payer

This includes all costs that a payer would incur like:

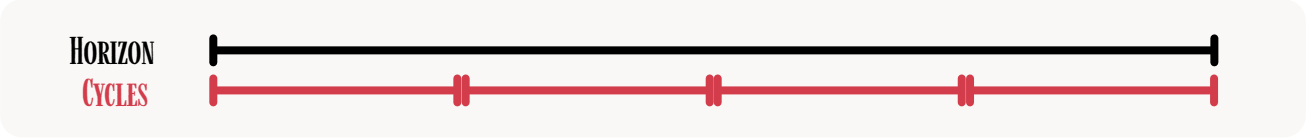
- Cost of appointments
- Cost of medication
- Costs of ambulance

These numbers are hard to determine in many health systems as payer costs may vary across many factors. However, this may be possible in systems with stable pricing.

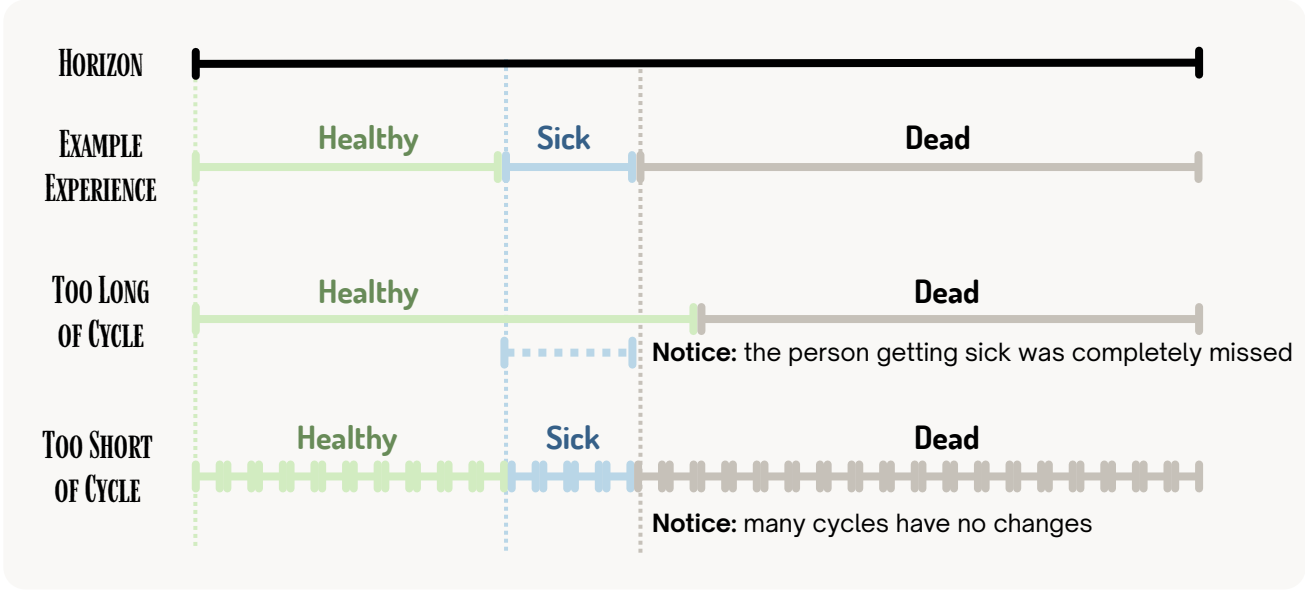
Cycle Length

One key component of building a simulation model is determining a cycle length. Many models use a year. However, there are many research questions and conditions that require a different time frame (e.g., pregnancy would need monthly or weekly and stroke might need daily or hourly.) Your initial literature review will reveal if a different length is commonly used for your condition.

The horizon is the entire length of your model (e.g., Lifetime). The cycle length is how you want to break that continuous time into segments (e.g., Yearly). Decision trees only run on a horizon.



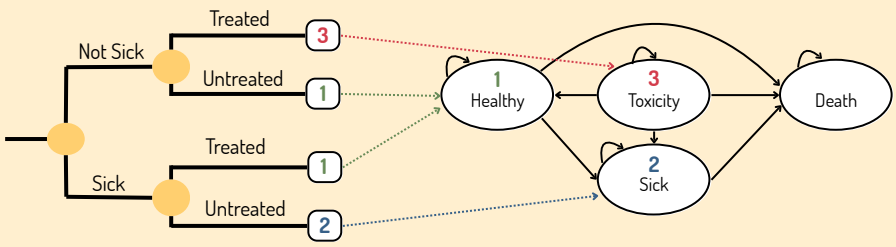
When determining cycle length, you need to balance the risk of longer cycles introducing competing risks against the high computational burden of shorter cycles, which may provide minimal additional information.



Ultimately, the cycle length should be determined by the condition including things like treatment length, time until progression, and acute vs chronic treatment.

Markov Tree

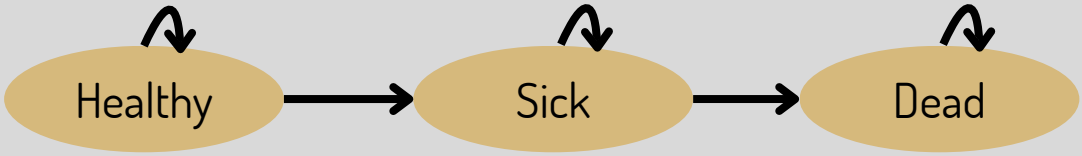
If there are a lot of short-term, upfront changes that are impacting the cycle length, consider creating a decision tree that flows into a Markov model. The tree will help determine how many people start in each health state.



