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`: $R_d = 0$

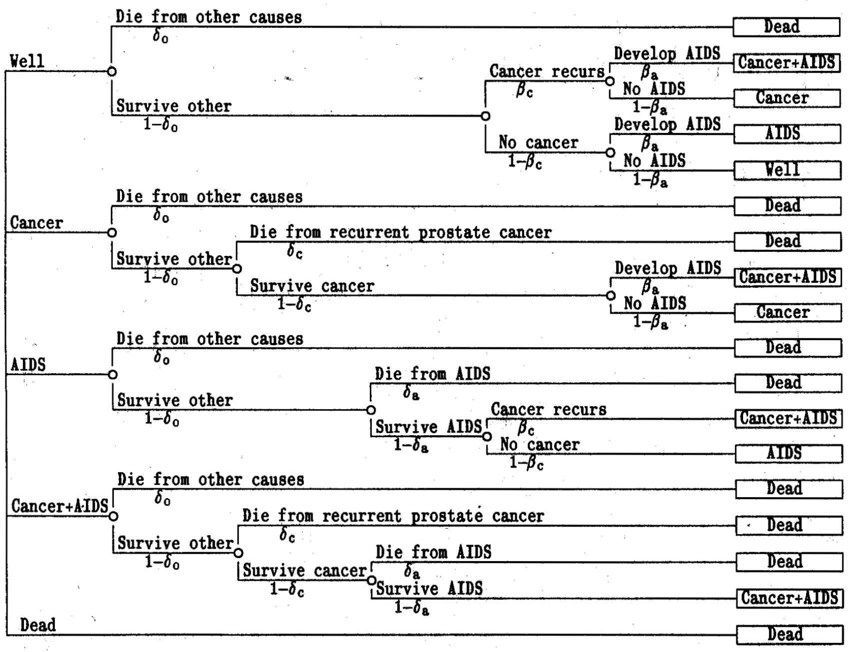
Note that we will not include discounting.

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).



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.

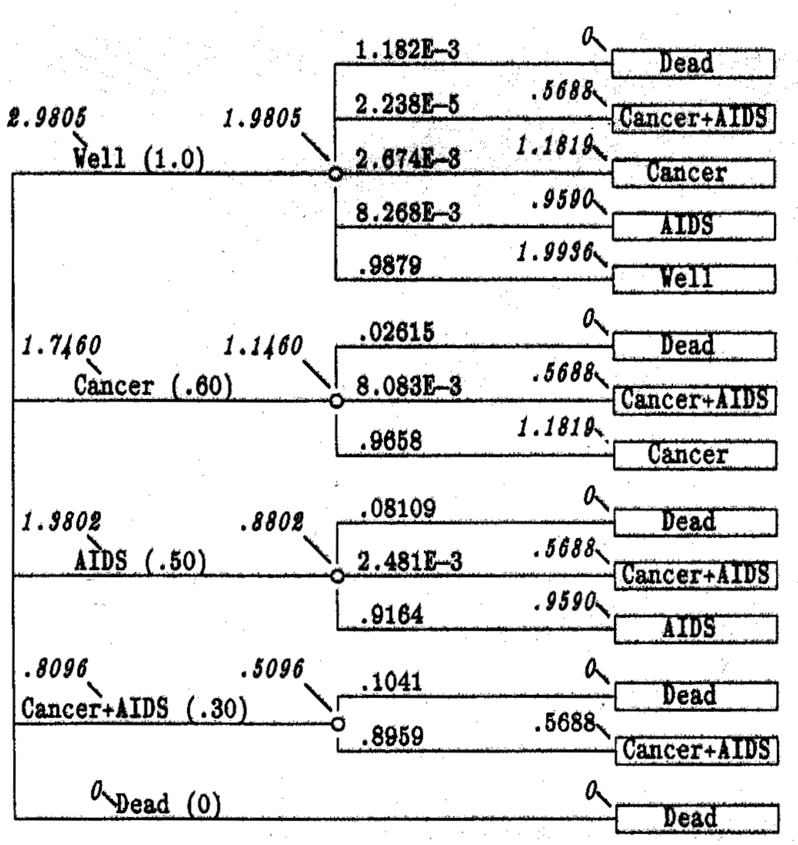
3. One-cycle Markov-cycle tree

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.

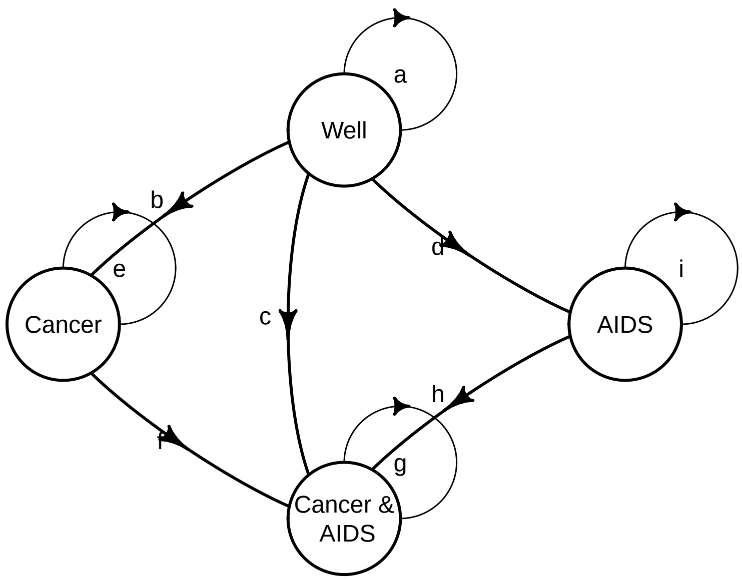
So for the below figure, the right-most numbers are the mean quality-adjusted durations for cycle 2, the left-most numbers are the mean quality-adjusted durations for cycle 3 and the numbers in brackets are the mean quality-adjusted durations for cycle 1. Hazen (1992) steps through this calculation in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

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

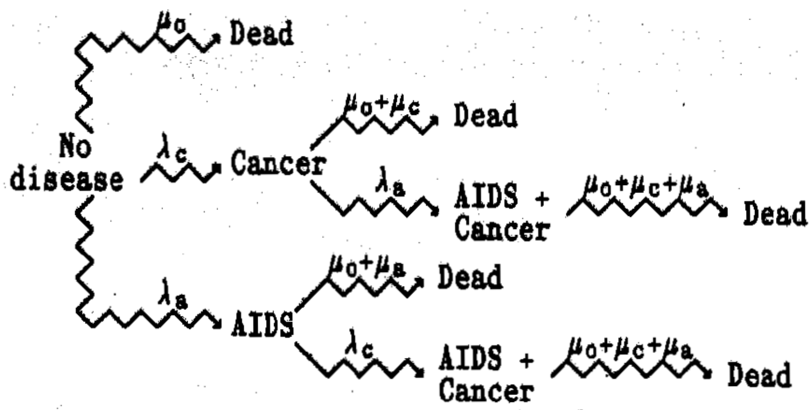
6. (BONUS CHALLENGE): Roll back stochastic tree

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

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

Written by Nathan Green

nathan.green@imperial.ac.uk

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.