

Introduction to Medical Decision Making and Decision Analysis

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Outline

- Decision analysis
 - Components of decision analysis
 - Building a tree: Example
 - Sensitivity analyses
- Markov models
 - Background
 - Constructing the model
 - Example
 - Monte Carlo simulations

Decision Analysis

- Decision analysis is a quantitative, probabilistic method for modeling problems under situations of uncertainty

Making a Decision

- We make a decision when we irreversibly allocate resources.
- We typically use the following steps:
 - gather information
 - assess consequences of the alternatives
 - take an action
- Goal of decision analysis is to clarify the dynamics and trade-offs involved in selecting one strategy from a set of alternatives
- Usually, in everyday decision-making, we do not take the time to thoroughly analyze the decision

Decision Analysts

- Deliberately seek out new, creative alternatives
- Identify the possible outcomes
- Identify relevant uncertain factors
- Encode probabilities for the uncertain factors
- Specify the value placed on each outcome
- Formally analyze the decision.

Decisions Vary in Degree Of:

- Complexity -- large number of factors, multiple attributes, more than one decision-maker
- Time factor -- static (no change over time) vs. dynamic (time-dependent)
- Uncertainty -- *deterministic vs. probabilistic*.
Deterministic means there is no uncertainty and the problem can be solved with a set of precise equations

Decision Analysis is Most Helpful

- For important, unique, complex, nonurgent, and high-stakes decisions that involve uncertainty
- “Decision Analysis = Decision Therapy.”
 - » A great deal of work is done to decompose the decision problem, work out the relation between factors, specify probabilities for uncertain events, and identify what is at stake and how it might be affected by the decision
 - » Constructing the tree, even before “solving” it mathematically, can provide important insights.

Cost-Effectiveness Analyses

- Cost-effectiveness analysis (CEA) is a methodology for evaluating the tradeoffs between health benefits and costs
- CEA is aid to decision making, not a complete resource allocation procedure

Cost-Effectiveness Ratio

Compares a specific (new) intervention to a stated alternative (old) intervention

$$\text{Cost}_{\text{new}} - \text{Cost}_{\text{old}} / \text{Benefit}_{\text{new}} - \text{Benefit}_{\text{old}}$$

Incremental resources required by the intervention

Incremental health effects gained by using the intervention

Decision Model

- Schematic representation of all the clinical important outcomes of a decision.
- Used to combine knowledge about decision problem from many sources
- Computes average outcomes (e.g., QALYs, costs, etc.) from decisions.

Elements of Decision Analysis

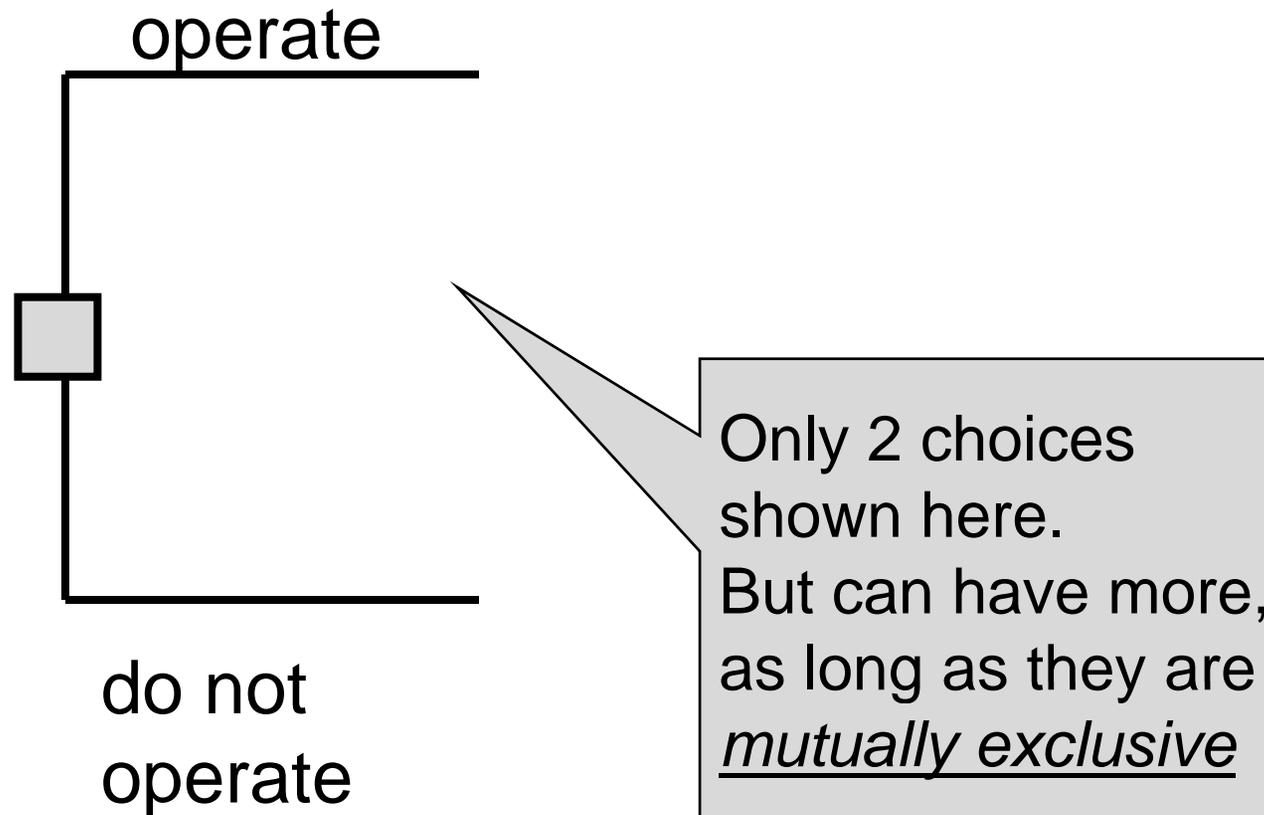
- Structure the problem
 - Identify decision alternatives
 - List possible clinical outcomes
 - Represent sequence of events
- Assign probabilities to all chance events
- Assign utility, or value, to all outcomes
- Evaluate the expected utility of each strategy
- Perform sensitivity analyses

Structuring the Problem

- Decision model (usually decision tree) is chosen to represent the clinical problem
- Model needs to be simple enough to be understood, but complex enough to capture the essentials of the problem
- Need to make a series of assumptions for modeling

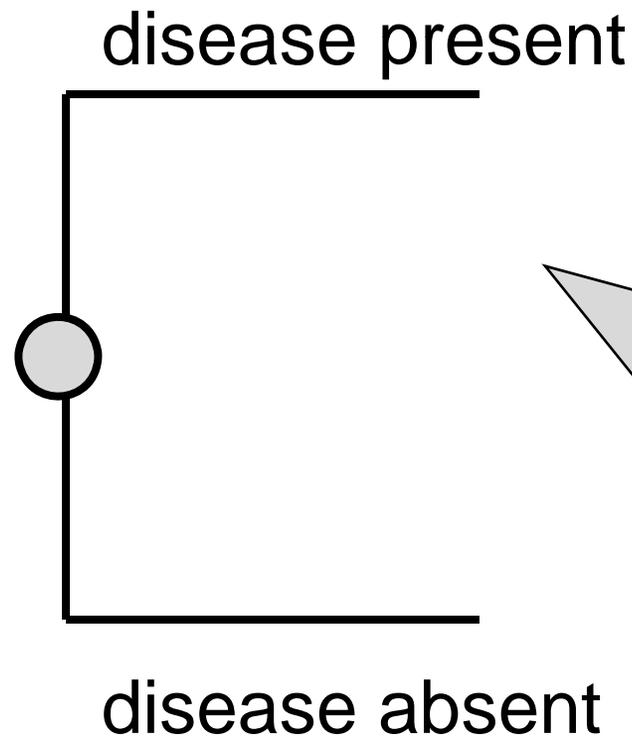
Decision Node:

A point in a decision tree at which several choices are possible. The decision maker controls which is chosen.



Chance Node:

A point in a decision tree at which chance determines which outcome will occur.



Only 2 outcomes shown here.
But can have more, as long as they are mutually exclusive and collectively exhaustive

Some Definitions

- Mutually exclusive
 - The intersection of the events is empty
 - One (and only one) of the events must occur
- Collectively exhaustive
 - Events taken together make up the entire outcome space
 - At least one of the events must occur

Terminal Node:

Final outcome state associated with each possible pathway

————— **20 LY**
Patient cured

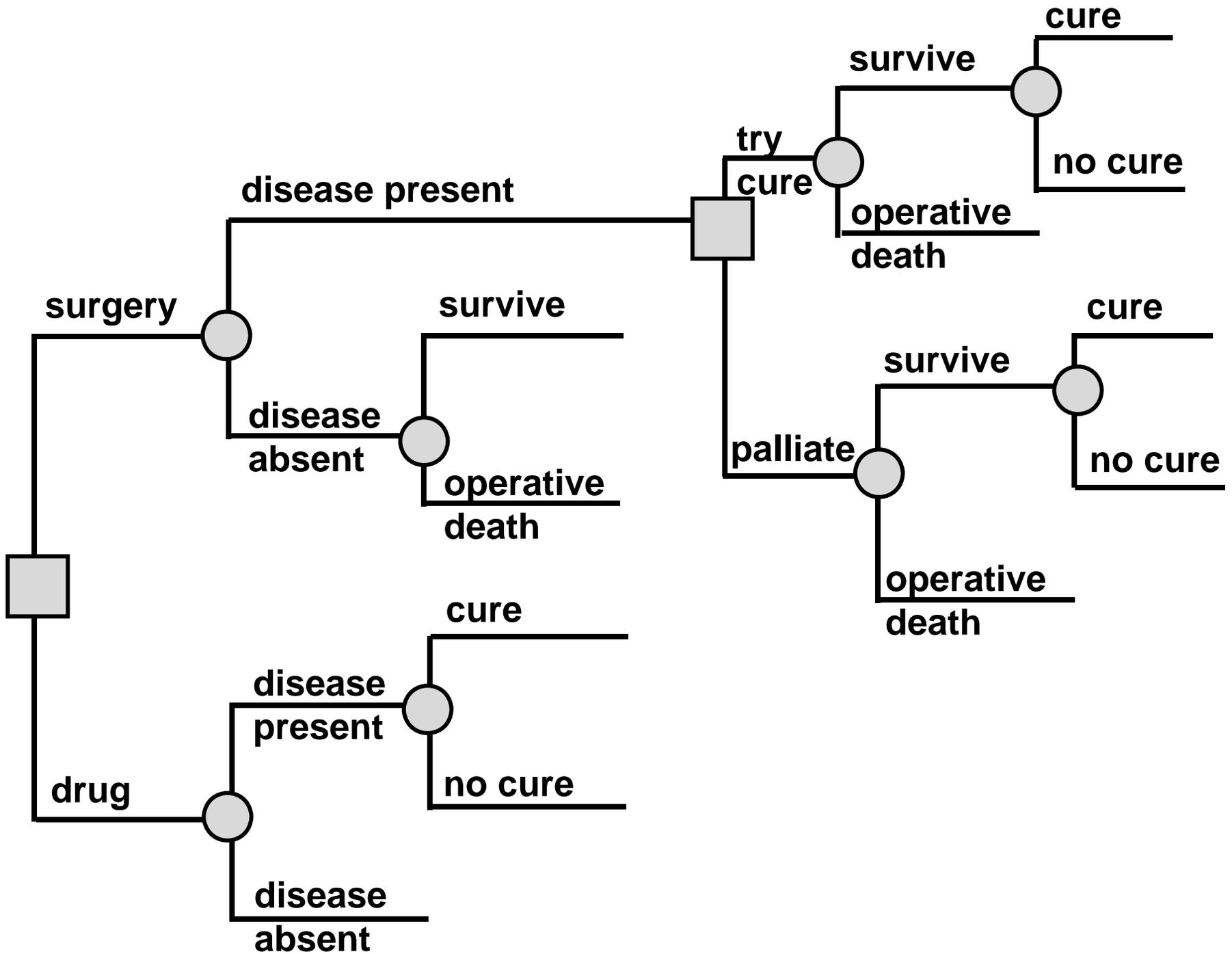
Some measure of value or worth needs to be applied to the terminal nodes (eg. LYs, QALYs, costs)

Outline

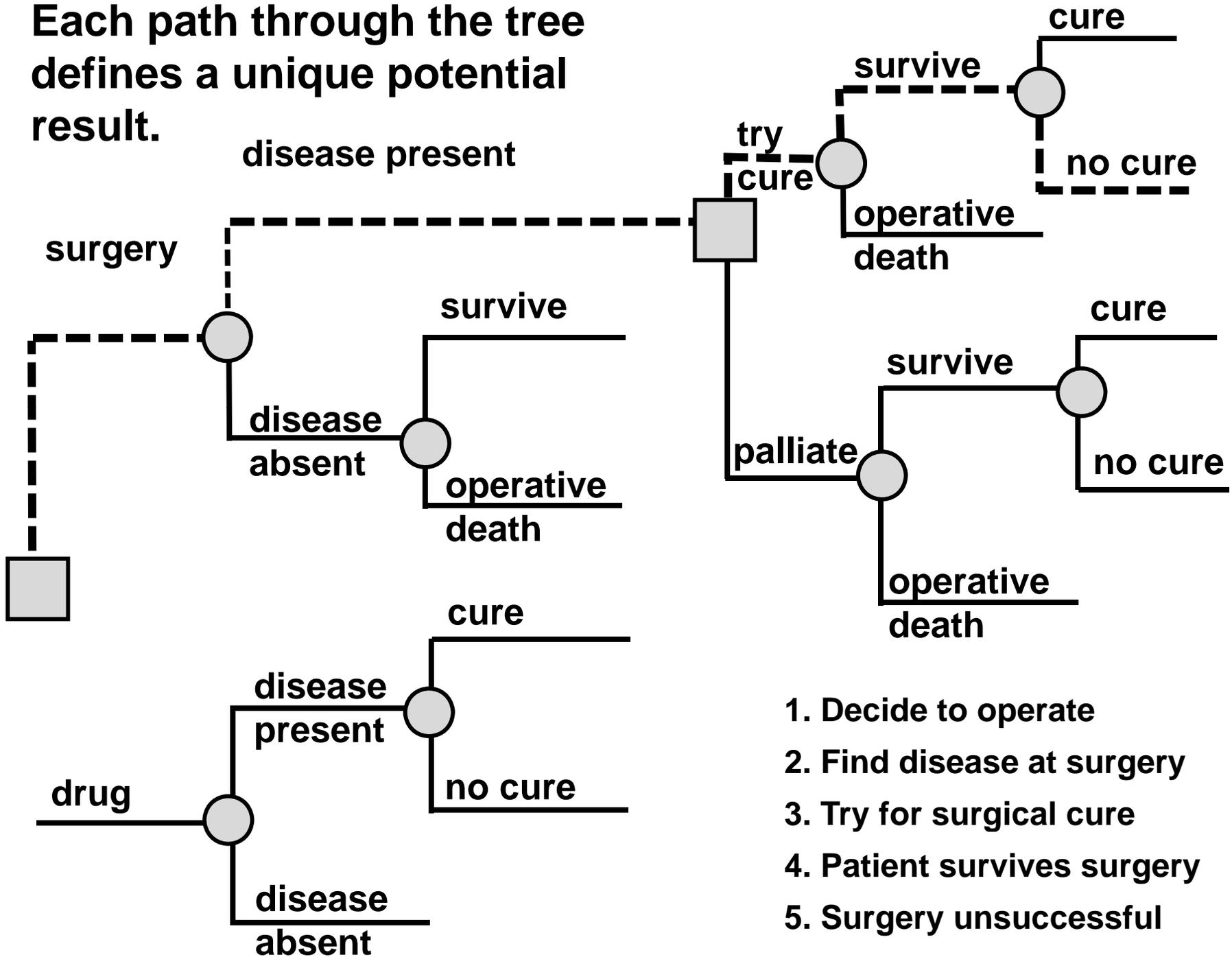
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Example

- Symptomatic patient:
 - operate (risky)
 - medical management
- If disease present at surgery, must decide whether try for cure or palliate
- Want to evaluate surgery vs. medical management

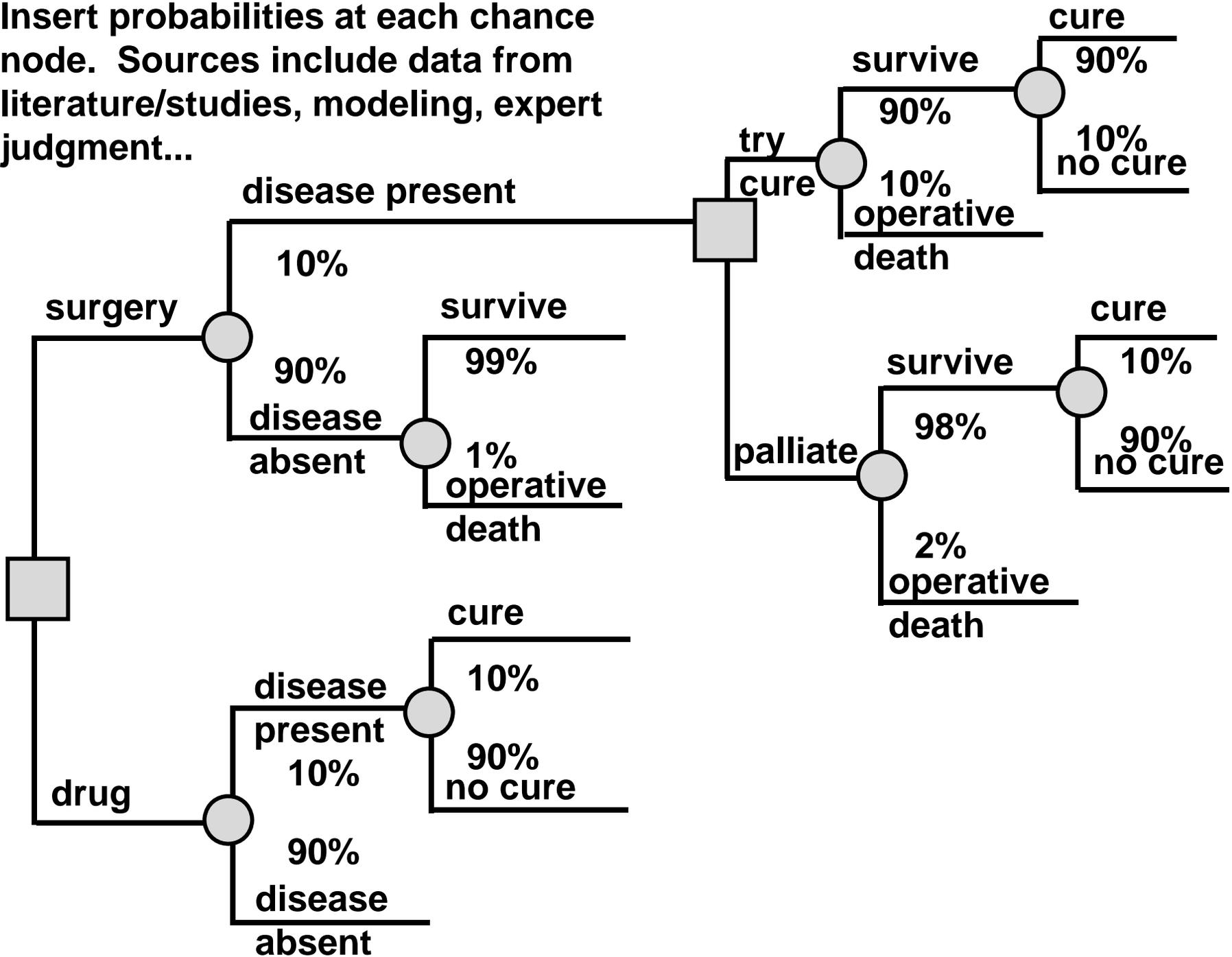


Each path through the tree defines a unique potential result.