Building a Bubble Diagram

Bubble diagrams are a visual representation of the process that a person will go through within the model. This step will help you determine the health states within the model.

Example



Rules of Bubble Diagrams:

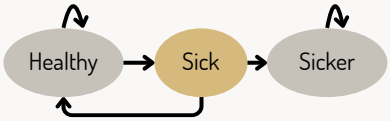
1. States can be repeatable, tunnel states or absorbing states.

Repeatable

Many states will be stayed in for multiple cycles. This is shown with a repeat arrow.

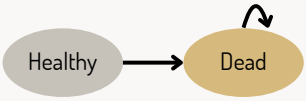
Tunnel

Tunnel states are only stayed in for one cycle. These can be used to take a count of an event. They do not have a repeat arrow.



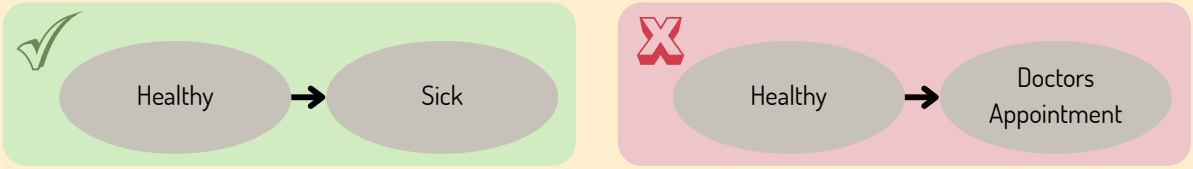
Absorbing

Once someone enters an absorbing state, they cannot leave it. This is typically death. It will have a repeat arrow but no other ways to exit the state.



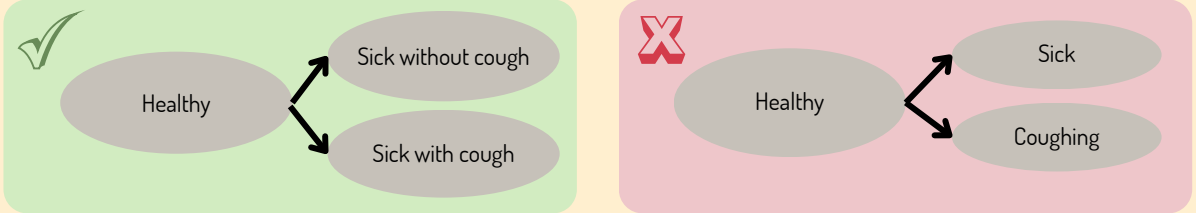
2. An individual must be able to stay in the state for the entire length of a cycle.

Example: For a year-long cycle, people can move to sick for a year but a doctor's appointment does not last a whole year.



3. Each state must be mutually exclusive. Each person can only be in one state at a time.

Example: If coughing is a side effect of being sick then it cannot be its own state because a person could be sick and coughing. They need to be made into states where all possibilities are captured.



Now that we have covered some rules, let's get started building one.

Steps

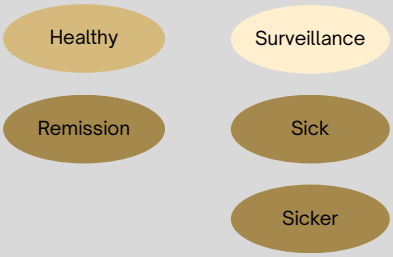
Example

My disease will start with everyone healthy. Initial symptoms will move an individual into a surveillance tunnel state where they will either heal naturally or progress. Individuals can then either stay in their disease state, progress, or enter remission. If their disease hits stage 3, then they have a chance of dying from the disease. All states have a chance of dying from causes not considered in the model. Since my disease takes a year to progress, I will use an annual cycle length.

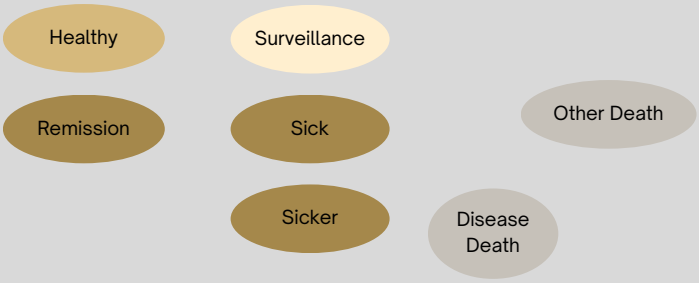
1. With the information you have collected, you will want to formalize your cycle length, starting states, and condition progression.

2. Identify the starting state(s) of your model. Will everyone start healthy? Or will they be split into multiple starting conditions?

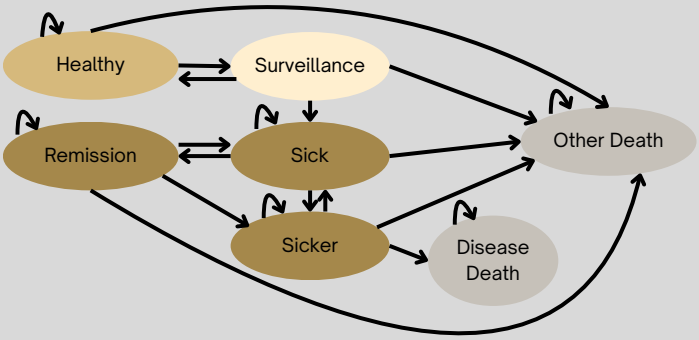
3. Identify the other states in your model, keeping in mind your cycle length. Ensure that all components of the condition that have large impact or are relevant to your research question are included.



