Code Challenges

The following exercises are for the virtual code challenge for participants in the R for trial & model-based cost-effectiveness analysis workshop taking place 9th July 2019 at University College London. See the associated GitHub repo for more details.

Jump to challenge here: C1, C2, C3, C4, C5, C6.

1. A simple decision tree

This example is taken from Hazen (1992). The problem is concerned with a competing risk cancer and AIDS decision tree. We will assume discrete time of single years. An individual starts in the `Well` state. They can transition into `Dead`, `Cancer & AIDS`, `Cancer`, `AIDS` or remain in the `Well` state.

Define the transition probabilities:

- Die from other causes: $\delta_0 = 0.001182$
- Die from recurent prostate cancer: $\delta_c = 0.025$
- Die from AIDS: $\delta_a = 0.080$
- Cancer recurs: $\beta_c = 0.0027$
- Develop AIDS: $\beta_a = 0.0083$

Each state has an associated utility or benefit (quality factor in Hazen (1992)) accrued by spending one cycle in each state. Define the state utilities:

- `Well`: $R_w = 1.0$
- `Cancer`: $R_c = 0.60$
- `AIDS`: $R_a = 0.50$
- `Cancer & AIDS`: $R_{ca} = 0.30$
- `Dead`: $R_d = 0$

Note that we will not include discounting.

C1. Define a (single year) decision tree and calculate the expected quality-adjusted value.

2. Markov-cycle tree

A Markov-cycle tree was introduced by Hollenberg (1984) and is a representation of a Markov process in which the possible events taking place during each cycle are represented by a probability tree. This is one way of simplifying determining probabilities from multiple paths.

The diagram for the Markov-cycle tree of the example in Hazen (1992) is given below (note that the order of the states is different on the left-hand side and right-hand side).

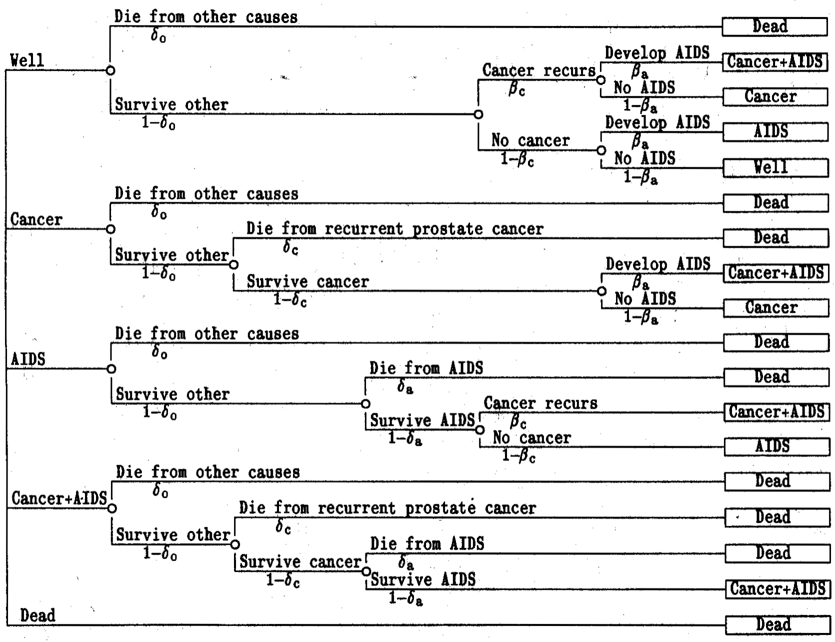


FIGURE 1. Markov-cycle tree for competing cancer and AIDS risks.

The terminal state are now root or source states, meaning the process returns to the left hand side to be repeated.

C2. Extend the model of C1 for multiple cycles and thus create a Markov-cycle tree. Calculate the mean quality-adjusted lifetime of 90.473.