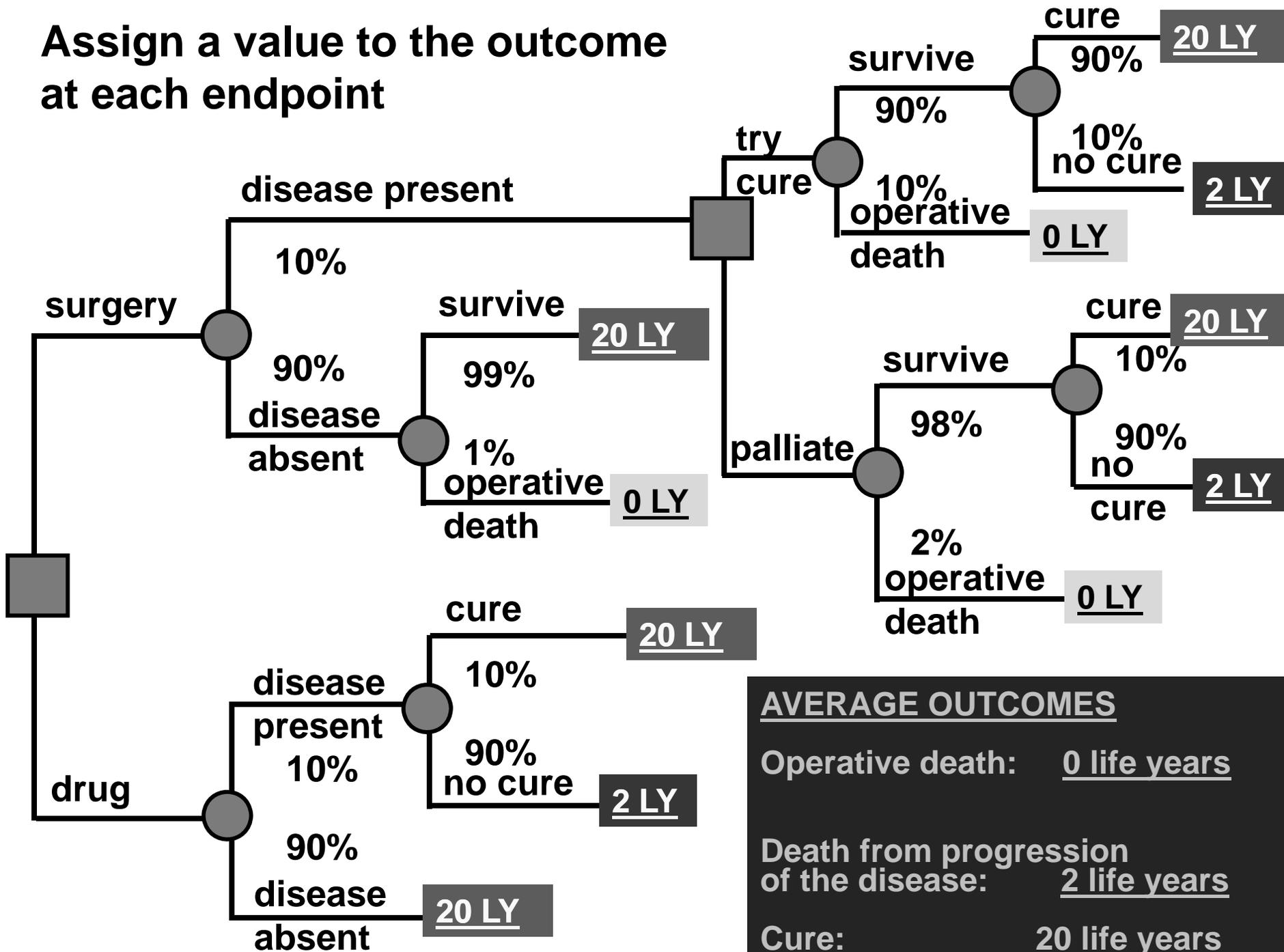


1. Decide to operate
2. Find disease at surgery
3. Try for surgical cure
4. Patient survives surgery
5. Surgery unsuccessful

Insert probabilities at each chance node. Sources include data from literature/studies, modeling, expert judgment...

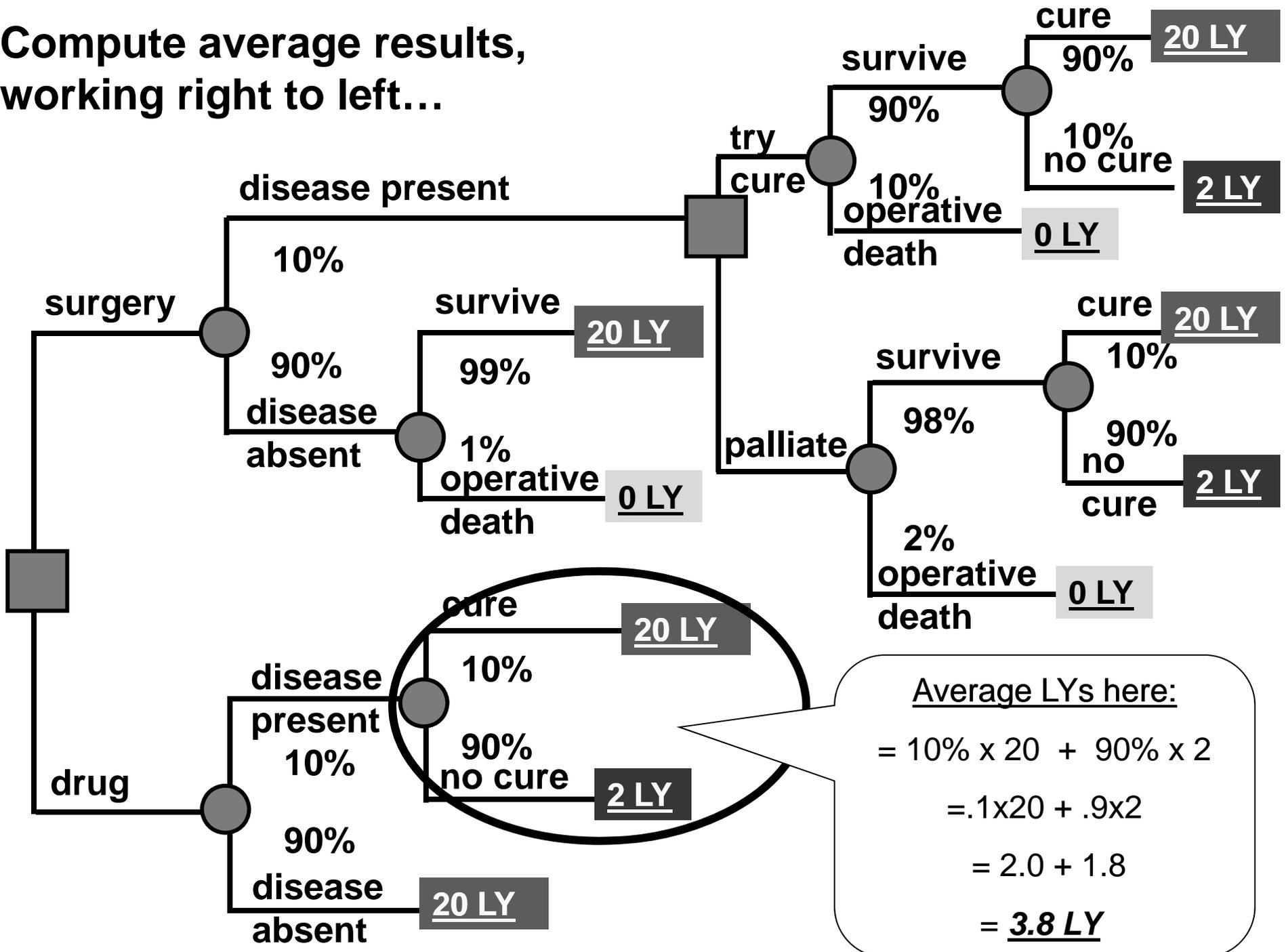


Assign a value to the outcome at each endpoint



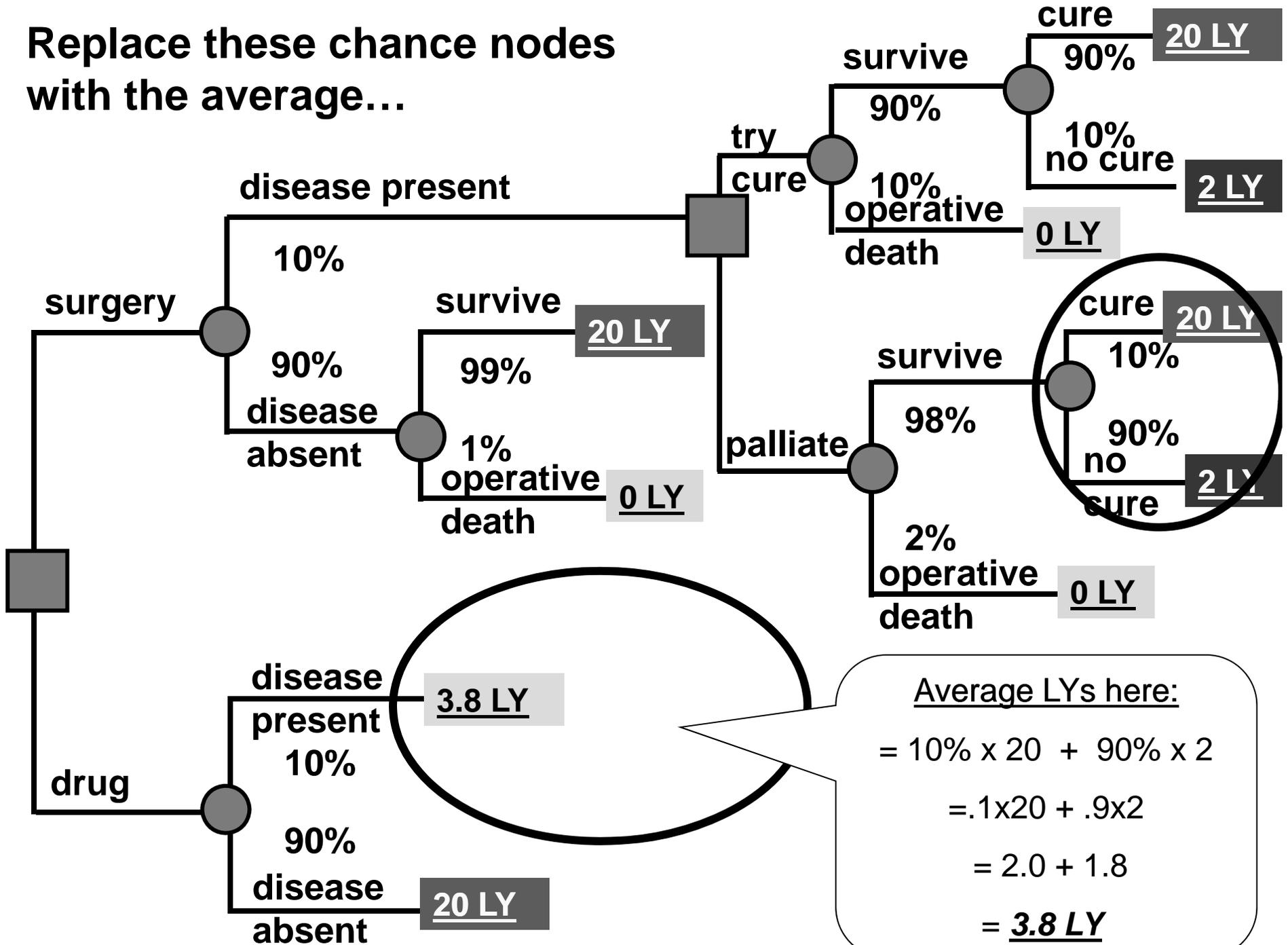
AVERAGE OUTCOMES	
Operative death:	<u>0 life years</u>
Death from progression of the disease:	<u>2 life years</u>
Cure:	<u>20 life years</u>

Compute average results,
working right to left...

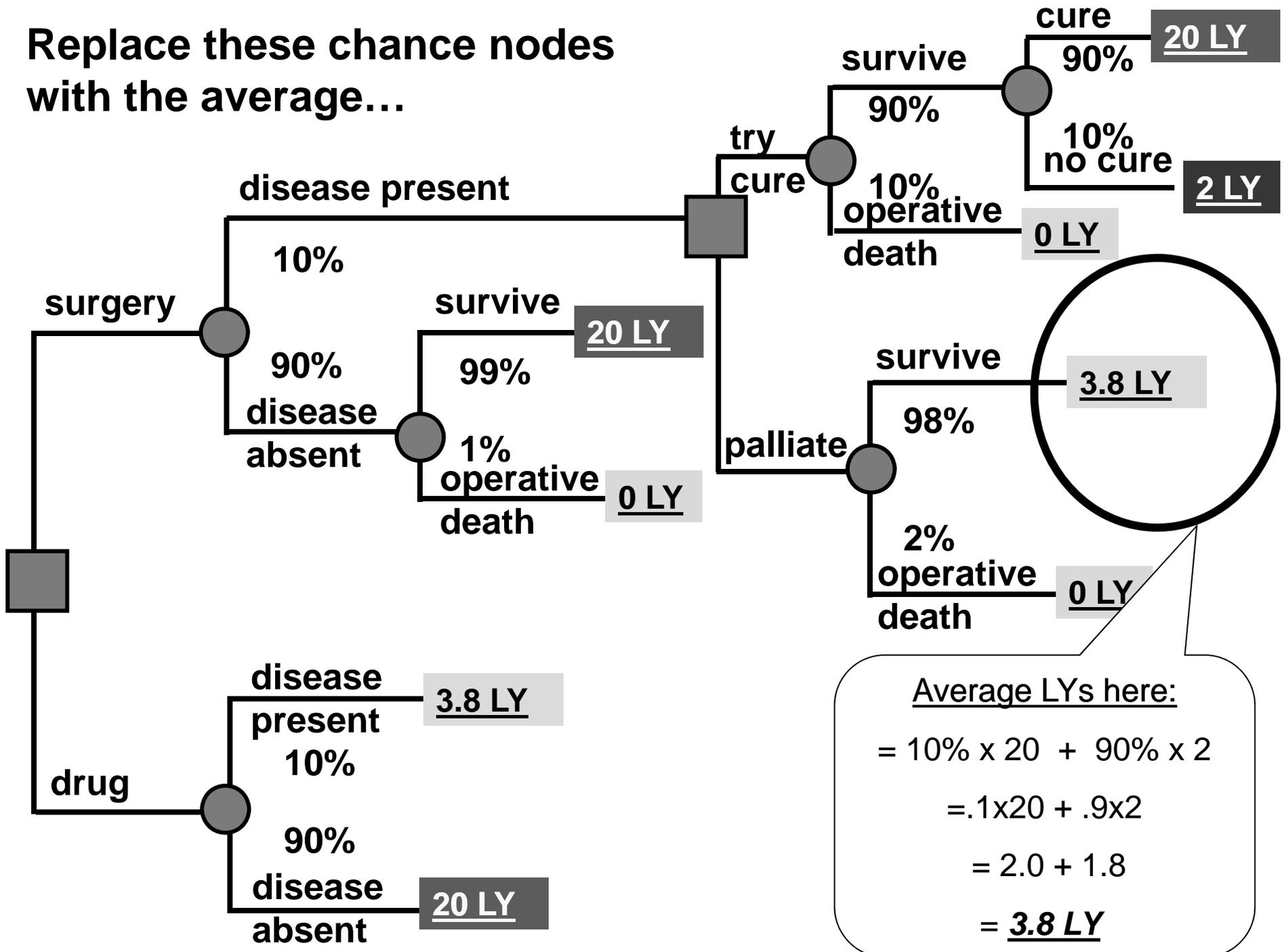


Average LYs here:
 $= 10\% \times 20 + 90\% \times 2$
 $= .1 \times 20 + .9 \times 2$
 $= 2.0 + 1.8$
 $= \underline{3.8 \text{ LY}}$