4. Determine what the end states of the model will be. For lifetime models, this is typically death. For a condition with high death rate, a separate death state can help create a count of disease death.

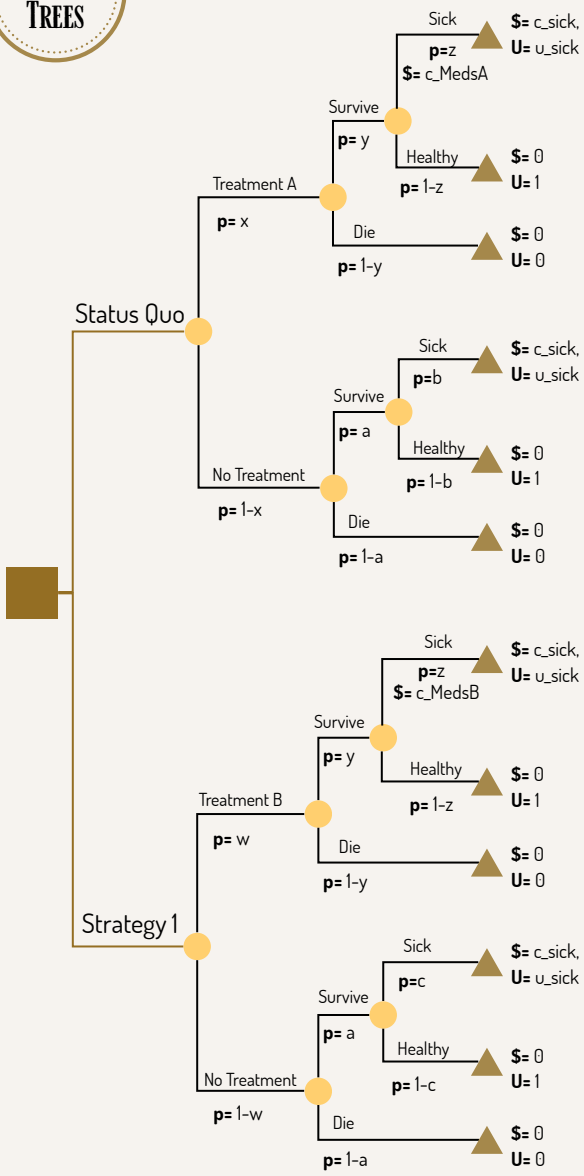


5. Add the arrows between the state to demonstrate all connections between the states



Model Framework - Decision Tree

Decision Trees



*It is often cleanest to model the events from most severe to least severe.

Decision Node: The initial choice between the different strategies of comparison.

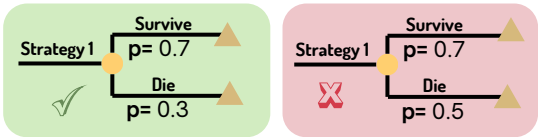
Decision Arm: The decision options (strategies) that are being modeled.

Chance Node: Denotes a chance for an event to happen.

Event Arm: Events that there is a chance of occurring or experiencing. With a beginner model it is often easiest to have only two arms per decision node.

p=

Event Probability: Each event has a probability of occurrence. All arms directly after a chance node must sum to 1.



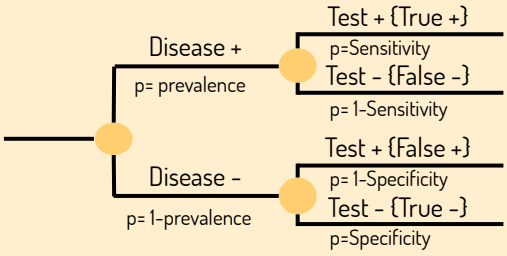
Terminal Node: This is the end of the model for decision trees. This is the outcome of a person's experience in the model. It often will be used with cost and utility.