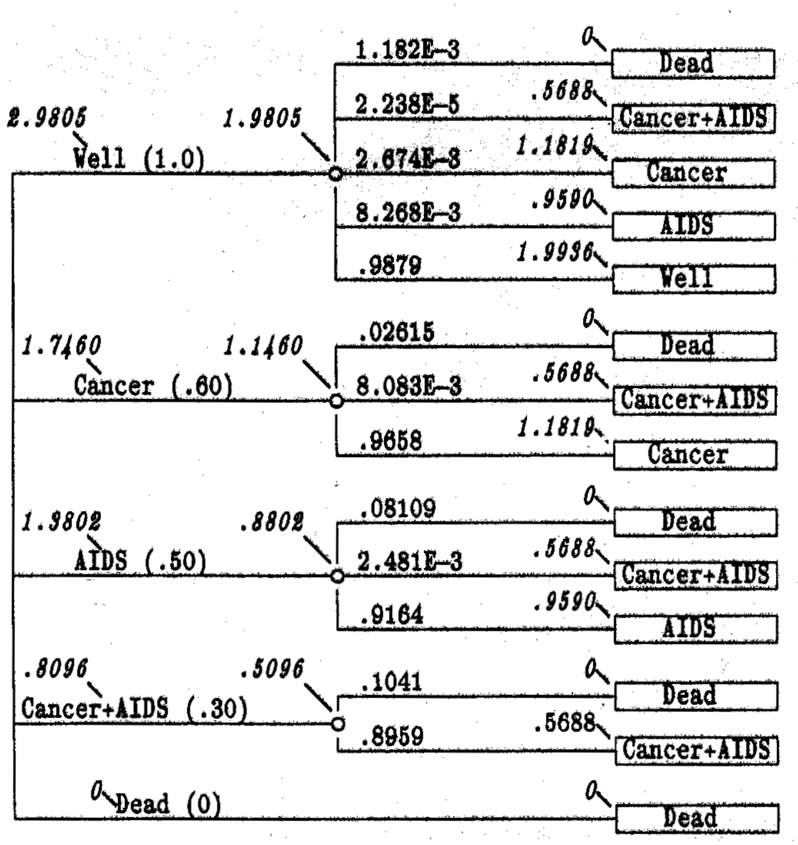
3. One-cycle Markov-cycle tree

We can rearrange the Markov-cycle tree to closer resemble a Markov model by collapsing the branches into a single cycle and simply combining the probabilities.

In the below figure

- The numbers above each branch are the one-cycle transition probabilities
- The numbers pointing at nodes and names are the mean quality-adjusted durations accrued through n cycles.
- The numbers in brackets are the mean quality-adjusted durations at the start of the cycle.

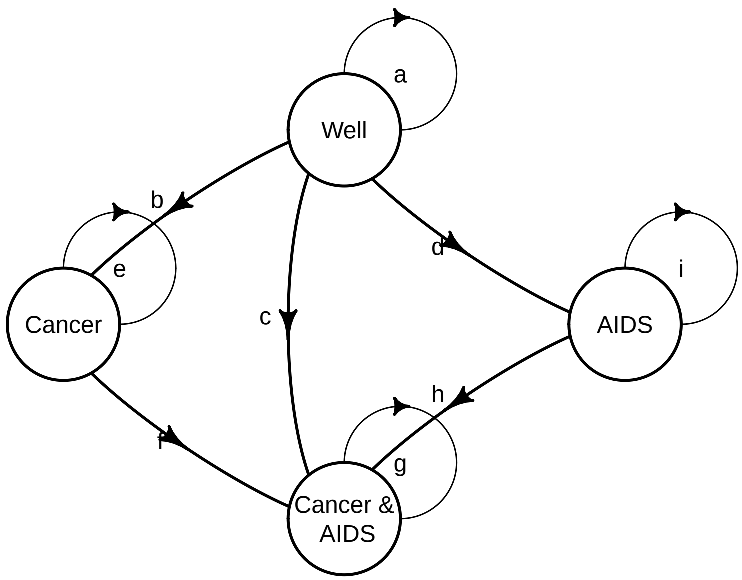
So for the below figure, the right-most numbers are the mean quality-adjusted durations for cycle 2, the left-most numbers are the mean quality-adjusted durations for cycle 3 and the numbers in brackets are the mean quality-adjusted durations for cycle 1. Hazen (1992) steps through this calculation in detail.