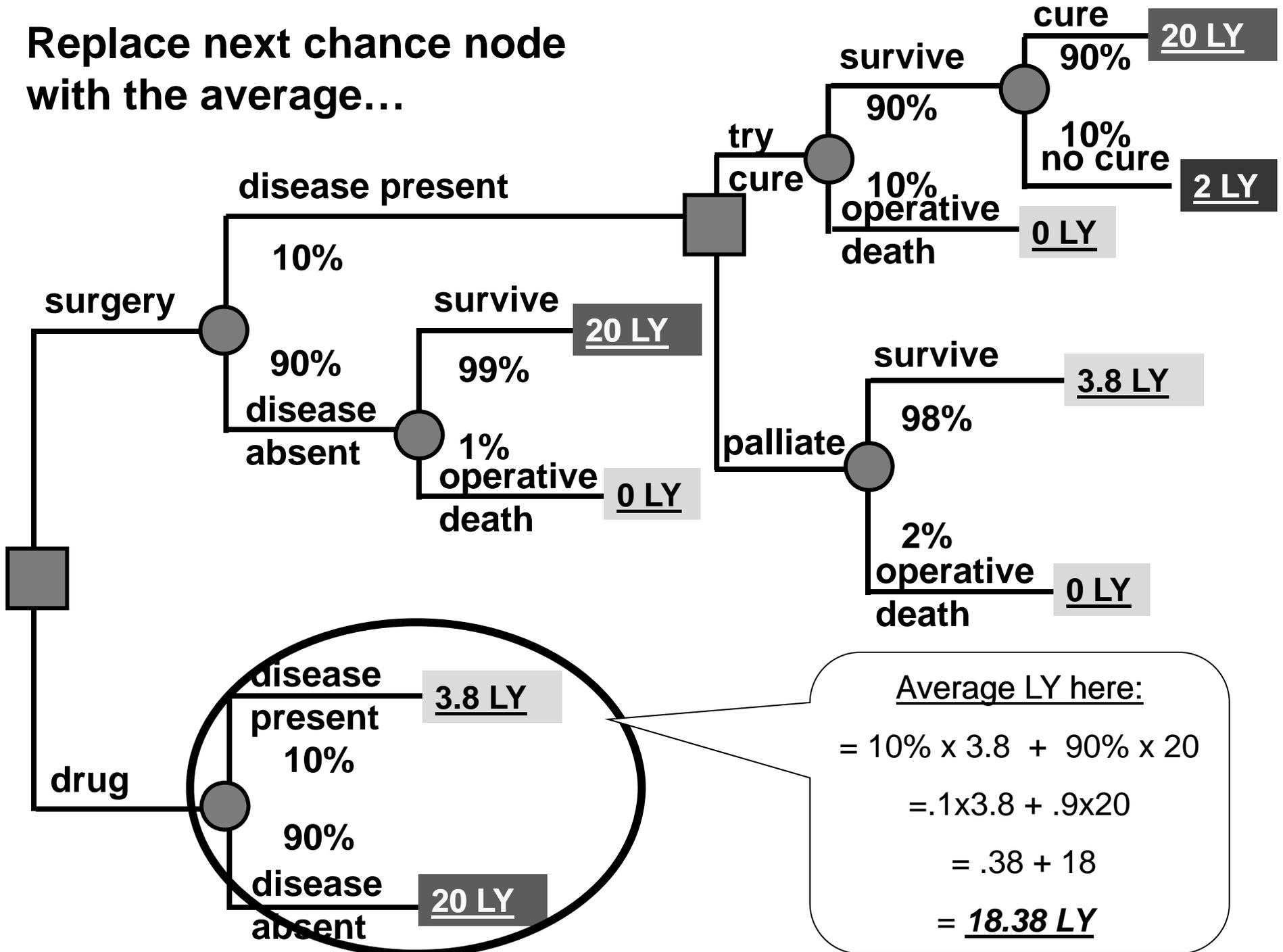
Replace these chance nodes with the average...



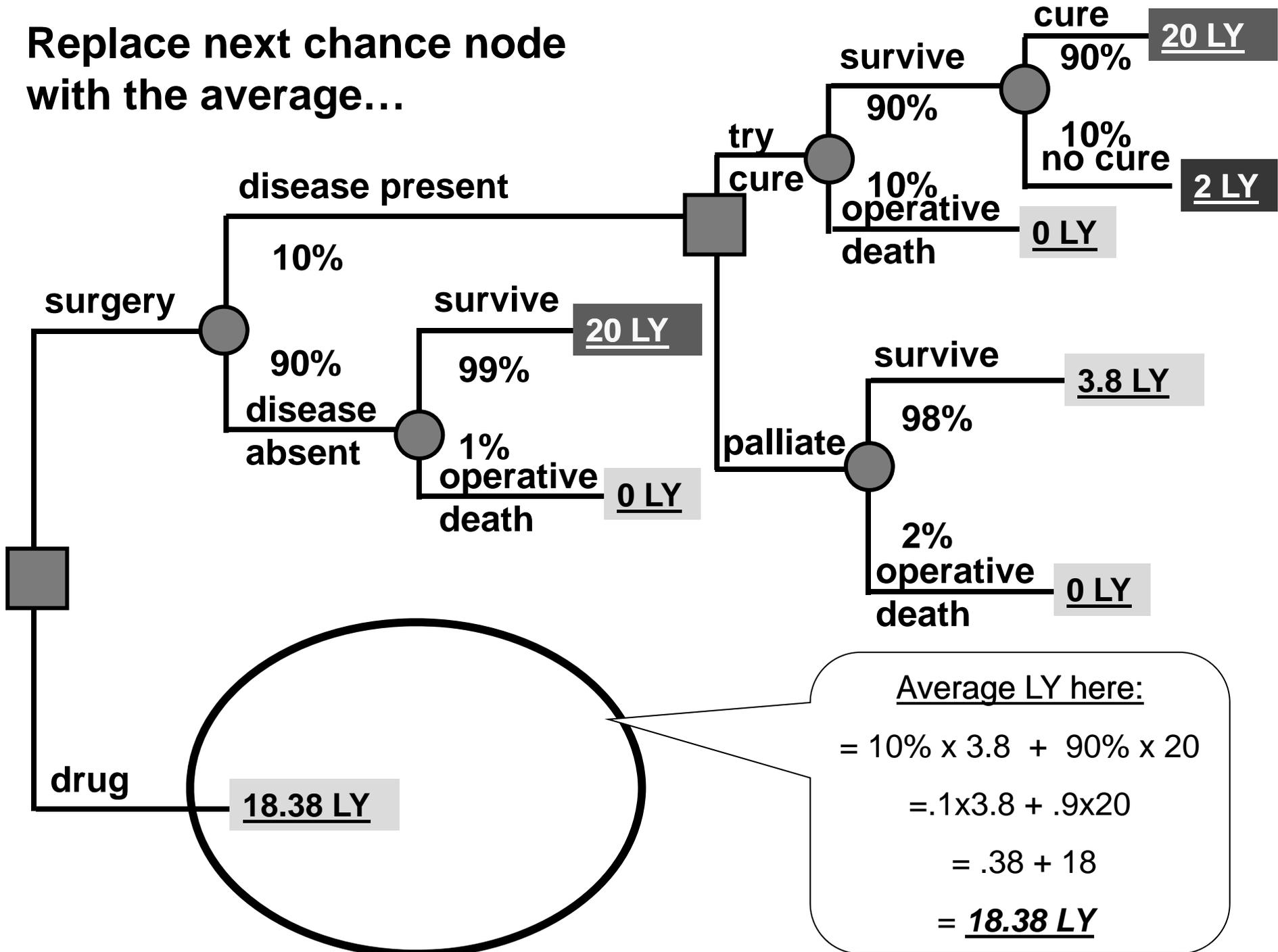
Replace these chance nodes with the average...



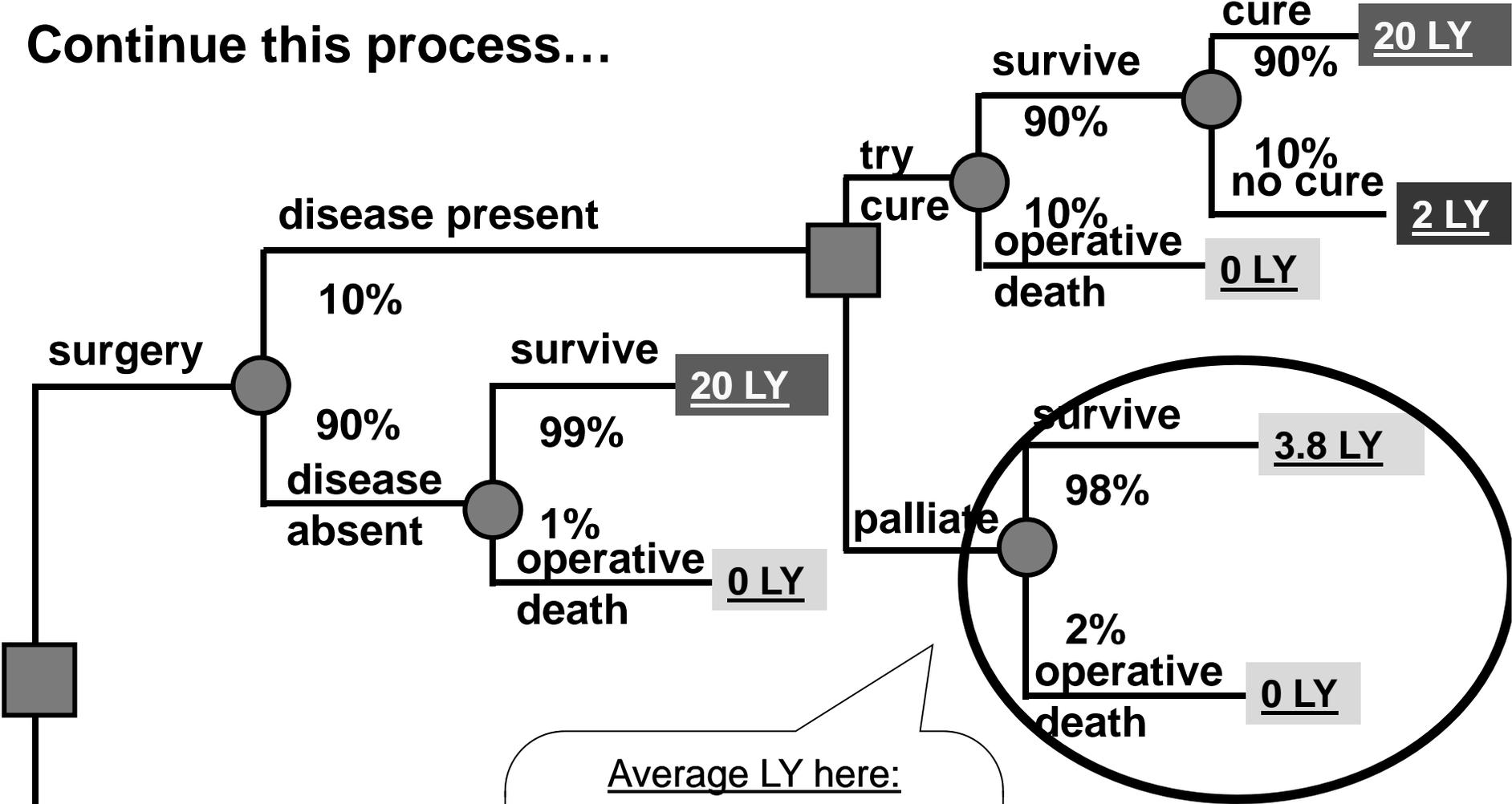
Replace next chance node with the average...



Replace next chance node with the average...



Continue this process...



Average LY here:

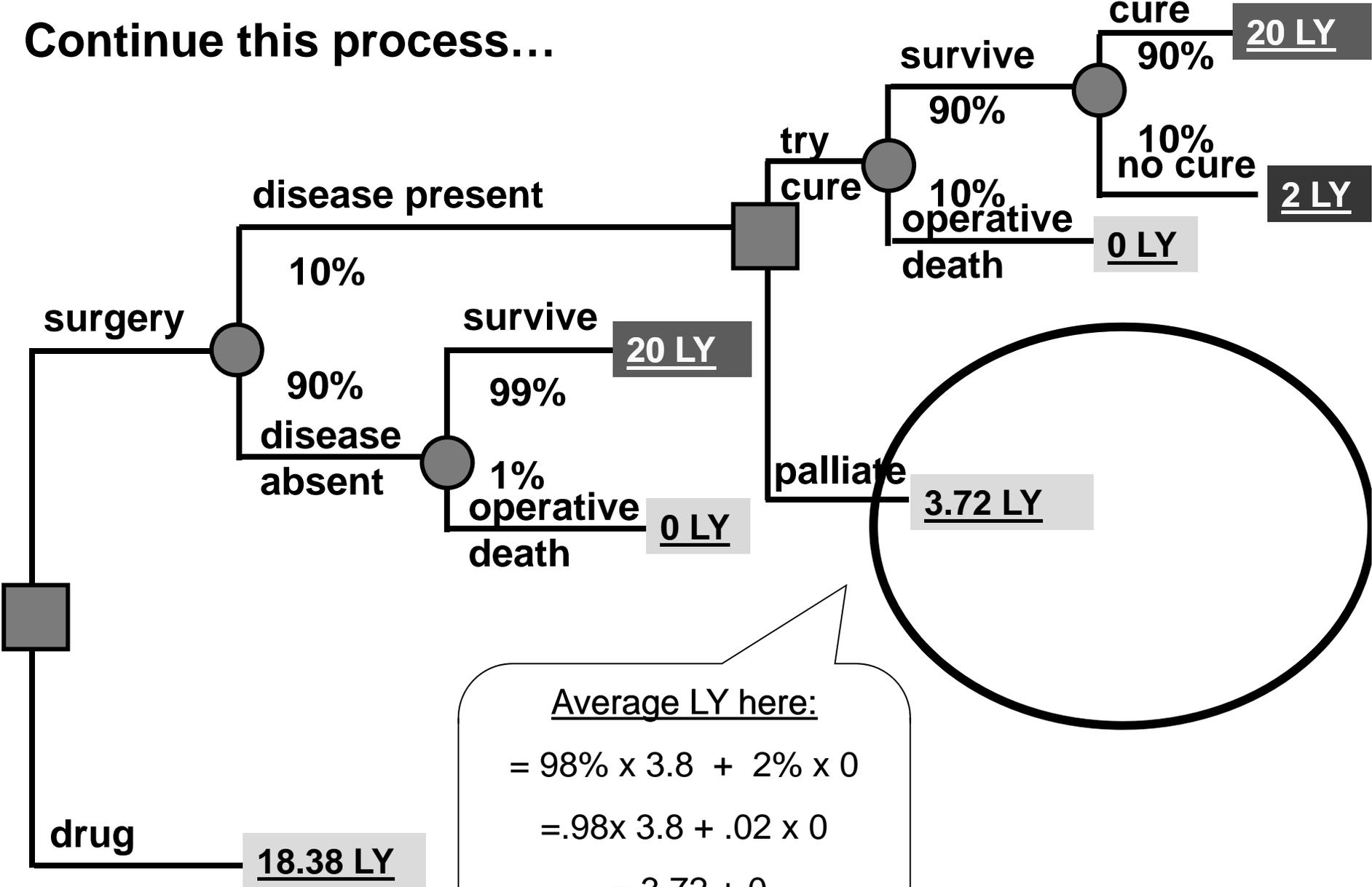
$$= 98\% \times 3.8 + 2\% \times 0$$

$$= .98 \times 3.8 + .02 \times 0$$

$$= 3.72 + 0$$

$$= \underline{\underline{3.72 LY}}$$

Continue this process...