$= , U=

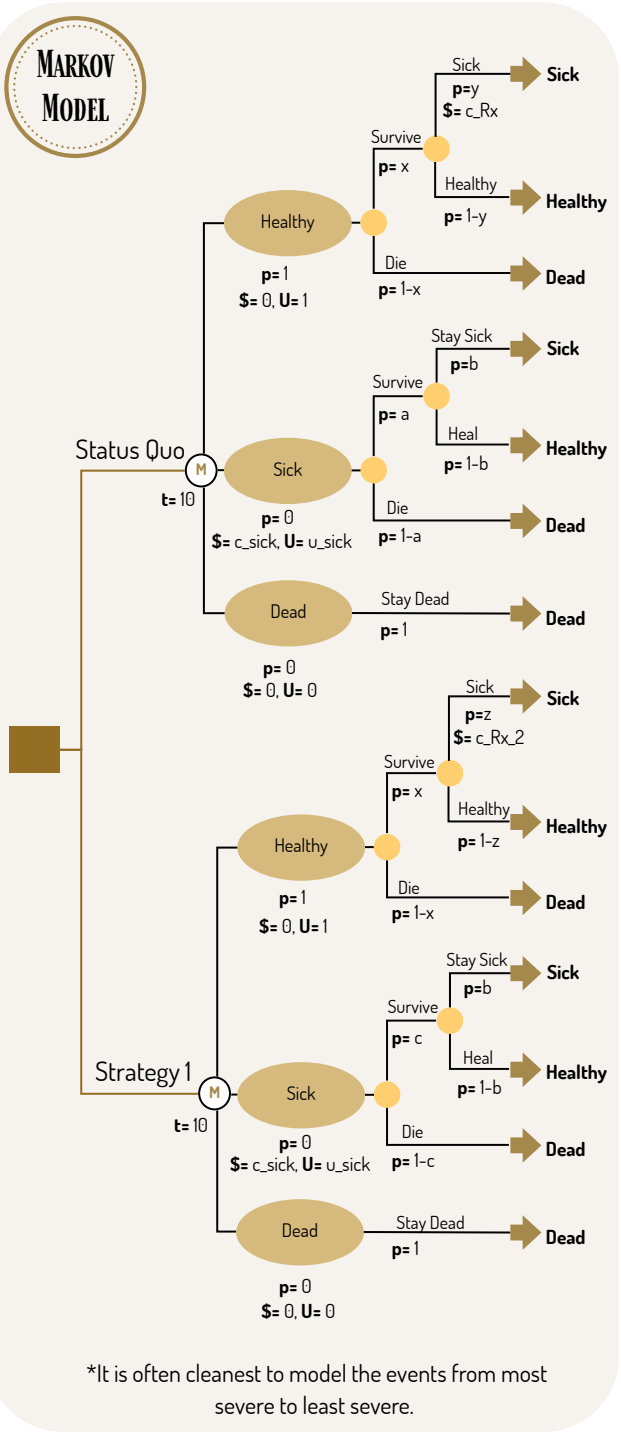
Outcomes: The tracked results (e.g., Cost and Utility). These can be on the terminal node or decision arms.

Working with Tests (Diagnostic, Screening, Etc.)

When working with tests it is important to capture all outcome possibilities. Here is an example of a typical format for a test.



Model Framework - Markov Models



*It is often cleanest to model the events from most severe to least severe.

Decision Node: The initial choice between the different strategies of comparison.

Decision Arm: The decision options (strategies) that are being modeled.

Markov Node: The start of the Markov model.

Termination Condition: The condition in which the model ends (total cycles).

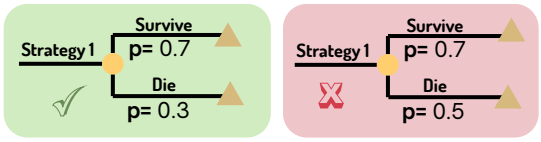
Health State: Each branch starts with a health state. Event arms show what can happen within that health state. Each strategy has all the possible health states. Each health state has a starting probability.

Outcomes: The tracked results (e.g., Cost and Utility). These can be on the Markov state or event arms.

Chance Node: Denotes a chance for an event to happen.

Event Arm: Events that there is a chance of occurring or experiencing. With a beginner model it is often easiest to have only two arms per decision node.

Event Probability: Each event has a probability of occurrence. All arms directly after a chance node **must sum to 1**.

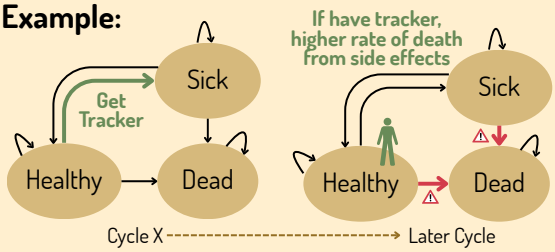


Health State Transition: Arms end with transition arrows stating where the person or cohort will move in the next cycle.

Microsimulation instead of Markov

Built similar to Markov models but use individual level risks. To alter the framework, trackers are added when events occur. These trackers are then be used to alter probabilities. Trackers can be added before or during the model.

Example:



Model Framework - Programs

There are many different methods for building a model including Excel, TreeAge, R, and AMUA.

AMUA is a free software that can be downloaded from and provides an easy to learn user interface.
https://github.com/zward/Amua/wiki/Getting-Started

DARTH offers free R tutorials for building models
https://github.com/DARTH-git

Data Collection - What Do I Need?

As you collect your data be sure to keep track of your sources and assumptions. These will need to be reported in publication. Based on your findings, you may need to refine your research question.

Not all below will apply to your model and there will be other data points specific needed. Review them all to see what you have, what you can get, and where you will need to make assumptions.

Condition Parameters

- What is a good cycle time length?
- How long should the model run?
- Who is the population impacted by this condition?
  - Are there underlying features of this population that could lead to a change in condition probabilities?
- What is the progression of the condition?
- What is the "standard of care" for the condition?

Probabilities

- What is the likelihood (rate, probability, hazard ratio, etc.) for each part of the model?
  - Getting the condition
  - Getting a screening test
  - Tests being accurate (sensitivity/specificity)
  - Getting a vaccination
  - Getting a treatment
  - Getting and/or treating a side effect
  - Medication/treatment compliance
  - Behavior change
  - Success of treatment/transplant
  - Needing a secondary treatment/transplant
  - Condition progression
  - Death from condition
- Do any of the above change over time?

Costs

- How much does treatment of the condition cost?
  - Medication(s)
  - Treatment(s)
  - Operation(s)
  - Screening(s)/test(s)
  - Vaccination(s)
  - Doctor Appointments/surveillance
  - Treatment of side effects
  - Implementation cost(s)
  - Staff training
- Do any of the above change over time?