C3. Modify the model of C2 to create a one-cycle Markov-cycle tree. Calculate the mean quality-adjusted lifetime.

4. Discrete-time Markov model

Clearly, the Markov-cycle tree can also be represented as a discrete-time Markov model. The transition probabilities can be calculated by combining relevant path probabilities from the decision tree as done for the one-cycle Markov-cycle tree. The model is shown below (note that death is not shows for simplicity).



C4. Create the equivalent discrete-time Markov model to the one-cycle Markov-cycle tree. Calculate cumulative proportion of patient cycles in each state and take product with health utilities for each respectively to obtain the mean quality-adjusted lifetime.

5. Roll back Markov-cycle tree

A neat strength is that we can calculate the mean quality-adjusted lifetime using the one-cycle Markov-cycle tree representation without calculating the cumulative proportion of time of patient cycles in each health state. This is done by rolling back using the recursive equation (value iteration):

$$V_n(i) = R(i) + \sum_j p_{ij} V_{n-1}(j)$$

where $V_n(i)$ are the values at node i at step n, in our case the expected QALYs.

C6. Calculate the mean quality-adjusted lifetime using the one-cycle Markov-cycle tree and value iteration.

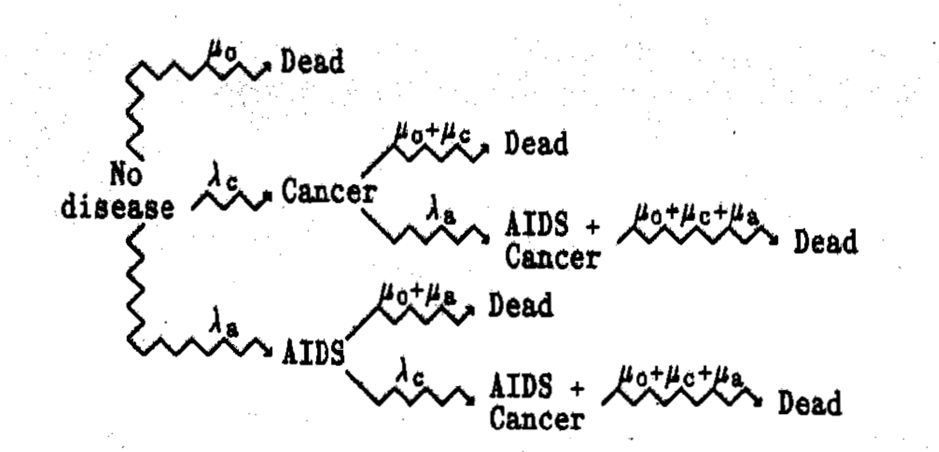
6. (BONUS CHALLENGE): Roll back stochastic tree

So far we have only considered discrete time. The Markov-cycle tree representation can be extended to continuous time as a *stochastic tree* (see Hazen (1992) for details). Probabilities are now replaced by rates. This change is represented by zigzag lines in the diagrams. This is clearly a more compact representation.

We can calculate mean quality-adjusted lifetime in an analogous way to the discrete-time case by rolling back using the recursive equation:

$$V(S) = \frac{R(i)}{\sum_j \lambda_j} + \sum_j p_j V(S_j)$$

The new model diagram is given below.



The rates for state transitions are:

- `Cancer`: $\lambda_c = 0.03250$/year
- `AIDS`: $\lambda_a = 0.10$/year
- `Dead from Cancer`: $\mu_c = 0.3081$/year
- `Dead from AIDS`: $\mu_a = 0.9970$/year
- `Dead other`: $\mu_o = 0.014191$/year

C7. Create the stochastic tree model and calculate the mean quality-adjusted lifetime using value iteration.

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References

Hazen, Gordon B. 1992. "Stochastic Trees : A New Technique for Temporal Medical Decision Modeling." *Medical Decision Making* 12 (3): 163–78. https://www.researchgate.net/publication/21642929_Stochastic_Trees_A_New_Technique_for_Temporal_Medical_Decision_Modeling/stats.

Hollenberg, JP. 1984. "Markov cycle trees: a new representation for complex Markov processes." *Medical Decision Making* 4: 529.