Average LY here:

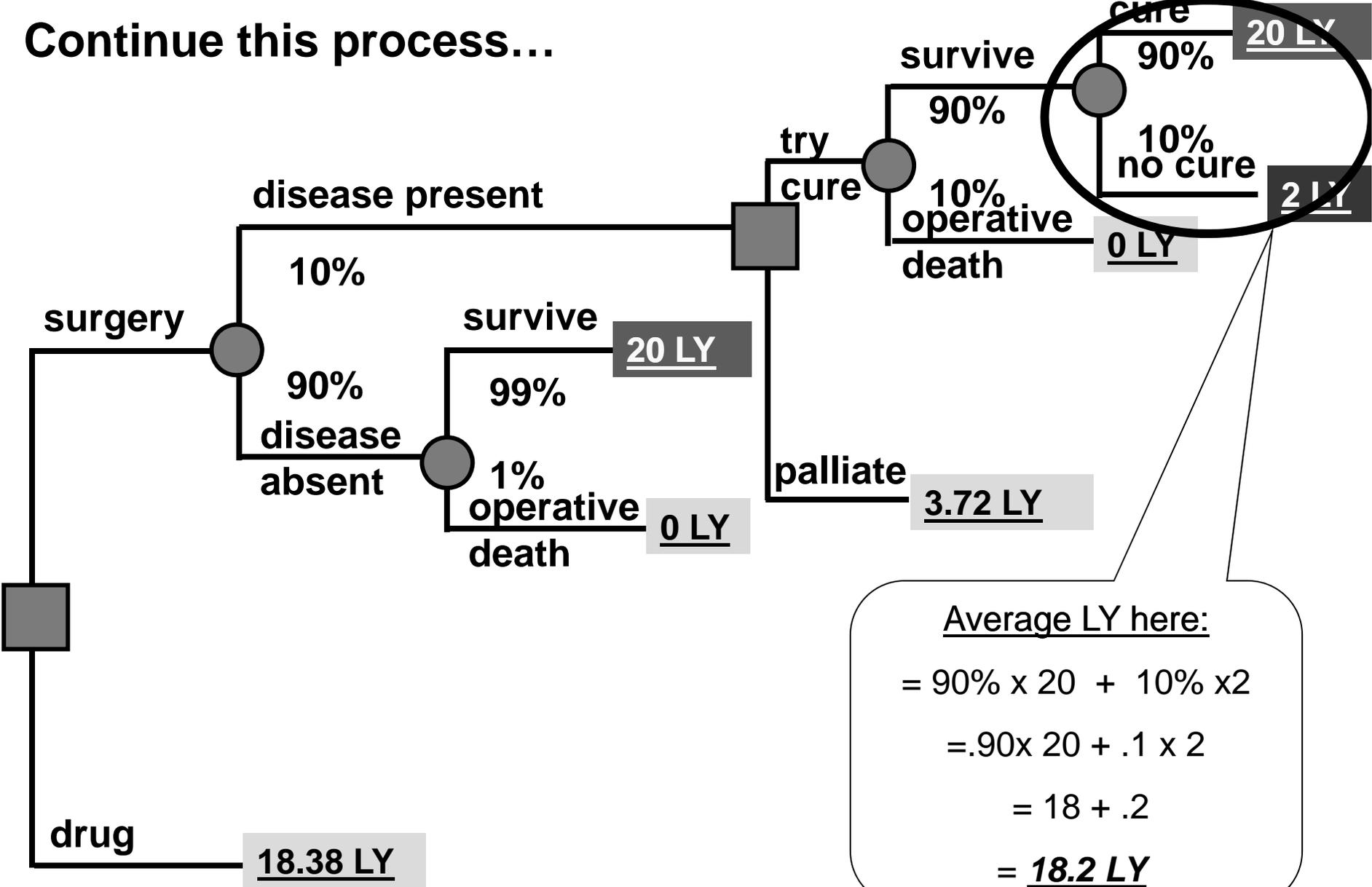
$$= 98\% \times 3.8 + 2\% \times 0$$

$$= .98 \times 3.8 + .02 \times 0$$

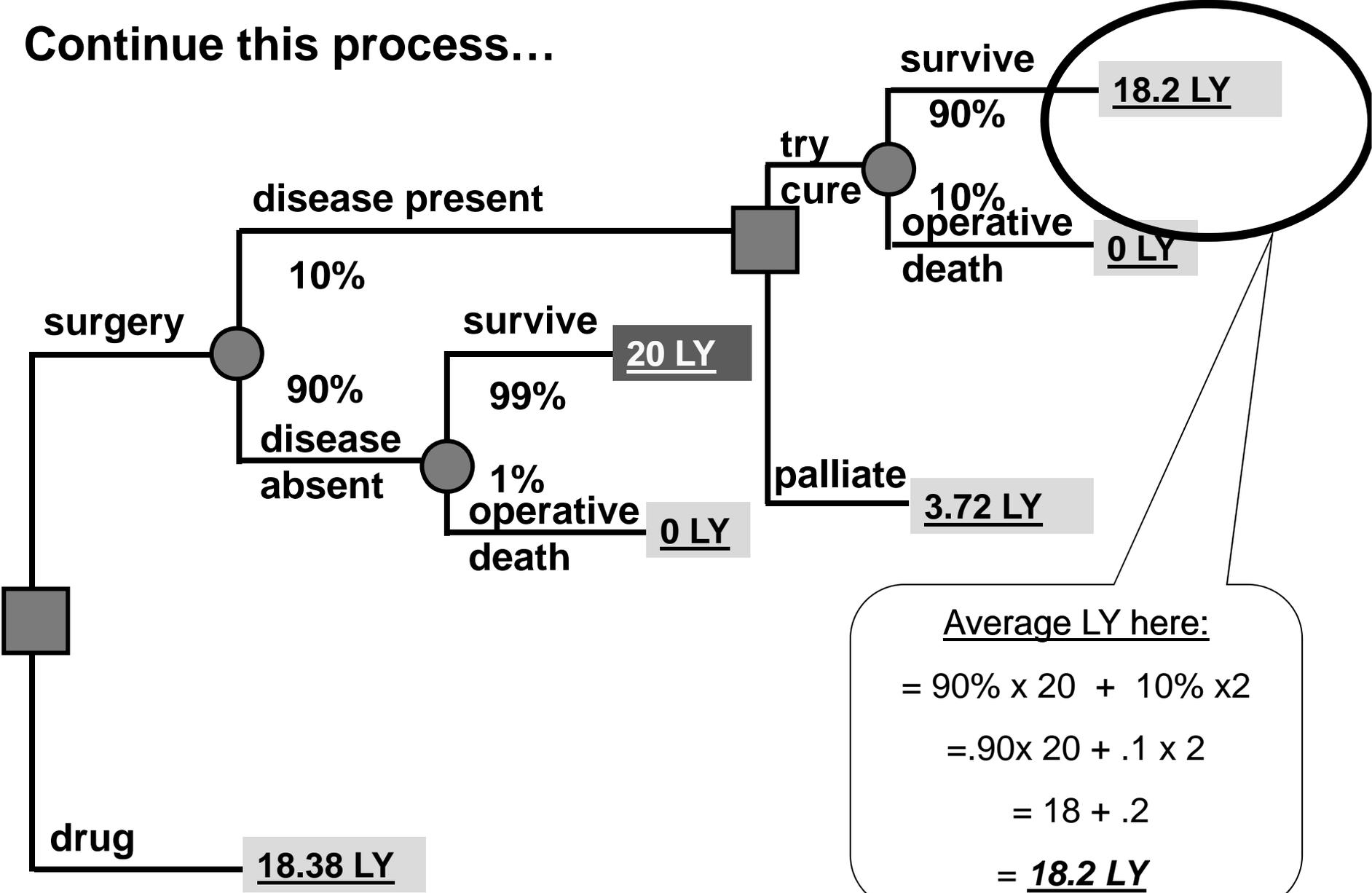
$$= 3.72 + 0$$

$$= \underline{\underline{3.72 LY}}$$

Continue this process...

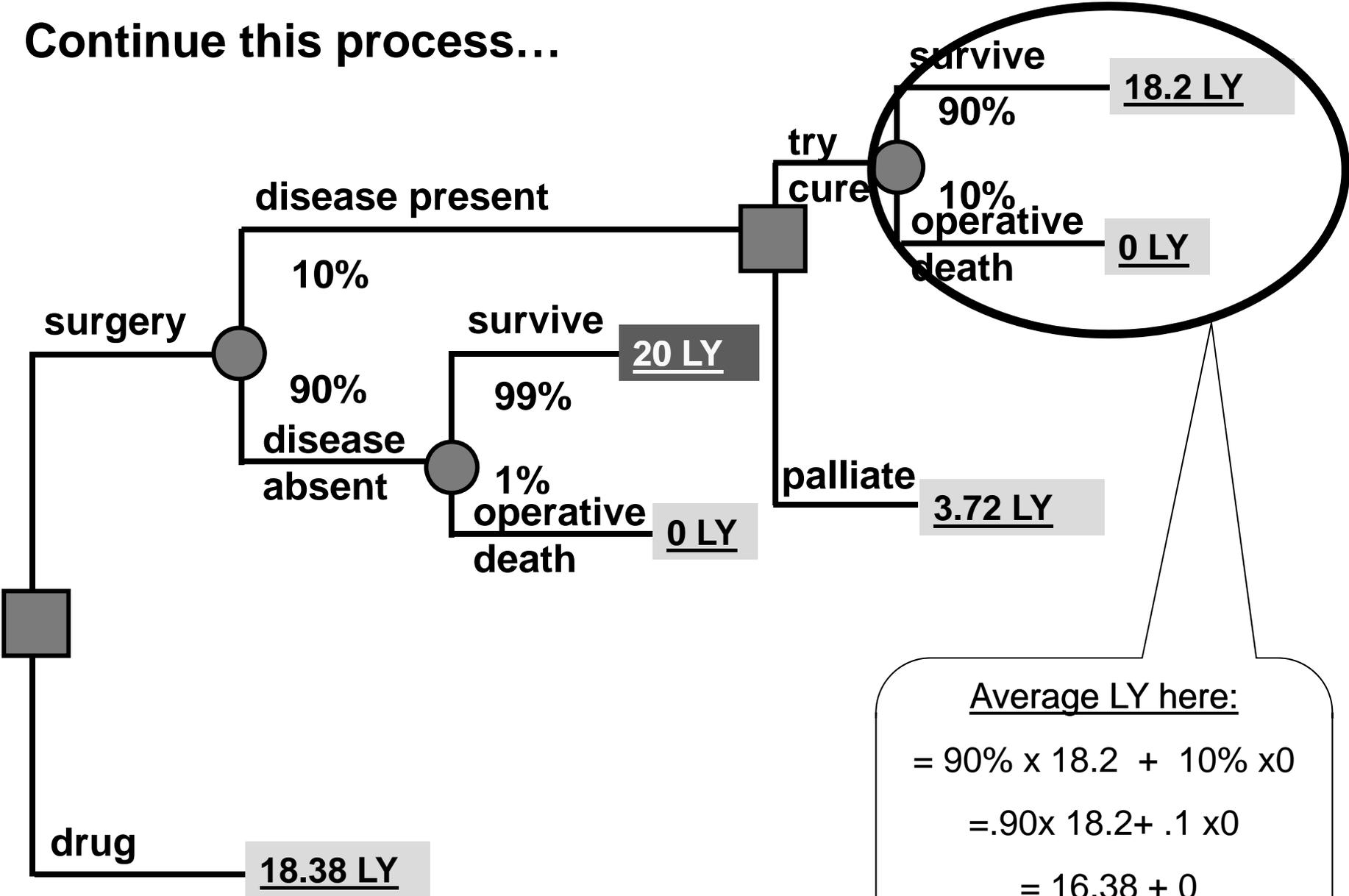


Continue this process...

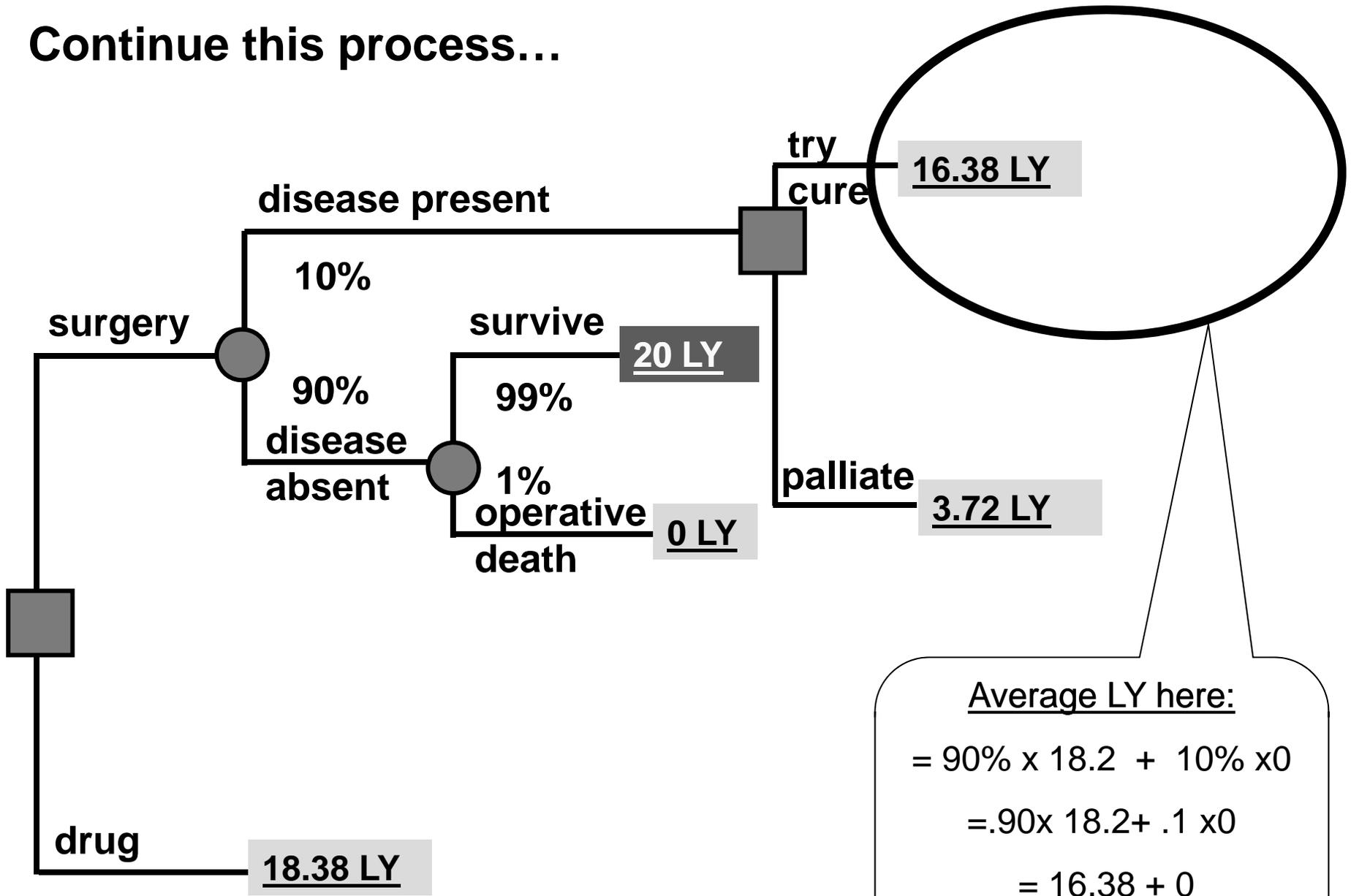


Average LY here:
= 90% x 20 + 10% x 2
= .90x 20 + .1 x 2
= 18 + .2
= 18.2 LY

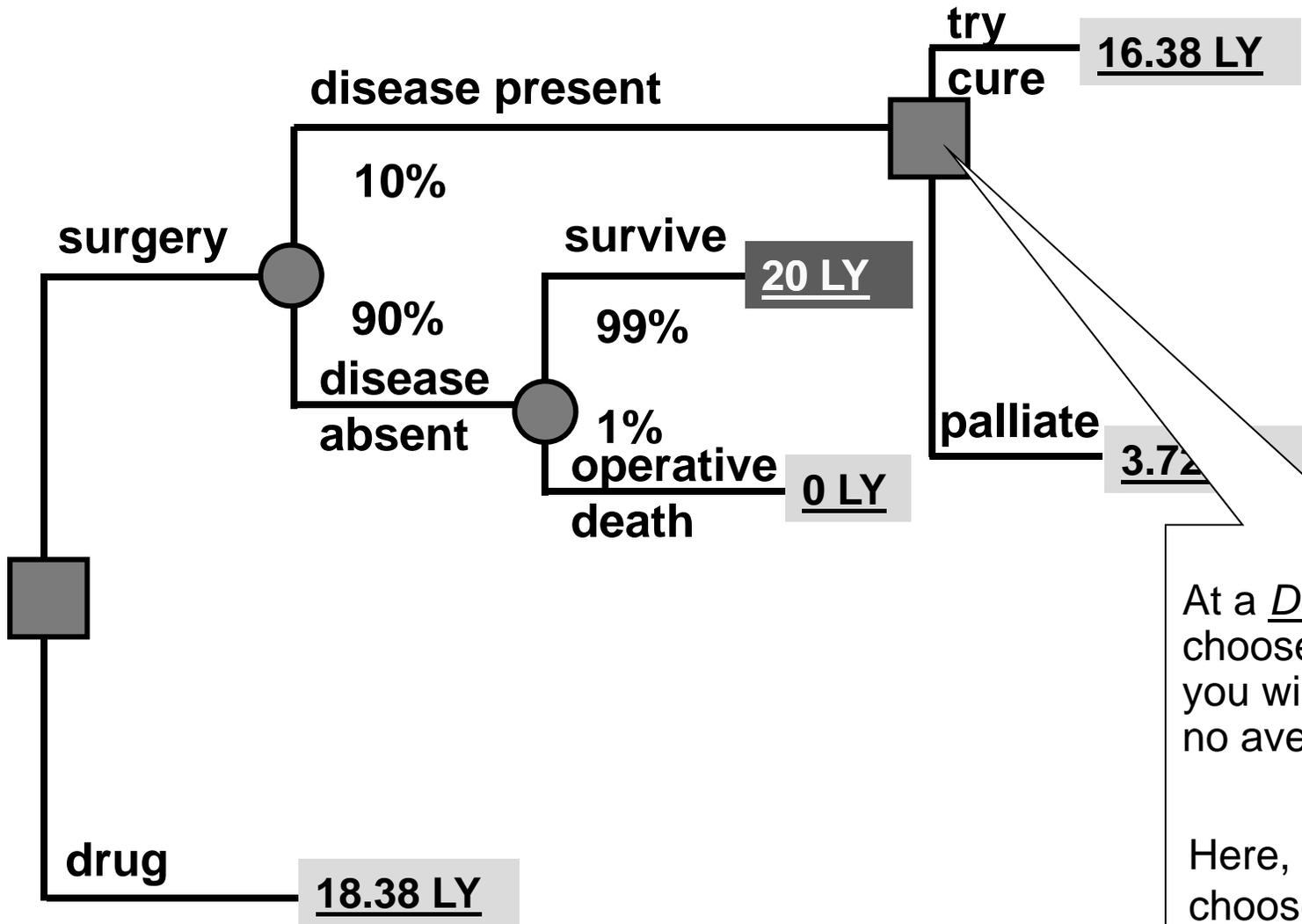
Continue this process...