Utility

- How does the condition and treatment impact quality of life? (Note: can be utility or a decrement to utility)
  - Medication side effects
  - Medication benefits
  - Operation/treatment recovery
  - Condition stages/progression
  - Condition/treatment side effects
- Do any of the above change over time?

For All Metrics:

How do these change between strategies?

Data Collection - Where Do I Find It?

You will need to locate all the parameters needed for your model. For each data point, collect the base case or population average that will be used in the model. In addition, record the confidence interval or maximum and minimum values for each metric to use in sensitivity analysis. Data will come from a variety of sources. Locations of data vary but here are some common examples.

Condition
- Clinical Expertise
- Treatment Guidelines

Costs
- Government Databases
- Costing Studies

Probabilities
- Clinical Trials
- Patient Surveys

Utility
- Utility Trials
- Tufts CEA Database

Some parameters will need to be calculated with a formula. Record sources of the formula inputs and note the formula used in your parameter log.

Consider keeping a table with the following data:

Parameter	Base Case	Formula	Description	Notes	Distribution	Source
c_Disease	*$500*	*c_Meds + c_Doc_Visit*	*Cost of being Sick*	*Annual, 2020 USD*	*gamma(shape = 12, scale = 83.3)*	*2024, V. Andy et Al*

It is important to capture death in a model because even the healthiest people have a chance of death. Using a life table allows death to vary by age as it would in real life. If your condition accounts for a decent proportion of overall death, you will need to remove those deaths from the probability.

Finding a Life Table:

Institute for Health Metrics and Evaluation (IHME)
Global Burden of Disease
www.healthdata.org

World Health Organization (WHO)
Mortality Database
www.who.int

Outcomes

Based on the research question that you have chosen, you will need to determine the appropriate outcomes. Simulation models can be used to get counts of events or predictions on future happenings. They can also be used for things like cost-effectiveness where outcomes like cost and utility are needed.

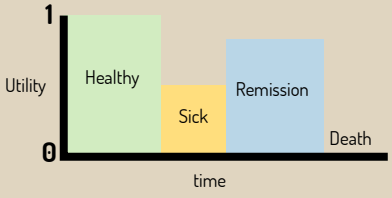
Commonly used outcomes in models include:
- Event occurrences
- Deaths from disease
- Costs
- Health Adjusted Life Years
- Life Years

All of these can be used to answer different research questions.

What is Utility:

Utility is a method used to put a value on the quality of one's life. For most conditions healthy has a utility of 1 and death a utility of 0.

These values are collected through surveys and research studies of utility. Using this scale allows for comparability between different conditions.



Data Manipulation

Once you have collected your data, you need to ensure that you understand each metric.

Steps	Action	Example
Know the Classification of the Metric	Consider how rates vs probabilities are used and can be manipulated.	• Rates • Other • Probabilities
Know the time scale of the metric	Time scales may need to be altered to match the time scale (cycle length) of your model	10 year probability to an annual probability.
Standardize Costs	All costs should be adjusted to one standard currency and year to account for inflation.	USD 2024

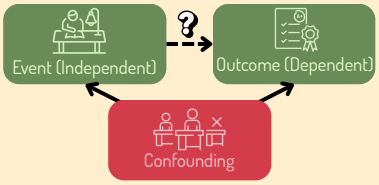
Differentiating Strategies

Modeling the differences between strategies is the backbone of simulation modeling. This variation is how we understand the unique costs, utilities, and outcomes of each strategy. These differences can be throughout any or all parameters.

To help visualize the differences, consider a comparison table:

Example	Cost	Late-Stage Diagnoses	Participate in Screening	Deaths
Status Quo: No Screening	Low	High	No interest	High
Strategy 1: Screen all	High	Low	People assume low risk and skip screening	Medium
Strategy 2: Screen high risk	Medium	Low	People more likely to screen due to risk	Low

⚠ Be careful ⚠
to model causality correctly.



If not included, confounders that influence both the chance of an event and a model outcome can bias the model and cause inaccurate results.

Putting the Data into the Model

Once your numbers are ready to be put into the model there are two best practices we want to note.

1 Do not hardcode any value you put into your model. This applies to models made in Excel, AMUA, R, or anywhere else. These all have ways to create and name variables for each data point. If you do not use named variables, the sensitivity analysis will not work. Additionally, this makes edits to the model faster to complete.

2 Use consistent naming! Consider:

type	prefix
Probability	p_
Rate	r_
Table	tbl_
Cost	c_
Utility	u_
Hazard Ratio	hr_

Sub-Group Analysis

A technique that may be needed to answer your research question is running the model on sub-groups of a population. Before completing this analysis ask yourself the following:

1. Is there a distinction between the sub-groups that would make this analysis informative?

2. Can I collect unique data points for each group to properly model the differences?

If you answered yes to both, try running your model on different populations to compare results. Otherwise, consider if an analysis is truly important to your research question. If it is, you will need to spend more time collecting data.

Scenario Analysis:

Scenario Analysis allows us to look at the model under different assumptions. This analysis does not look at parameter uncertainty like the methods mentioned in the "Other Analyses" section (pg. 21).