Continue this process...

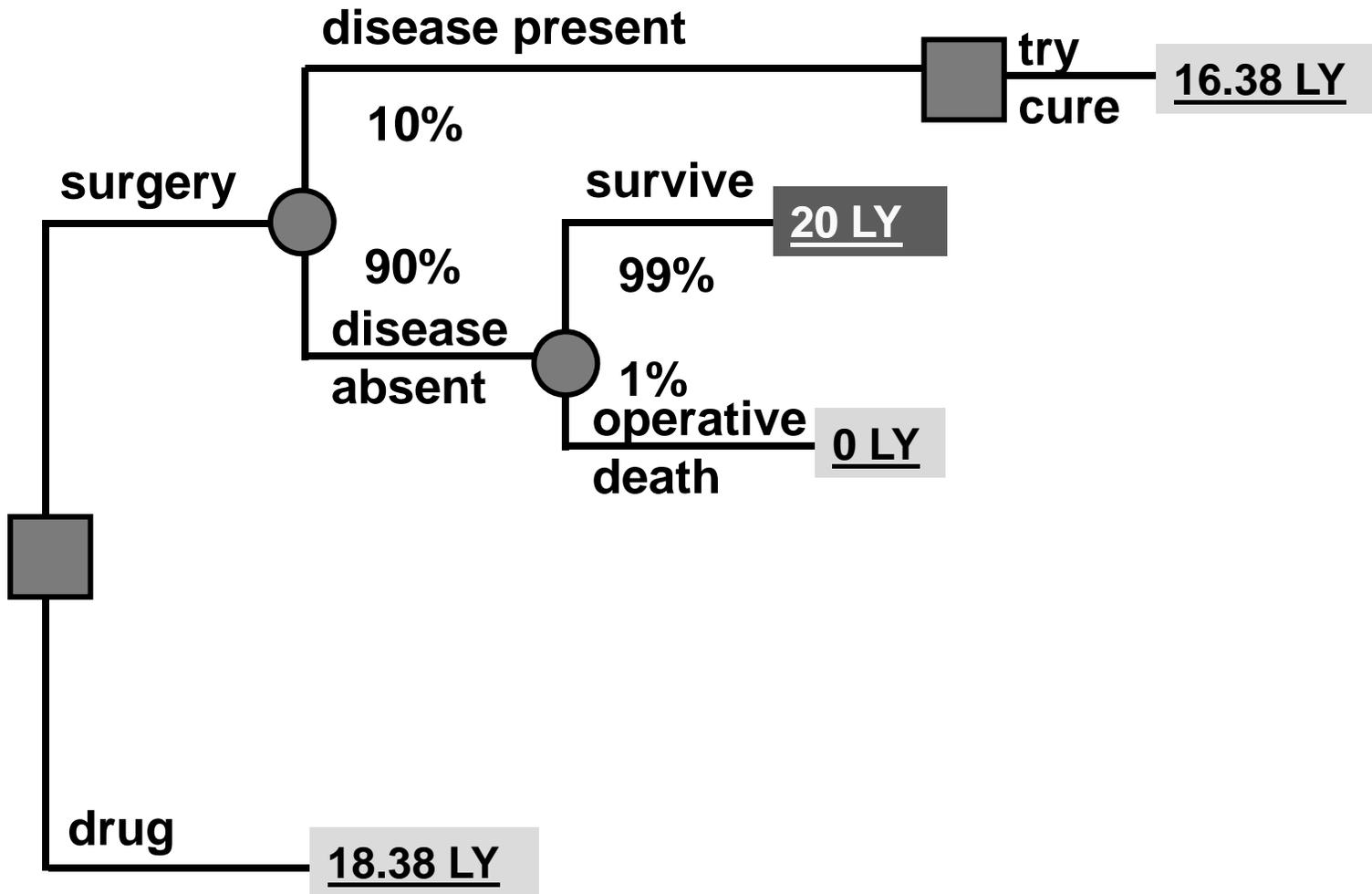


Average LY here:
= 90% x 18.2 + 10% x 0
= .90x 18.2+ .1 x 0
= 16.38 + 0
= 16.38 LY

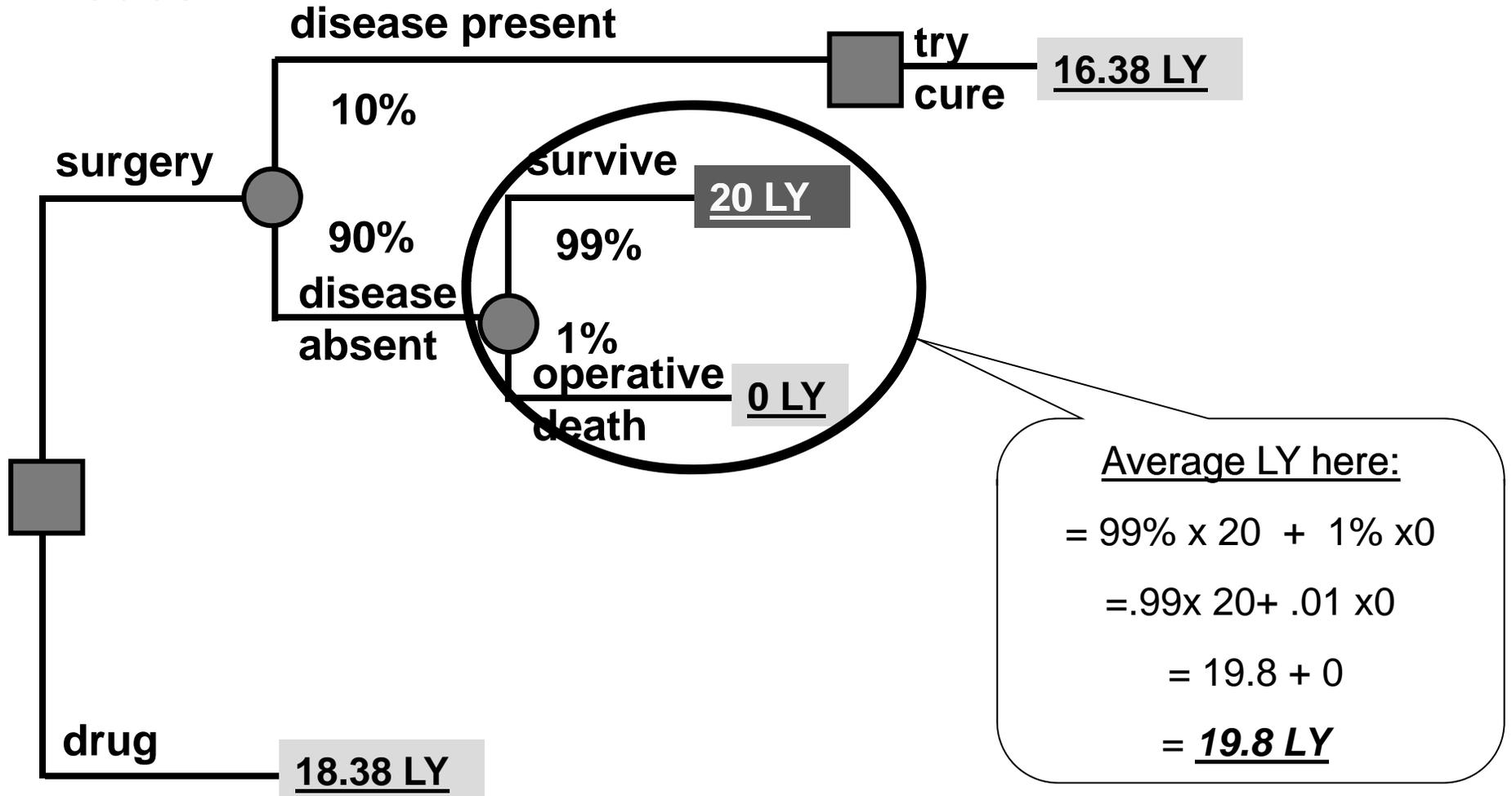


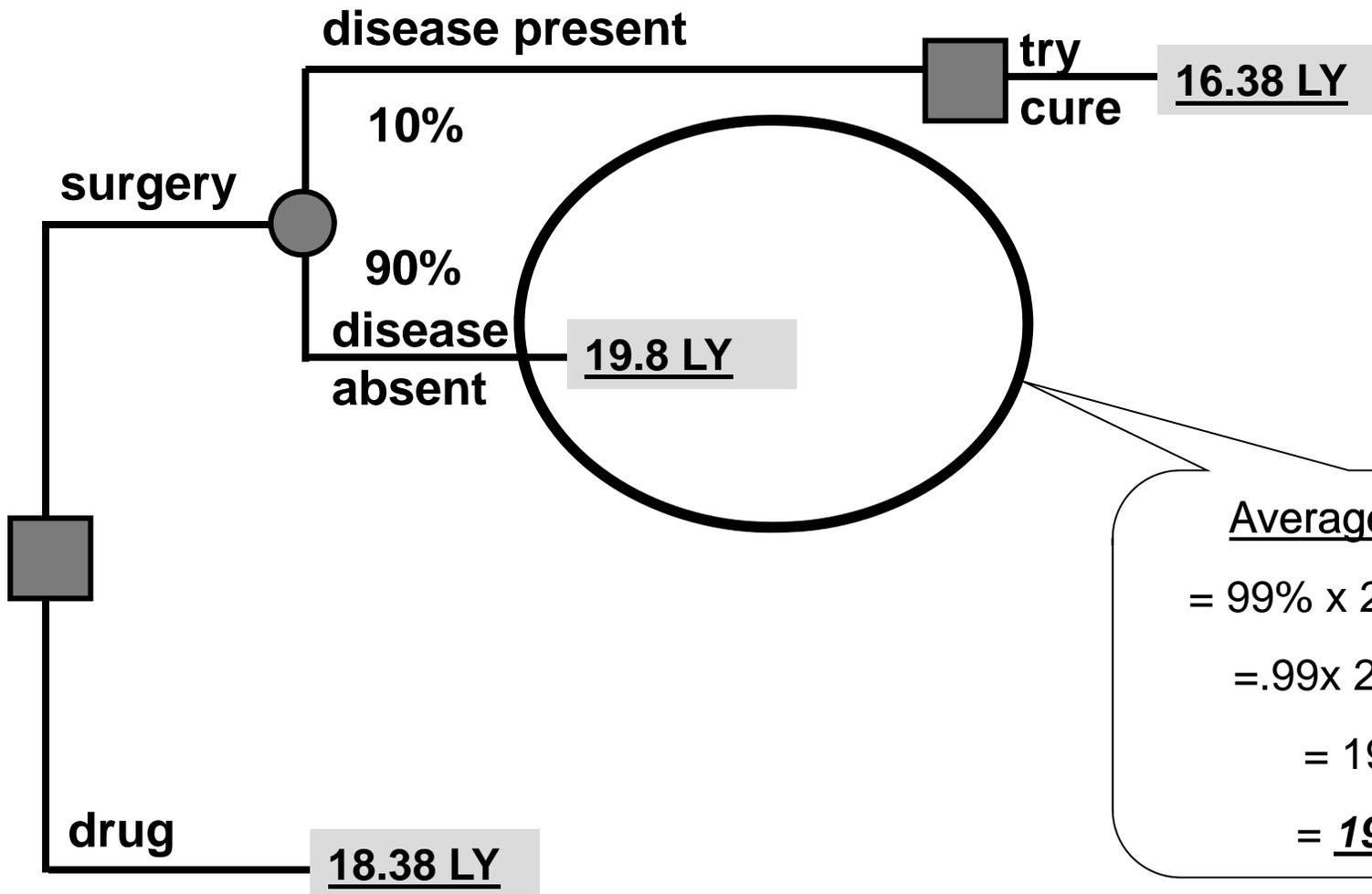
At a Decision Node you choose which path you wish to take -- no averaging!

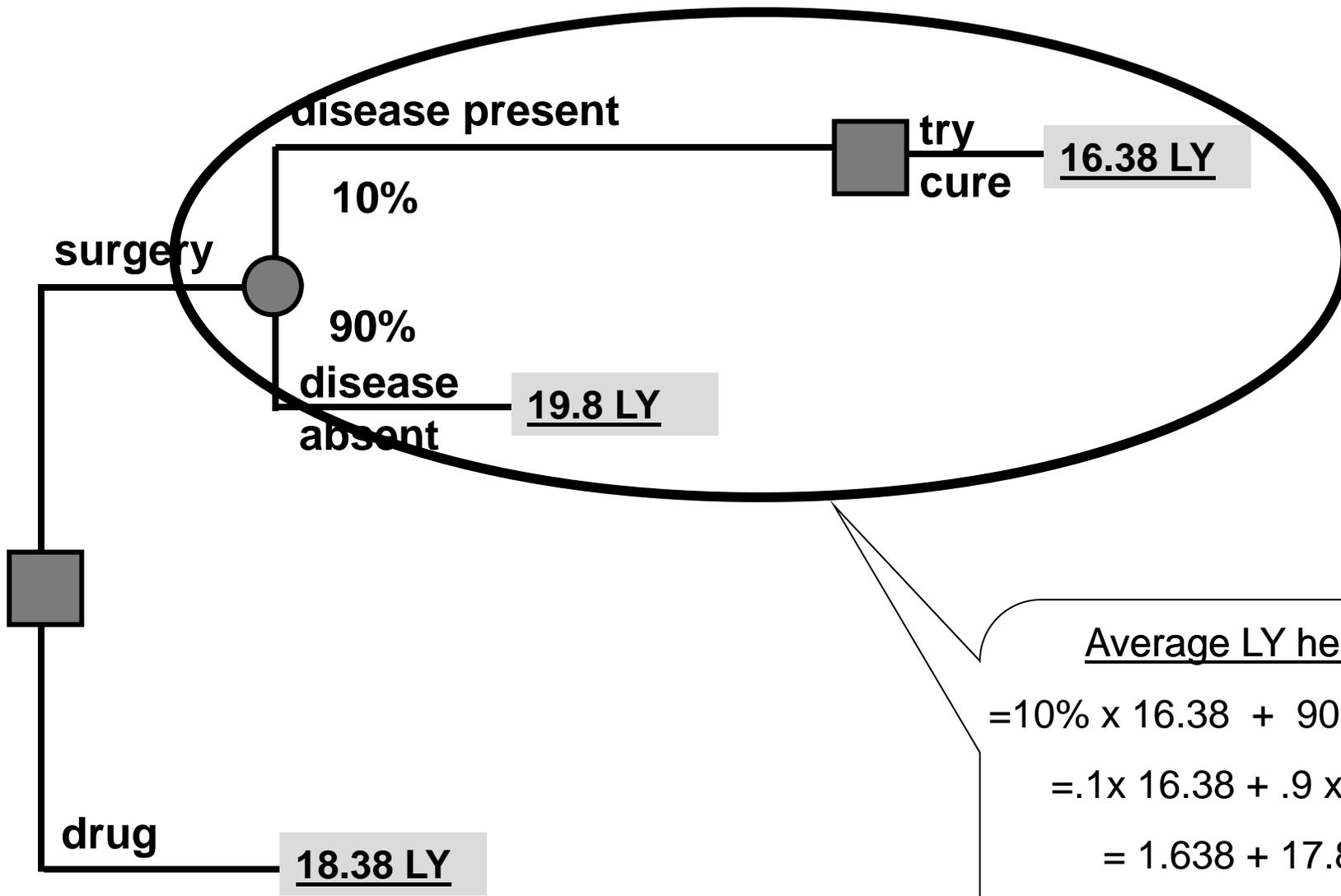
Here, we would choose to try for cure -- obviously!



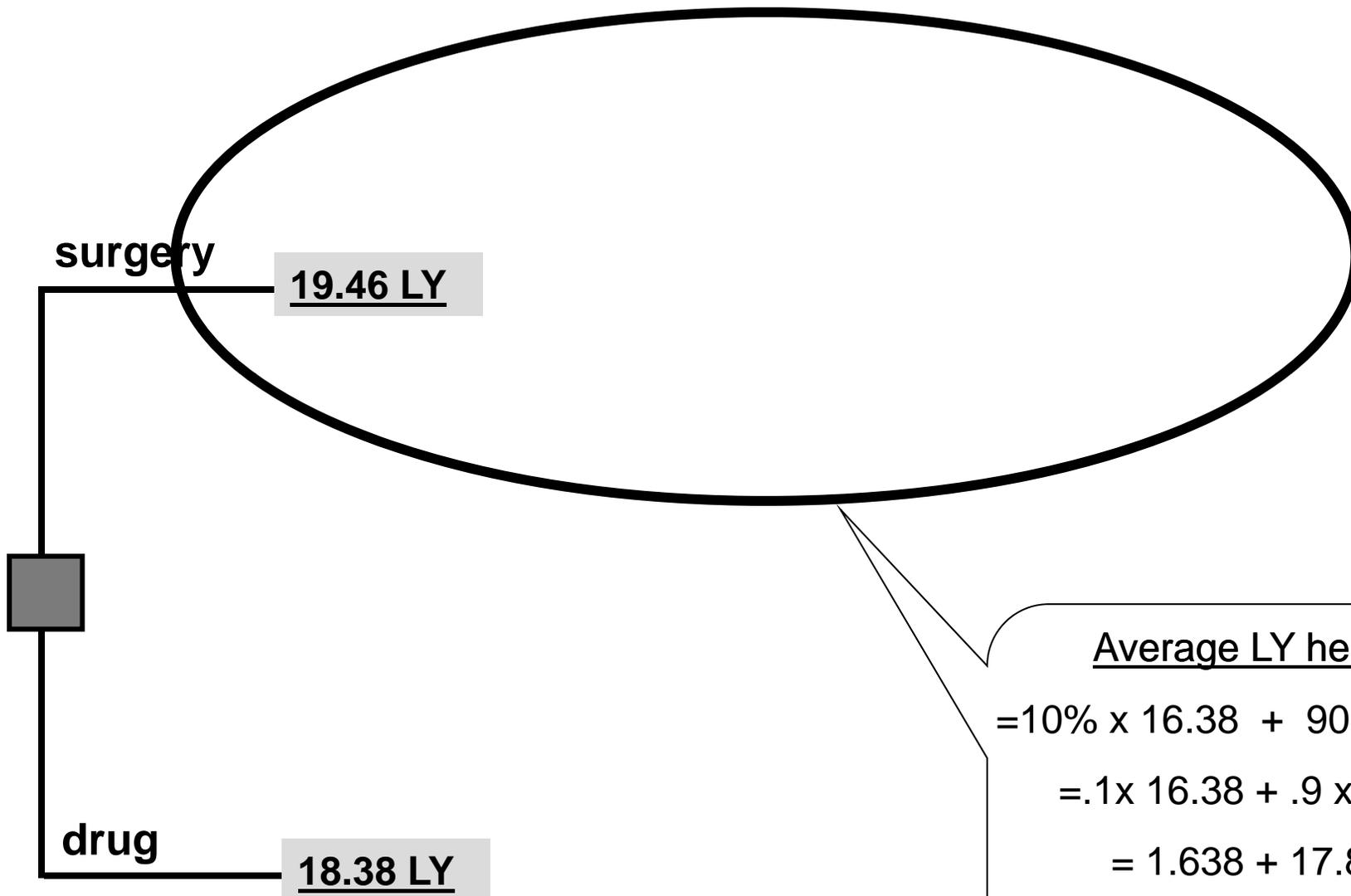
Continue working from right to left, averaging out at **Chance Nodes**, and choosing best branch at **Decision Nodes**...





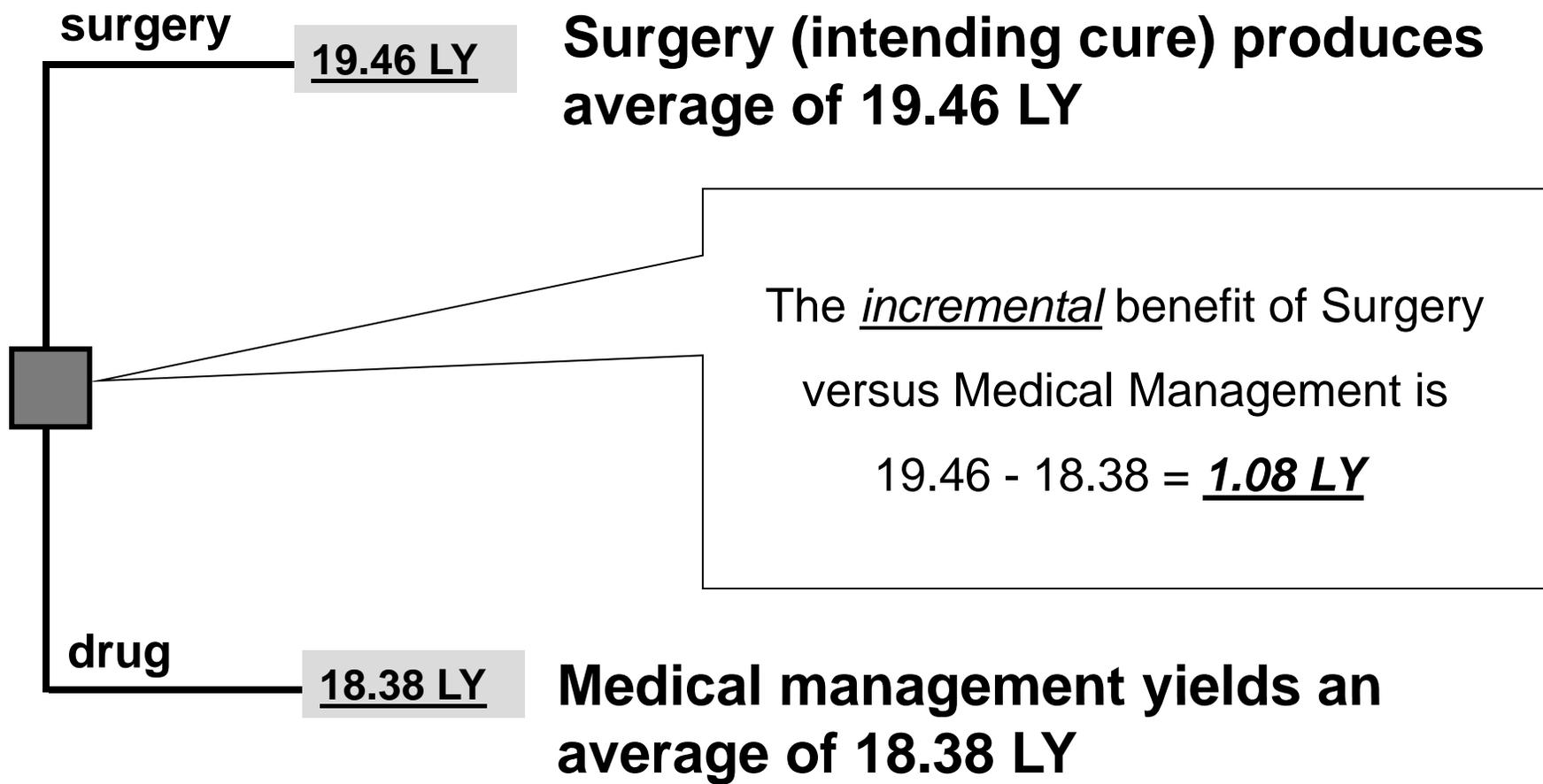


Average LY here:
 $= 10\% \times 16.38 + 90\% \times 19.8$
 $= .1 \times 16.38 + .9 \times 19.8$
 $= 1.638 + 17.82$
 $= \underline{19.46 LY}$



Average LY here:
=10% x 16.38 + 90% x19.8
=.1x 16.38 + .9 x19.8
= 1.638 + 17.82
= 19.46 LY

The outcome for each decision is more apparent now:



Repeat this Decision Analysis Using Other Outcome Measures

- Instead of just using average life years, can use QALYs at each endpoint.
- If you use both costs and QALYs at each endpoint:
 - Then can calculate the incremental cost effectiveness of surgery versus medical management

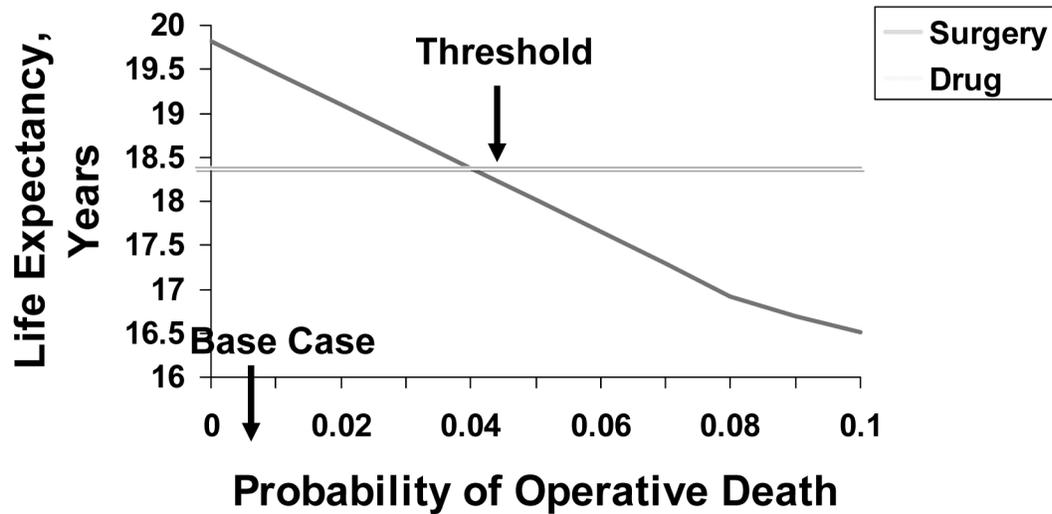
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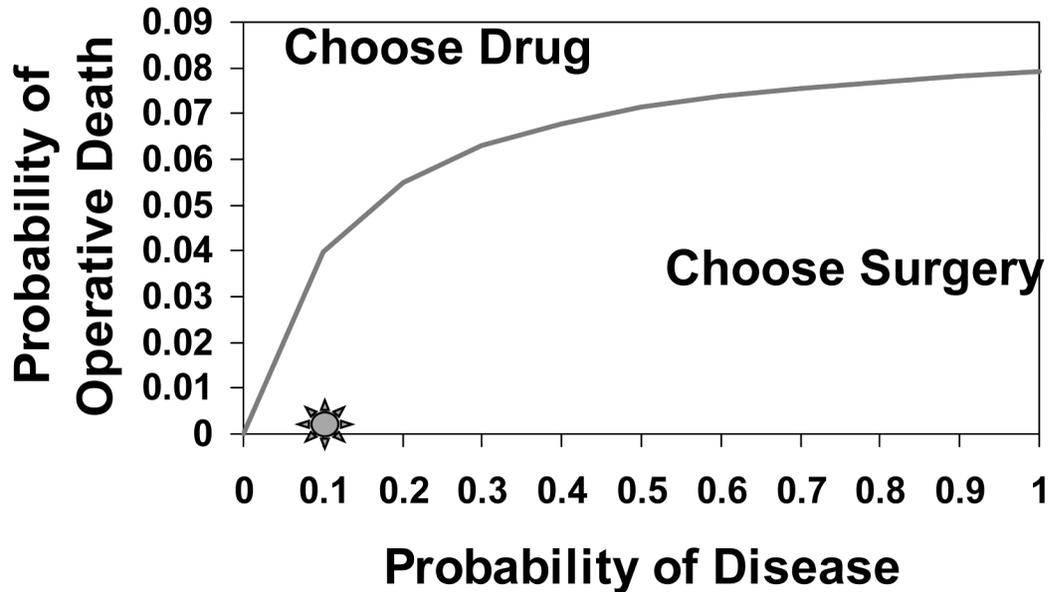
Sensitivity Analysis

- Systematically asking “what if” questions to see how the decision result changes.
- Determines how “robust” the decision is.
- Threshold analysis: one parameter varied
- Multi-way analysis: multiple parameters systematically varied

Sensitivity Analysis: Probability of Operative Death



Two-Way Sensitivity Analysis: pDisease vs. pOperativeDeath



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What is a Markov Model?

Mathematical modeling technique, derived from matrix algebra, that describes the transitions a cohort of patients make among a number of mutually exclusive and exhaustive health states during a series of short intervals or cycles

When to use a Markov Model?

- Problem involves risk that is continuous over time
- Timing of events is important
- Important events may happen more than once

Properties of a Markov Model

- Patient is always in one of a finite number of health states
- Events are modeled as transitions from one state to another
- Contribution of utility to overall prognosis depends on length of time spent in health states
- During each cycle, the patient may make a transition from one state to another

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Constructing a Markov Model

- Choose set of mutually exclusive health states
- Determine possible transitions between these health states
 - State transitions
 - Transition probabilities
- Determine clinical valid cycle length

Cycle Length

- Clinically meaningful time interval
- Entire life of patient, relatively rare events → yearly
- Shorter time frame, frequent events, rate changing rapidly over time → monthly or weekly
- Availability of probability data?

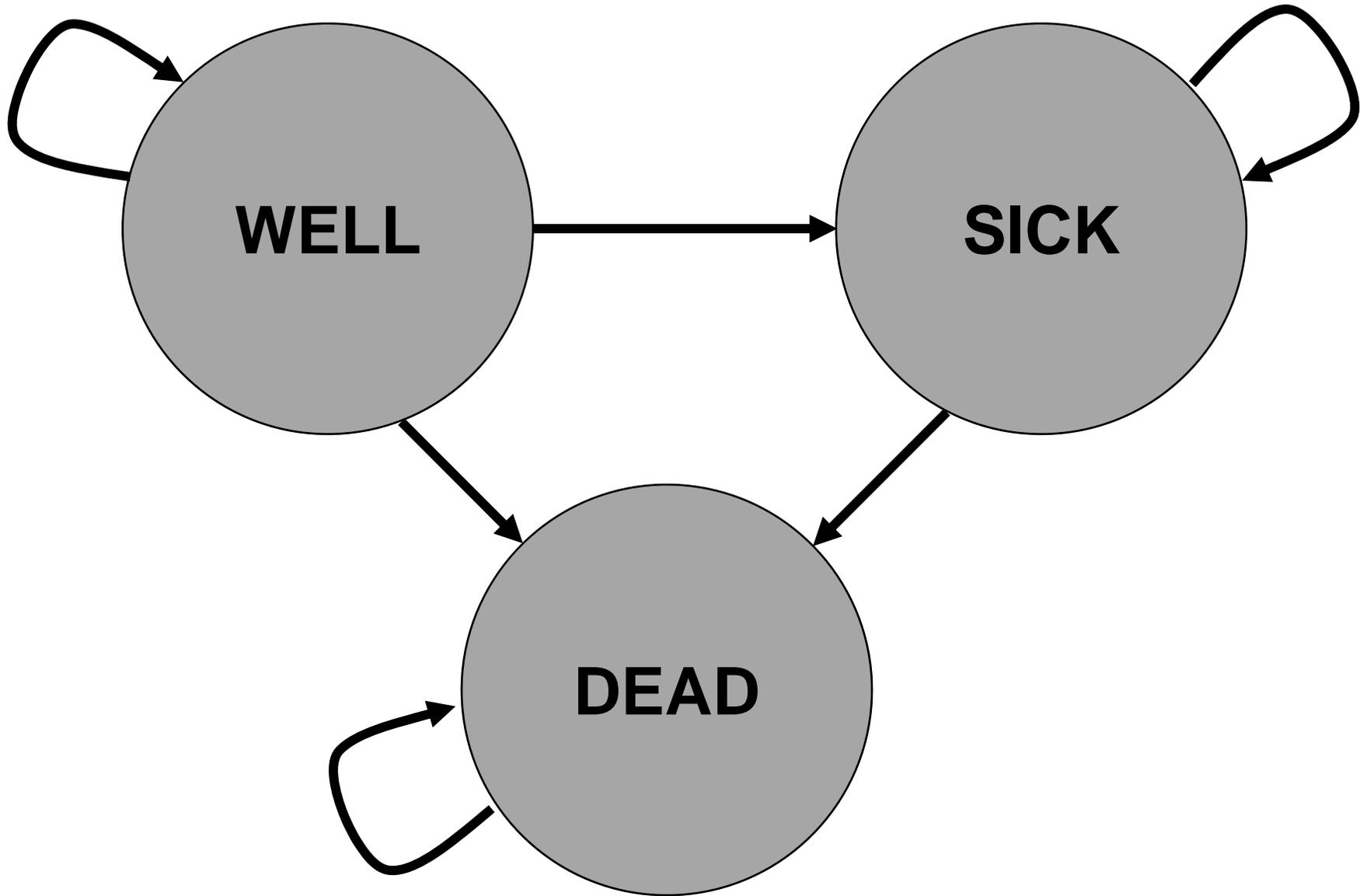
Markovian Assumption

- Behavior of the process subsequent to any cycle depends only on its description in that cycle
 - No memory of earlier cycles
- How do we get around this?
 - New health states
 - Tunnel states