This allows us to look at different things, like:

Starting Conditions	Subgroups	Perspectives	Timeframes
All on Medication vs Half on Medication	Age, Race, Gender, Risk Level	Healthcare vs Societal	Time to Taper off of Medication

Half-Cycle Correction

In real life, time is continuous and therefore events can happen at any time in a cycle. However, in Markov and microsimulation models, events occur at the beginning or the end of the cycle. To remediate the overcounting or undercounting this can cause, half-cycle correction is applied to the model. There are other forms of correction but half-cycle is enough for most models.

cyc	H	S	D	U	C
0	10	0	0	10	0
1	8	2	0	8.6	30
...	...	...	...	...	...
9	0	3	7	0.9	45
10	0	1	9	0.3	15

Step 1

Run the model and get the trace.

Step 2

Multiply the outcomes by 1/2 in the first and last cycle.

cyc	H	S	D	U	C
0	10	0	0	**5**	**0**
1	8	2	0	8.6	30
...	...	...	...	...	...
9	0	1	9	0.3	15
10	0	0	10	**0.15**	**7.5**

Learn More:

Naimark DMJ, Bott M, Krahn M. The Half-Cycle Correction Explained: Two Alternative Pedagogical Approaches. Medical Decision Making. 2008;28(5):706-712. doi:10.1177/0272989X08315241

Discounting

When events happen over time, it's not just the outcome that matters, but also when it happens. People generally value immediate benefits more than future ones. Discounting adjusts the outcomes to account for this factor. A 3% discount rate is typically used in health modeling but other rates can be used if reasonable for your model. You will need a discount rate for each outcome (e.g., cost and utility), you can use the same discount rate or different rates. Discounting is applied to all cycles.

Formula

$$\text{Present Value} = \frac{\text{Future Value}}{(1+\text{Rate})^{\text{Time}}}$$

Example

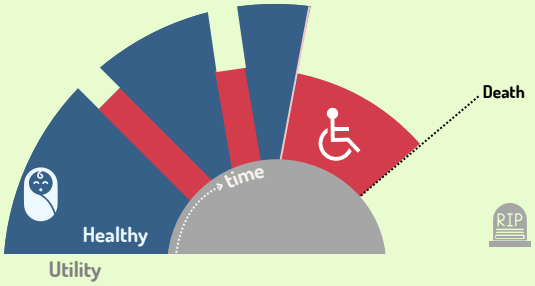
$20 is worth more to me now than the promise of $20 in 2 years

Cyc	Cost	Discounting (3%)	Cost*Discounting
0	$20	1.00000	$20
1	$20	0.99263	$19.85
2	$20	0.98532	$19.71

QALY vs DALY

Quality Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs) both provide summaries of health and allow us to make comparisons between diseases and over time. QALYs rely on utility studies but are easier to calculate. DALYs tend to be used in developing countries as they don't require utility studies but instead just disability weights, which can be found from the Global Burden of Disease Study.

Quality Adjusted Life Years



QALY =

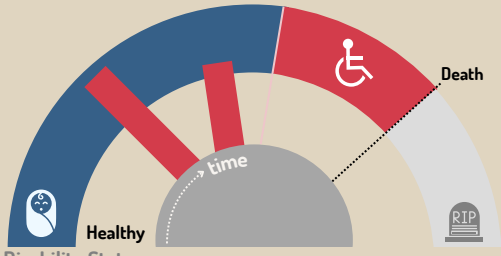
$$(\text{time}*\text{utility})_{H1} + (\text{time}*\text{utility})_{S1} + (\text{time}*\text{utility})_{H2} + (\text{time}*\text{utility})_{S2} + (\text{time}*\text{utility})_{H3} + (\text{time}*\text{utility})_{S3}$$

QALYs measure the quality of life.
(i.e., level of health)
1 QALY = 1 year of perfect health.

Gained = Better

Disability Adjusted Life Years

*disability is any health condition that reduces quality of life



DALY =

Years lived with disability (YLD) (time * disability weight) + Years of life lost (YLL) due to premature death

DALYs measure the burden of disease.
1 DALY = 1 year of premature death **OR**
1 year of full health lost to disability

Averted = Better

When using DALYs with discounting additional considerations are required.

The following paper can help walk you through methods to successfully calculate the correct values.

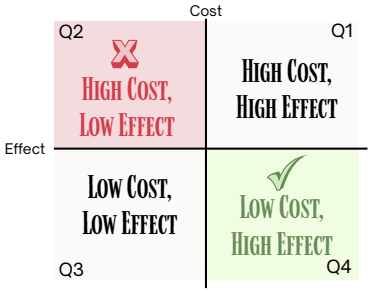
Leech AA, Zhu J, Peterson H, et al. Modeling Disability-Adjusted Life-Years for Policy and Decision Analysis. Medical Decision Making. 2025;0(0). doi:10.1177/0272989X251340077

Model Results

Cost Effectiveness Analysis (CEA) is used to determine the best use of money while also balancing the impact of quality of life. It is NOT a method to help find cost savings.

Ideally you want a strategy that is low cost and high effect (Q4) and you want to remove strategies in with high cost and low effect (Q2).

However, in reality, most strategies fall in Q1 and Q3. These strategies have a trade off in cost and effect. CEAs allow us to compare these tradeoffs.



ICER (Strategy A vs Strategy B):

$$ICER = \frac{\text{Incremental Cost: } Cost(A) - Cost(B)}{\text{Incremental Utility: } Utility(A) - Utility(B)}$$

Closest to willingness-to-pay threshold (pg 20) without going over.

Incremental cost-effectiveness ratios (ICERs) provide a measure of how efficiently health is gained and are expressed as cost per health unit (e.g., Strategy A is $1,000 per QALY). ICERs cannot be used if the denominator is undefined. It is best practice to not report negative ICERs. These are misleading because they could be in Q2 or Q4.

An incremental CEA will produce a table with information on the ICER and the status of each strategy. Anything that is dominated should not be considered for recommendation. From the remaining strategies, you will want to recommend the ICER closest to the willingness-to-pay threshold (pg 20) without going over.

How to do an Incremental CEA:

1. Calculate the Cost and Effect (QALY or DALY) for each strategy
2. Sort table by cost in ascending order
3. Calculate the ICER for each strategy
4. Determine the dominated strategies (Q2)
5. Re-calculate the ICER after eliminating dominated strategies
6. Determine strategies ruled out by extended dominance
7. Re-calculate the ICER after ruling out ALL dominated strategies

Strategy	Cost	QALYs	Incremental Cost	Incremental QALYs	ICER	Status
Status Quo	$16,453.99	17.33178	NA	NA	NA	
Strategy 3	$24,504.08	17.49126	$8,050.10	0.15948	50,478.23	
Strategy 2	$33,443.25	17.57951	$8,939.16	0.08825	101,291.69	
Strategy 4	$43,331.68	17.49126	NA	NA	NA	Dominated
Strategy 1	$21,456.58	17.40887	NA	NA	NA	Dominated (extended)

*Note that Strategy 3 is more expensive than Strategy 1. But Strategy 3 gains health MORE EFFICIENTLY. (Lower Cost/QALY)

Net Health Benefit (NHB) or Net Monetary Benefit (NMB) assumes that health has a particular value. Using this assumption we can calculate the monetary loss of choosing strategies with lower health outcomes. Note that these formulas rely on a set willingness-to-pay threshold (pg. 20). NHB and NMB can be calculated by strategy or incremental. The conclusions from either are identical.

Net Health Benefit

$$NHB = Utility - \frac{Cost}{WTP}$$

Higher = Better

Net Monetary Benefit

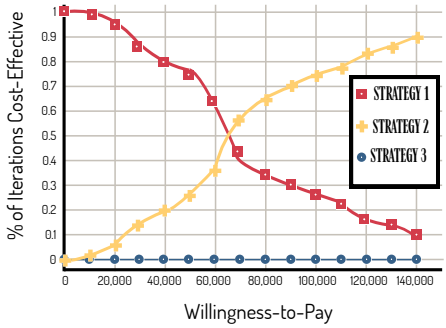
$$NMB = Utility * WTP - Cost$$

Higher = Better

Willingness - To- Pay (WTP) Threshold

All payers have a maximum budget. To help determine this, a willingness-to-pay threshold (WTP) is used to compare strategy effectiveness. Any strategy with with a higher ICER than the WTP will not be considered cost effective to the payer.

WTP varies by country and sometimes by condition. For the United States the WTP is considered to be $50,000 to $100,000 per quality-adjusted life year. One analysis that can be run on a completed model is a Cost-Effectiveness Acceptability Curve which displays how a decision will vary based on the WTP chosen (See “Other Analyses” pg 21).



Learn More:

USA: Vanness DJ, Lomas J, Ahn H. A Health Opportunity Cost Threshold for Cost-Effectiveness Analysis in the United States. Ann Intern Med. 2021 Jan;174(1):25-32. doi: 10.7326/M20-1392. Epub 2020 Nov 3. PMID: 33136426.

Global: Ochalek J, Lomas J, Claxton K. Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data. BMJ Glob Health. 2018 Nov 5;3(6):e000964. doi: 10.1136/bmjgh-2018-000964. Erratum in: BMJ Glob Health. 2019 Jun 4;4(3):e000964corr1. doi: 10.1136/bmjgh-2018-000964corr1. PMID: 30483412

Model Validation

After you have built a model, it is important to verify that the model is producing realistic results. It is **highly recommended** to undertake at least one validation method. Models can be validated internally or externally. External validation is considered the gold standard but may not be an option for your question.

Strength ↓ +

Face Validity	The determination, by a suitable group of experts, that the model reflects the current understanding of the science and available evidence.
Internal Validation	An assessment of whether the model has been implemented correctly and behaves as expected.
Cross-Model Validation	A comparison of results among different models of the same (or sufficiently similar) analyses.
External Validation	Comparison of model outputs with empirical observations that were not used in model development.
Predictive Validation	Assessment of the model’s ability to reproduce empirical results that were not available and were not used during its development.

Learn More:

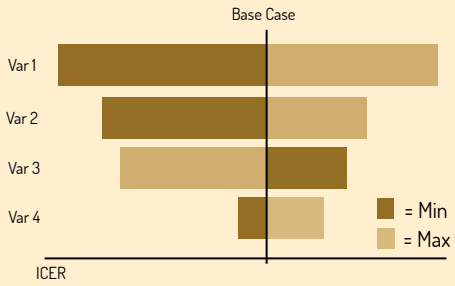
Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB; ISPOR-SMDM Modeling Good Research Practices Task Force. Model transparency and validation: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-7. Med Decis Making. 2012 Sep-Oct;32(5):733-43. doi: 10.1177/0272989X12454579. PMID: 22990088.

Other Analyses

There are many different methods to analyze your model. Four are briefly introduced below to help you understand as you are reading literature. However, you will need to do further research to complete these on your own model. It is highly recommended to complete some form of sensitivity analysis on the model as all inputs are never 100% accurate.