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State Transition Diagram



Evaluation

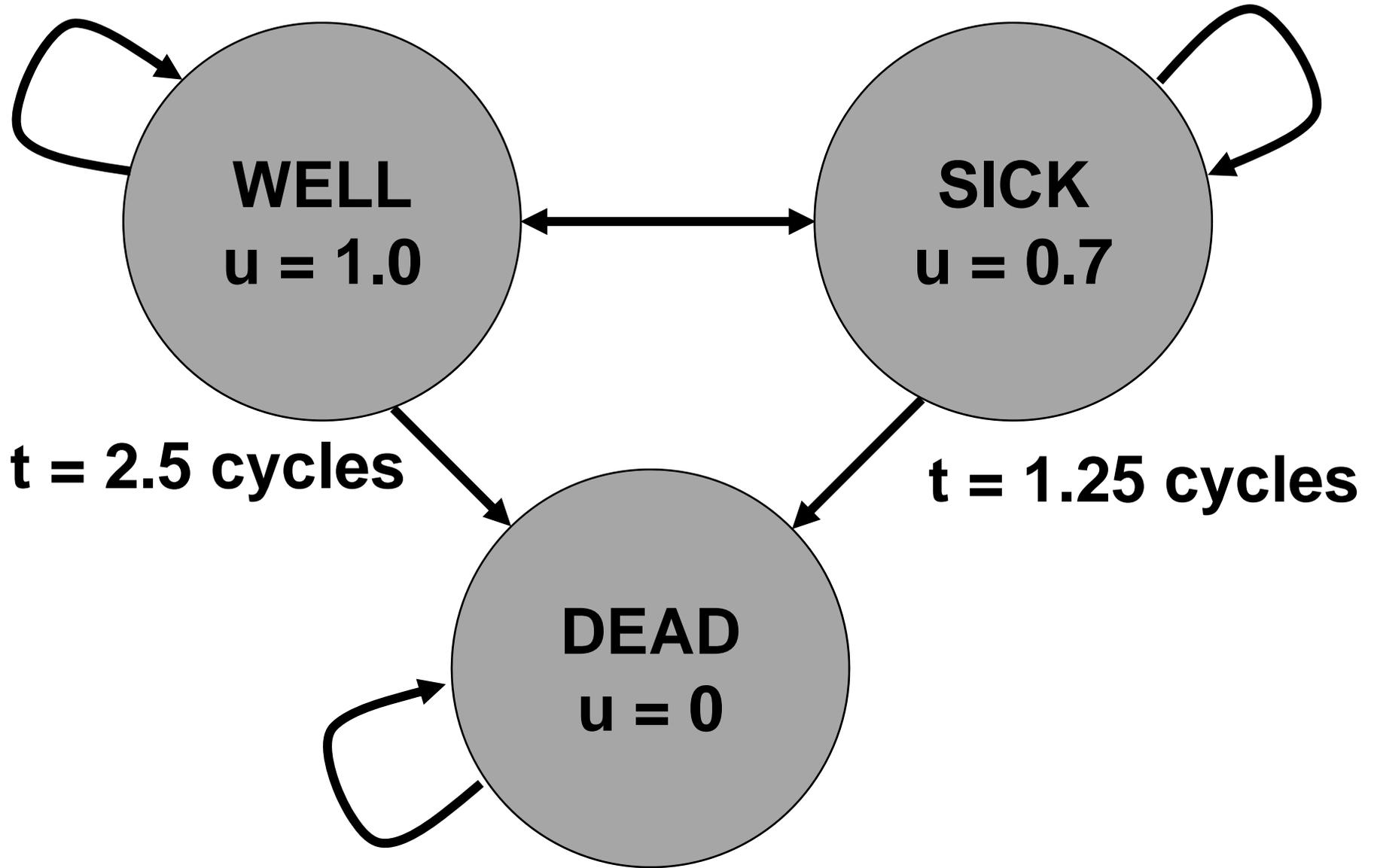
- Compute number of cycles spent in each health state

- Expected utility = $\sum_{s=1}^n t_s$

- Define incremental utility for spending a cycle in given health state

- Expected utility = $\sum_{s=1}^n t_s * U_s$

State Transition Diagram



Quality-adjusted life expectancy

$$= (t_w * u_w) + (t_s * u_s)$$

$$= (2.5 * 1) + (1.25 * 0.7)$$

$$= 3.9 \text{ QALYs}$$

Calculation of Outcomes with a Markov Model

- Assume absorbing health state (death)
- Methods:
 - Matrix algebraic solution
 - Markov cohort simulation
 - Monte Carlo simulation

Fundamental Matrix Solution

- Requires constant transition probabilities
- Does not require simulation
- Requires matrix algebra

Transition Probability Matrix

	Well	Sick	Dead
Well	0.75	0.20	0.05
Sick	0	0.70	0.30
Dead	0	0	1

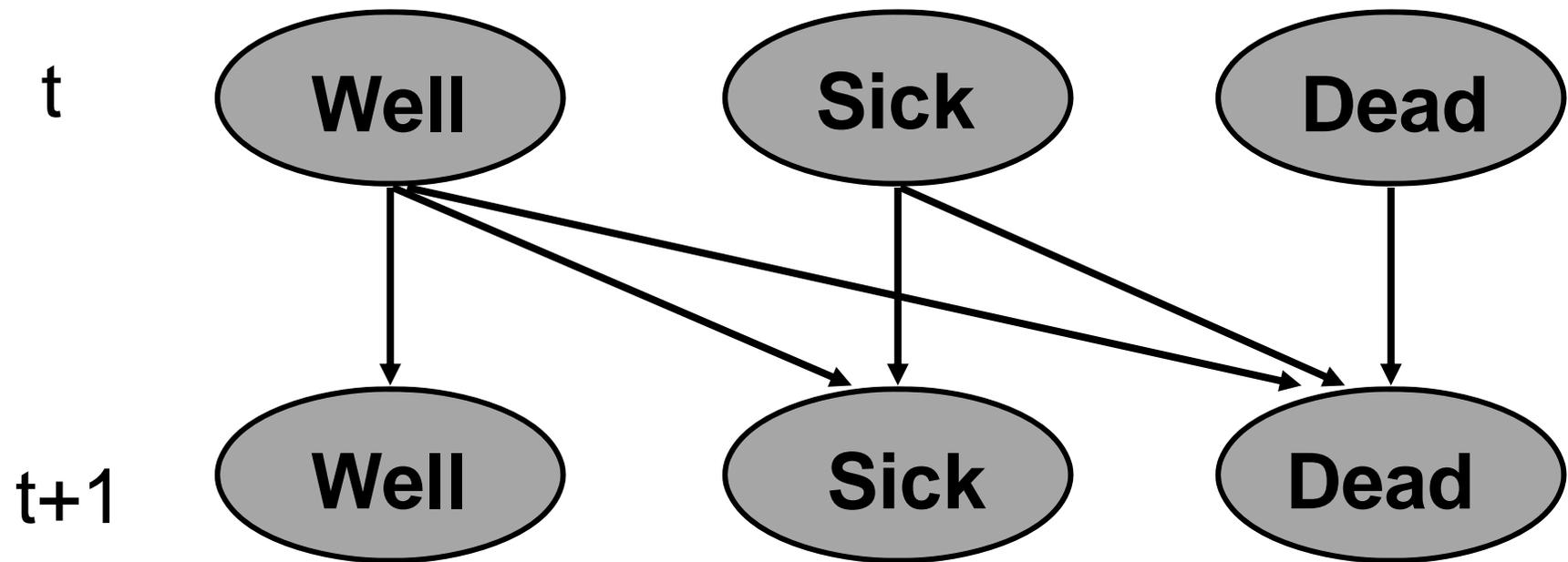
Starting Probability Vector: [1 0 0]

Markov Cohort Simulation

- Large number of patients are followed as a cohort
- Time dependent probabilities and utilities may be easily incorporated into the analysis
- Does not provide information on the distribution or variance of expected values