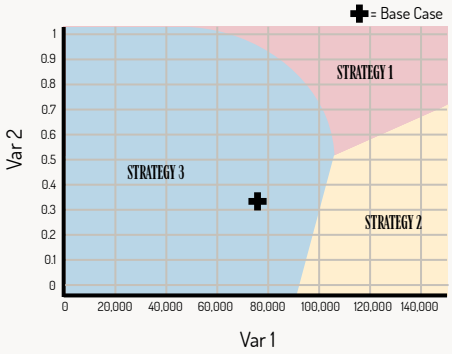
One-Way (OWSA)

One way sensitivity analysis looks at the impact that one parameter has on the model. The model is run on the minimum and maximum values of a parameter to understand uncertainty in the decision. This is usually repeated with many parameters and presented as a tornado diagram.



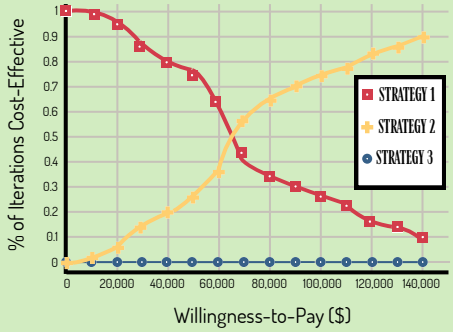
Two-Way

Two way Sensitivity analysis compares two parameters to understand how their interaction impacts the results of the model. Typically the graph will show the values of when each strategy is chosen and then a mark for the base case.



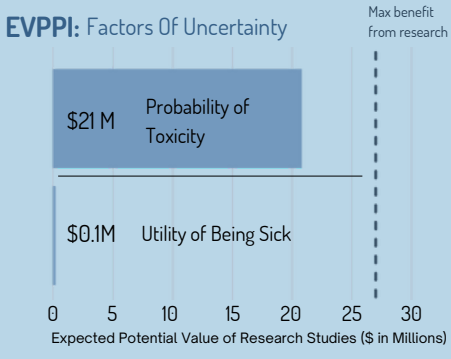
Probabilistic (PSA)

The probabilistic sensitivity analysis takes into account that parameters follow a distribution (beta, gamma, etc.). For this analysis, the model is run many times using various combinations of all distributed variables. As a result, this analysis takes high computation power.



Value Of Information (VOI)

This analysis looks at the value of gaining additional information. In other words, how much value is there in completing more research to inform this decision. The calculations determine the amount of uncertainty in the parameters and the monetary cost of that uncertainty. The University of Sheffield has created an online tool for a VOI analysis (https://savi.shef.ac.uk/SAVI/)



PUBLISHING RESULTS

Academic Publication: The Explanation and Elaboration Task Force Report created a best practice checklist to help assist in ensuring all necessary information is included in your academic publication.

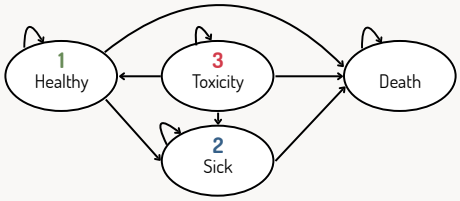
CHEERS Checklist www.equator-network.org/reporting-guidelines/cheers/

Policy Publication: If you are presenting to policy makers (internal or external) it is important to make the information understandable at their technical level. Bubble diagrams are a great way to demonstrate the complex model in an easy to understand visual. CEA tables are typically hard to read and therefore it might be more beneficial to present the impact instead of the table.

When presenting, it is important to include units on all values. Below is a simplified sample report.

Four strategies and a current best practice for prescribing Drug X were used to analyze the long-term impacts of improper prescriptions. Patients who receive the medication without being sick will gain toxicity. Strategies vary on prescribing recommendations.

Strategy	ICER ($/QALY)	Status
Status Quo	NA	
Strategy 3	50,478.23	
Strategy 2	101,291.69	
Strategy 4	NA	Dominated
Strategy 1	NA	Dominated (extended)



For the recommended $100,000/QALY willingness to pay threshold, Strategy 3 provides the most efficient gain of health with $50,478 per QALY. Strategies 1 and 4 should not be considered for implementation as they are inefficient compared to other strategies.

DISTRIBUTION-SENSITIVE COST-EFFECTIVENESS

Cost-Effectiveness tells us how to maximize our budget. This results in all QALYs being treated equally. However, decision makers likely care about many different things like financial risk protection, distribution of outcomes, and a fair treatment process.

As the field has evolved, new approaches have been developed to incorporate the distribution of outcomes across population subgroups (such as those defined by income, geography, or health status) into cost-effectiveness analysis.

Distributional Cost-Effectiveness Analysis

Asaria M, Griffin S, Cookson R. Distributional Cost-Effectiveness Analysis: A Tutorial. Med Decis Making. 2016 Jan;36(1):8-19. doi: 10.1177/0272989X15583266. Epub 2015 Apr 23. PMID: 25908564; PMCID: PMC4853814.

Extended Cost-Effectiveness Analysis

Verguet S, Kim JJ, Jamison DT. Extended Cost-Effectiveness Analysis for Health Policy Assessment: A Tutorial. Pharmacoeconomics. 2016 Sep;34(9):913-23. doi: 10.1007/s40273-016-0414-z. PMID: 27374172; PMCID: PMC4980400.