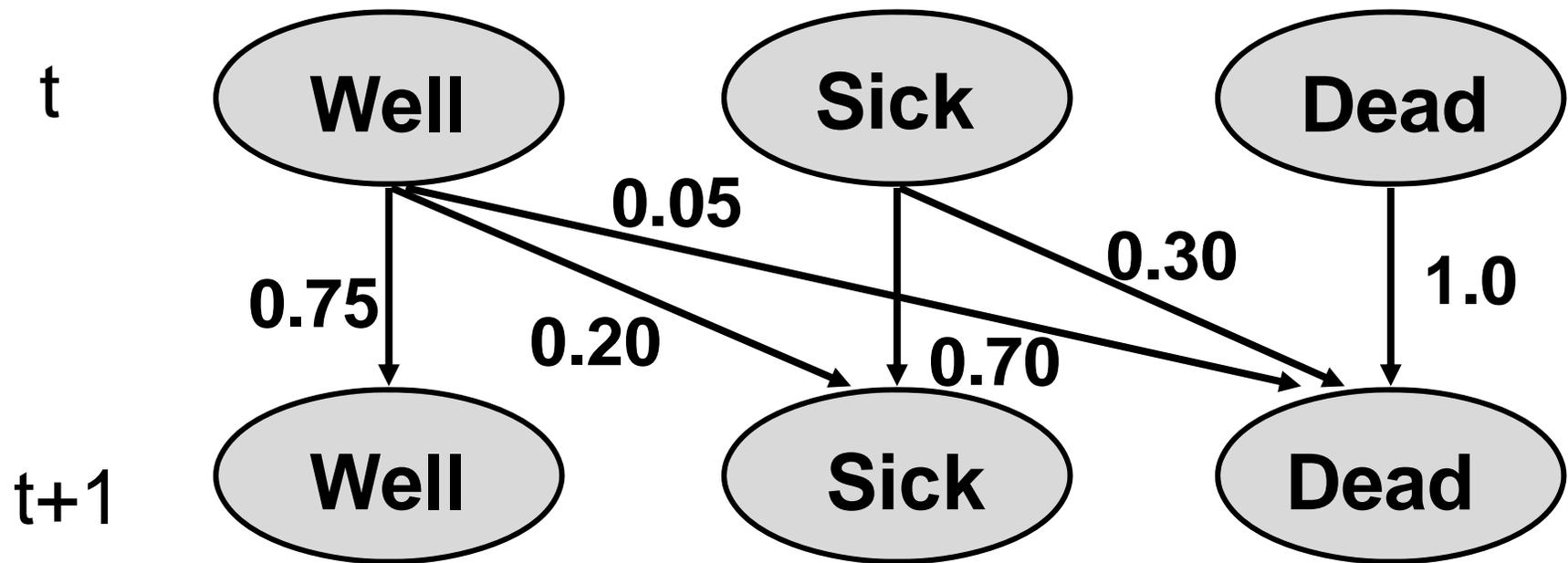
Markov Cohort Simulation

Time



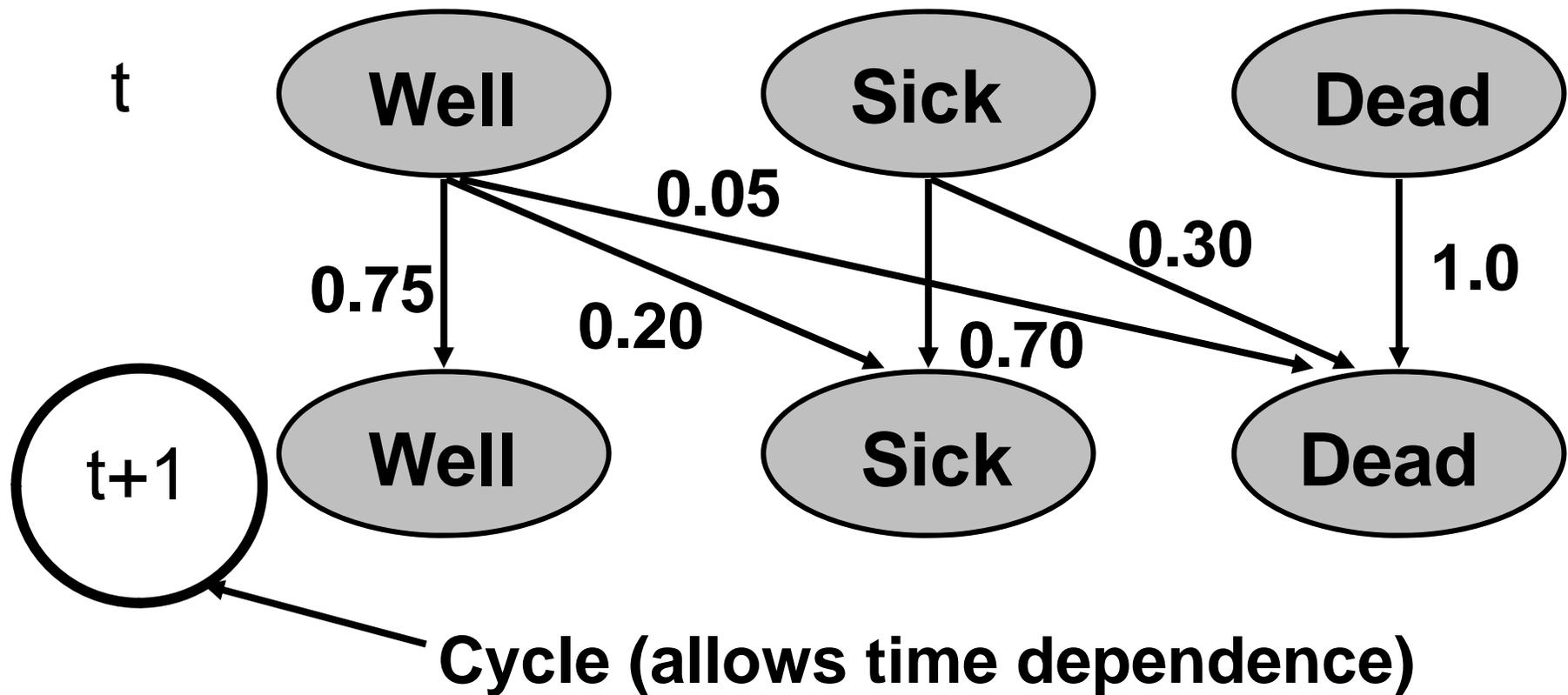
Markov Cohort Simulation

Time

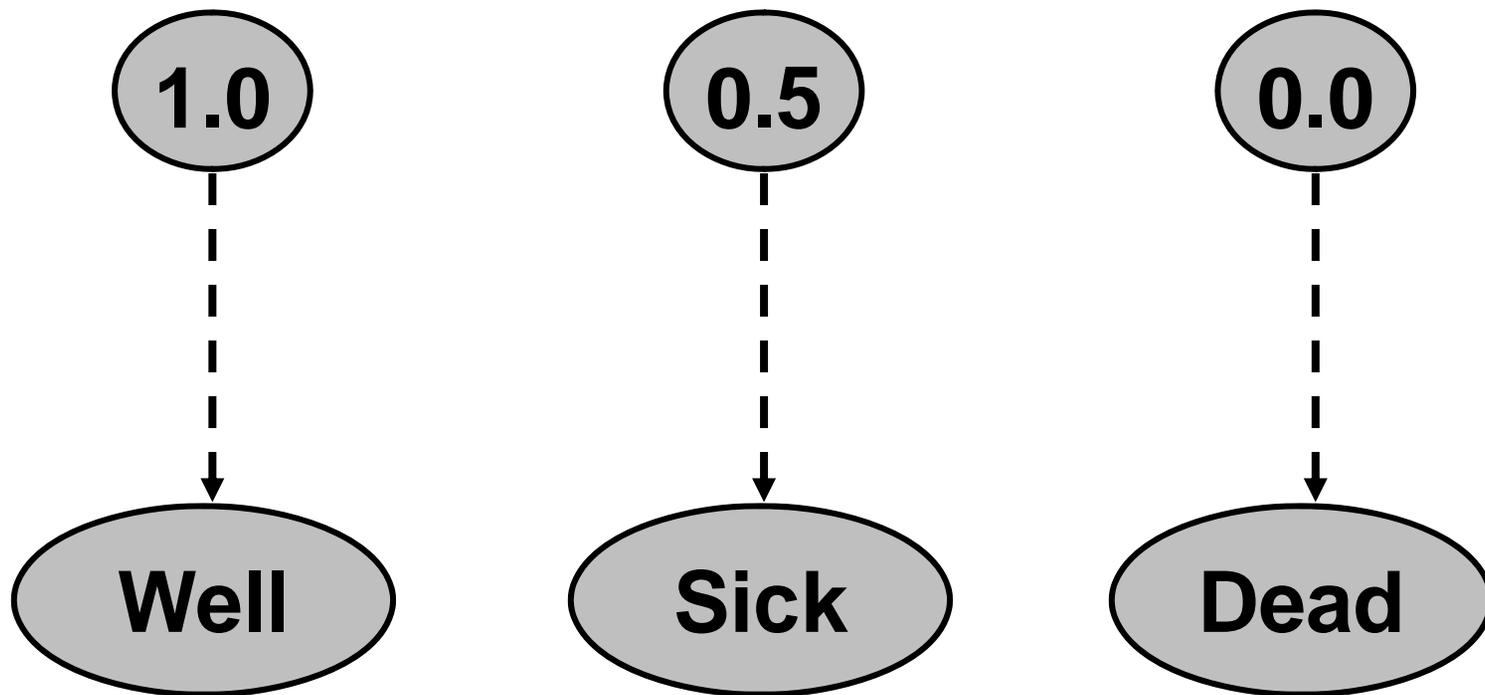


Markov Cohort Simulation

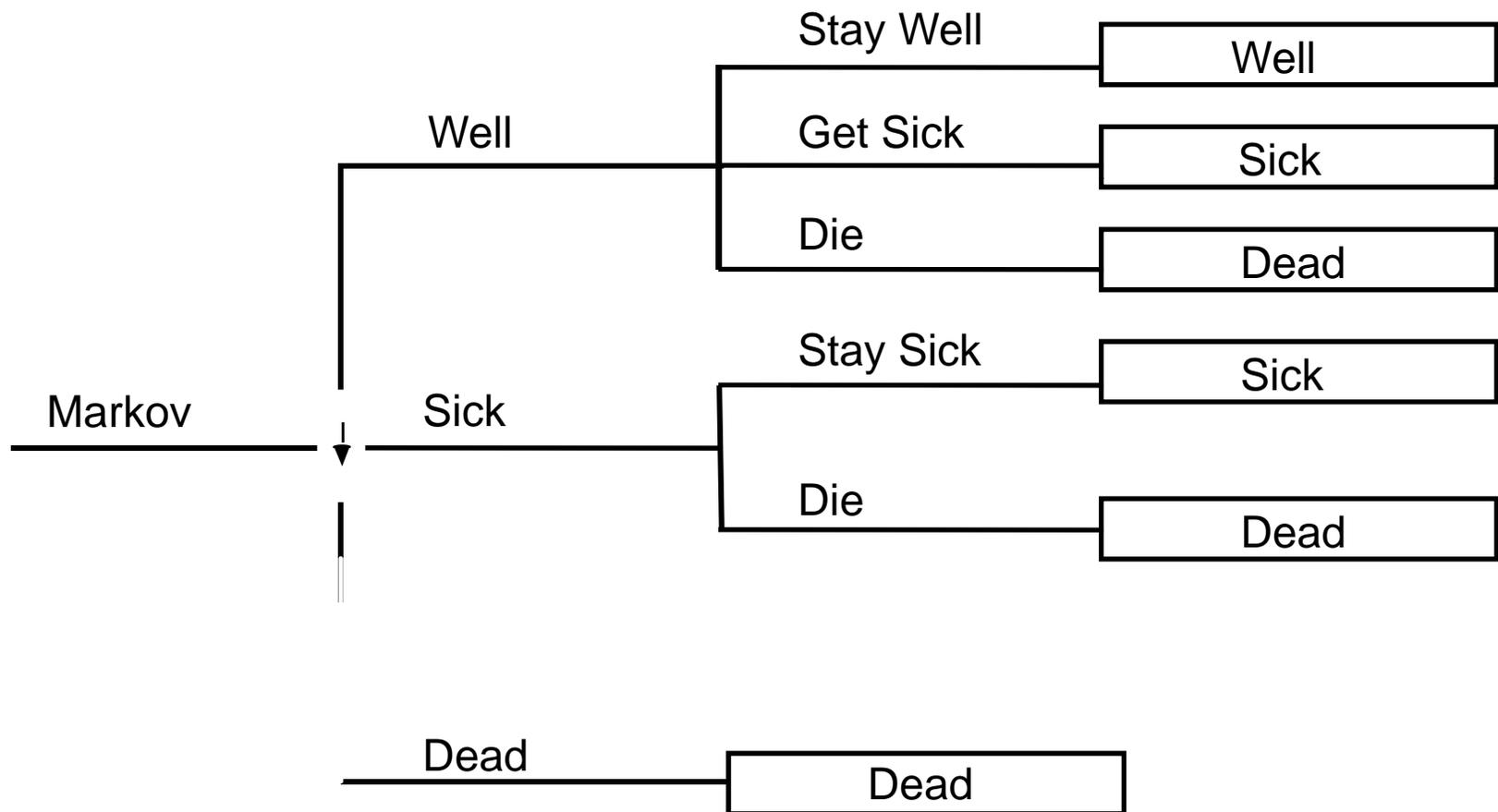
Time



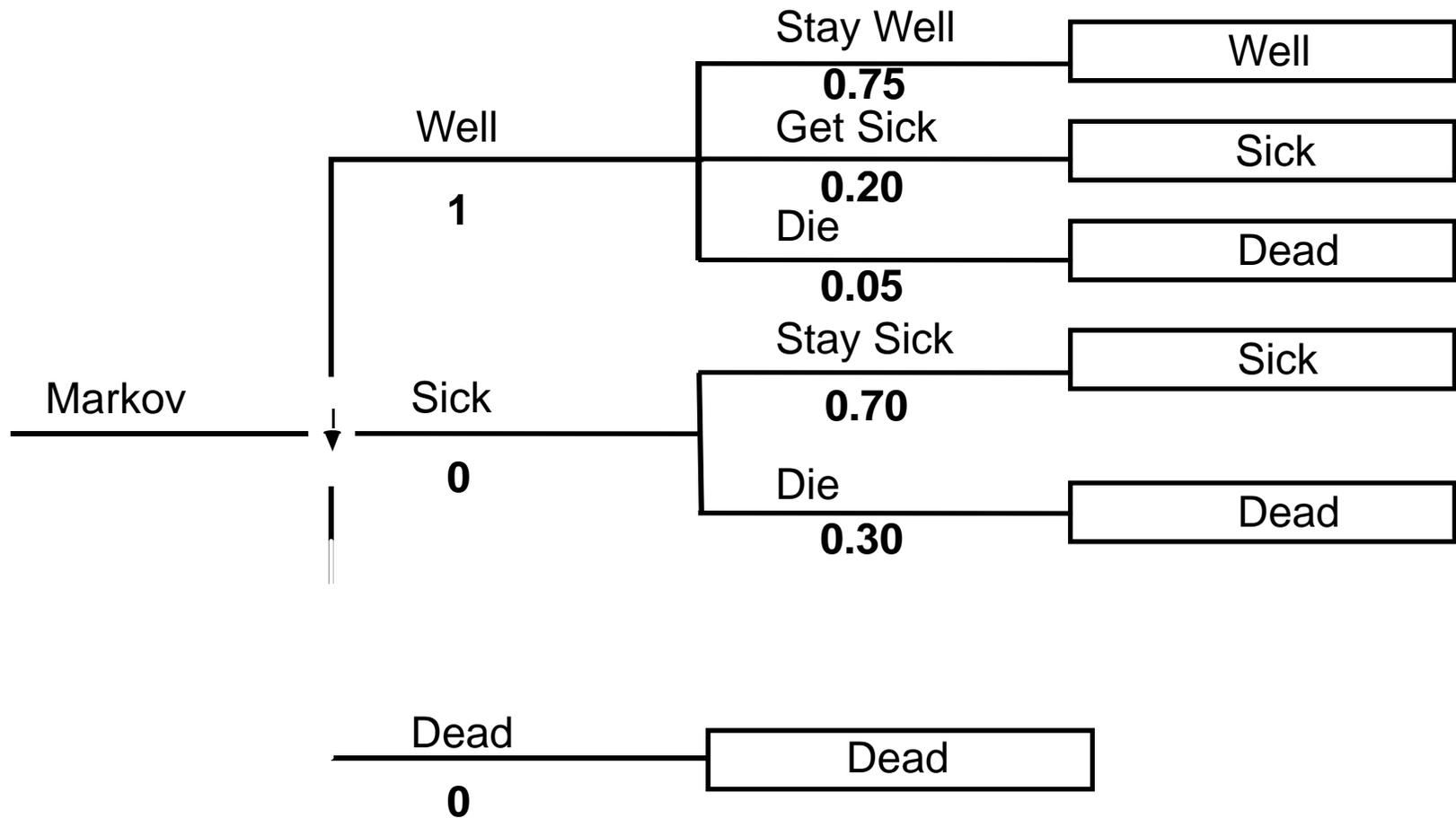
Quality-of-Life Adjustments



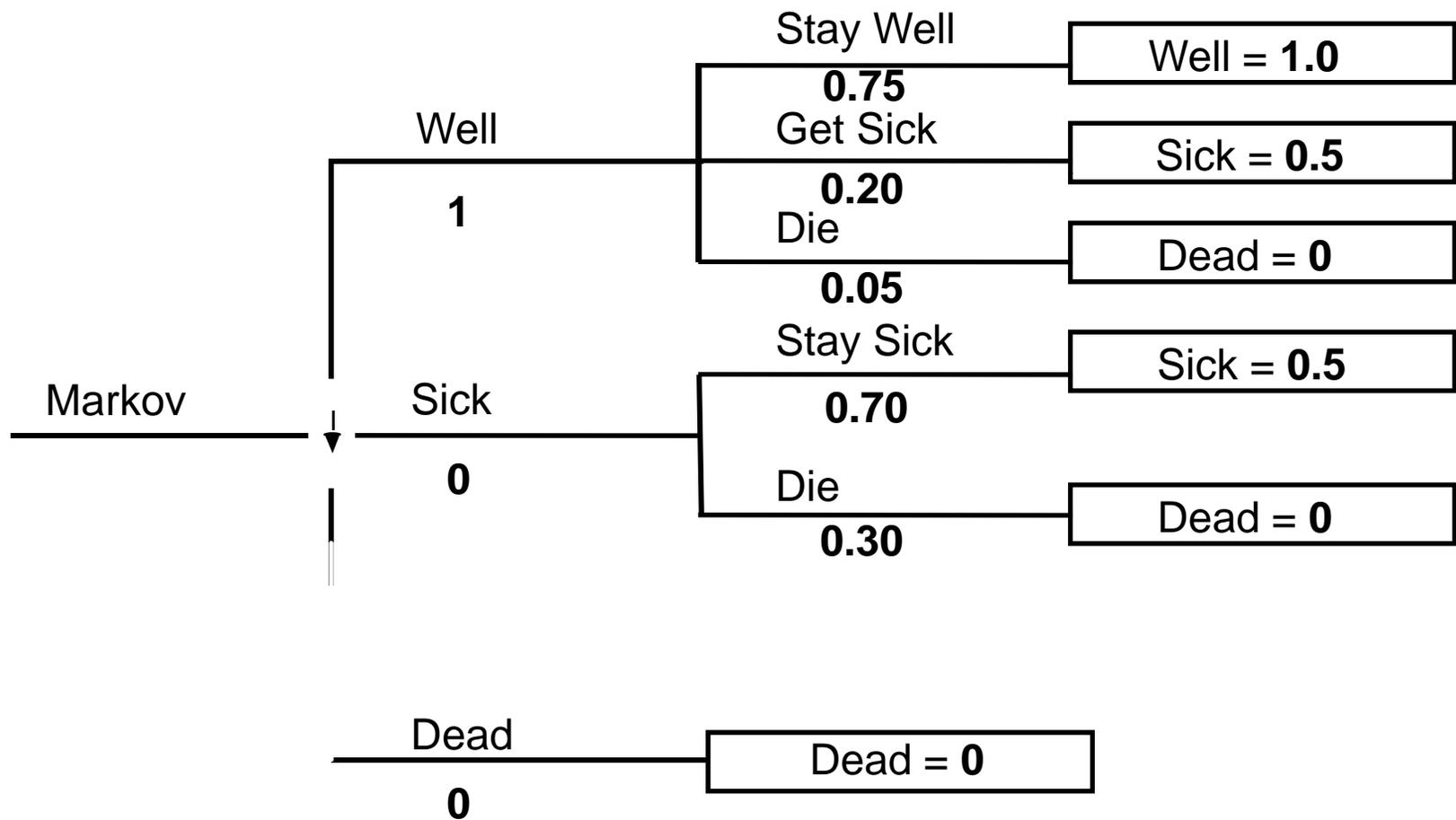
Expressed as a Markov Tree: Structure



Expressed as a Markov Tree: Transition Probabilities



Expressed as a Markov Tree: Utilities



Running the Model

Cycle	Well	Sick	Dead	Cycle Reward	Total Reward
0	1	0	0	0.5	0.5
1	0.75	0.20	0.05	0.85	1.35
2	0.56	0.29	0.15	0.71	2.06
3	0.42	0.32	0.26	0.58	2.64
4	0.32	0.31	0.38	0.47	3.11

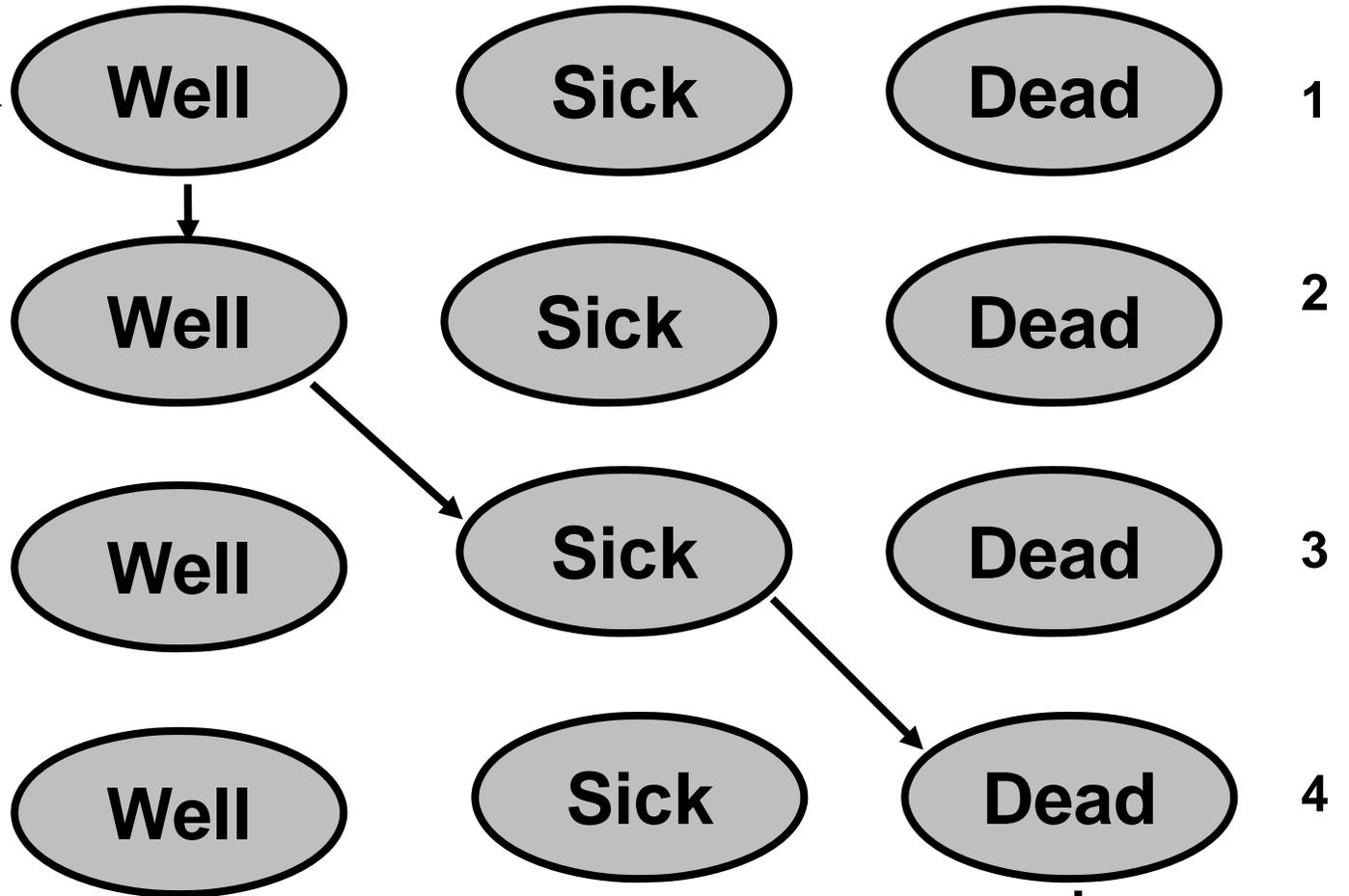
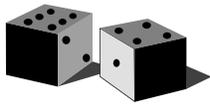
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Monte Carlo Simulation

- Determines the prognoses of a large number of individual patients
- Each patient runs through model until death – repeat large number of times ($\sim 10^4$)
- Provides a distribution of survival
 - Standard deviation
 - Variance

Monte Carlo Simulation



WWSD

Probabilistic Sensitivity Analysis (2nd order Monte Carlo)

- Decision tree estimates of probabilities and utilities are replaced with probability distributions (e.g. logistic-normal)
- The tree is evaluated *many* times with random values selected from each distribution
- Results include means and standard deviations of the expected values of each strategy

Characteristics of Markov Approaches

Feature	Markov Cohort	Monte Carlo	Matrix
Transition Probabilities	Time-dependent	Time-dependent	Constant
Incremental Utilities	Time-dependent	Time-dependent	Constant
Accuracy	Dependent on cycle length	Dependent on number of trials	Cycle-independent
Computation	Moderate	Most	Least
Variability Measures	No	Yes	Yes

Some Things to Remember

- Use of Markov models are appropriate in a number of situations
- Tradeoff between simplicity of conventional decision tree versus fidelity of Markov process
- When using decision trees OR Markov trees:
 - Assumptions and input variables should be as transparent as possible
 - Adequate sensitivity analysis should be performed
 - Modeling as well as clinical expertise should be consulted

Summary:

Medical Decision Analysis

- Clearly defines alternatives, events, and outcomes
- Formal method to combine evidence
- Can prioritize information acquisition
- Can help healthcare providers to make medical decisions under uncertainty

Decision Analysis Software

- Decision Maker
 - <http://infolab.umdnj.edu/windm/>
- DATA by TreeAge
 - <http://www.treeage.com>
- Excel spreadsheet models
- Other software packages

Where To Go For More

- Sox HC, Blatt MA, Higgins MC, Marton KI (1988) Medical Decision Making. Boston MA: Butterworth-Heinemann Publisher.
- Detsky AS, Naglie G, Krahn MD, Naimark D, Redelmeier DA. Primer on medical decision analysis: Parts 1-5. Med Decis Making. 1997;17(2):123-159.
- Sonnenberg FA, Beck JR. Markov models in medical decision making: a practical guide. Med Decis Making. 1993;13(4):322-38.
- Beck JR, Pauker SG. The Markov process in medical prognosis. Med Decis Making. 1983;3(4):419-458.
- Society for Medical Decision Making (<http://www.smdm.org>)