

## Code Challenges

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

Jump to challenge here: C1, C2, C3, C4, C5, C6, C7.

### 1. A simple decision tree

This example is taken from Hazen (2014). 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.

Event probabilities are

- $\delta_0 = 1.182 \times 10^{-3}$ : Die from other causes
- $\delta_c = 0.025$ : Die from recurrent prostate cancer
- $\delta_a = 0.080$ : Die from AIDS
- $\beta_c = 0.0027$ : Cancer recurs
- $\beta_a = 0.0083$ : Develop AIDS

C1. Define a (single year) decision tree.

### 2. Markov-cycle tree

A Markov-cycle tree was introduced by Hollenberg 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 (2014) is given below.

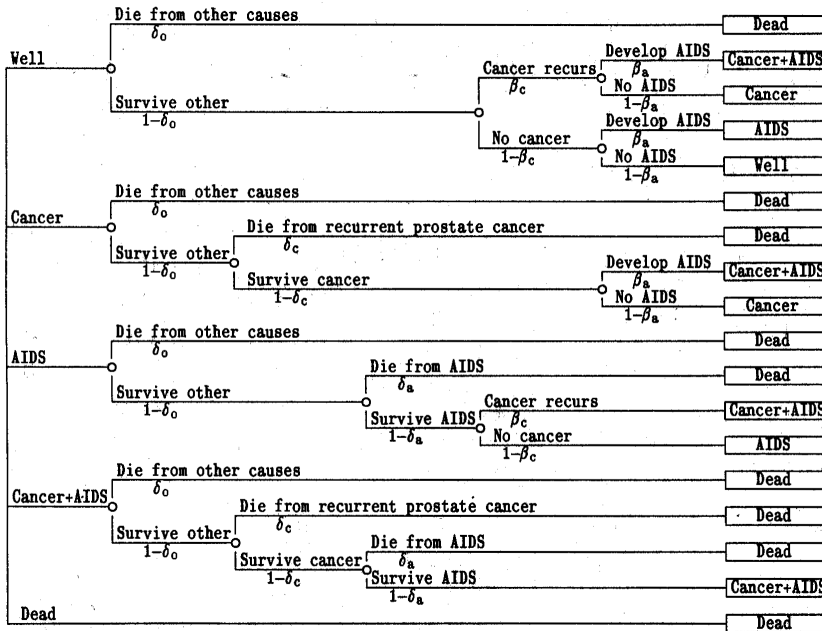


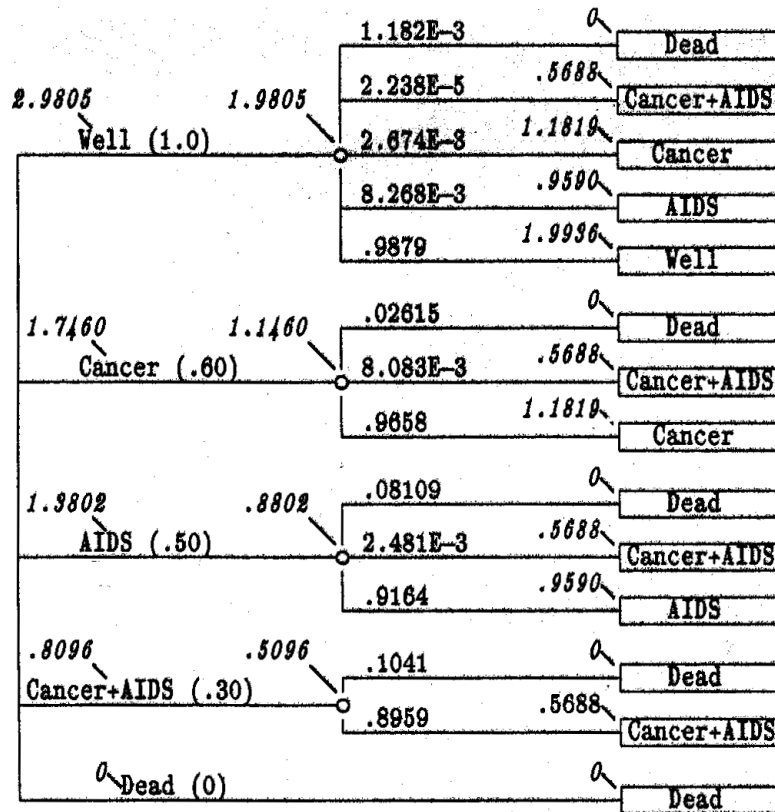
FIGURE 1. Markov-cycle tree for competing cancer and AIDS risks.

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.

### 3. One-cycle Markov-cycle tree

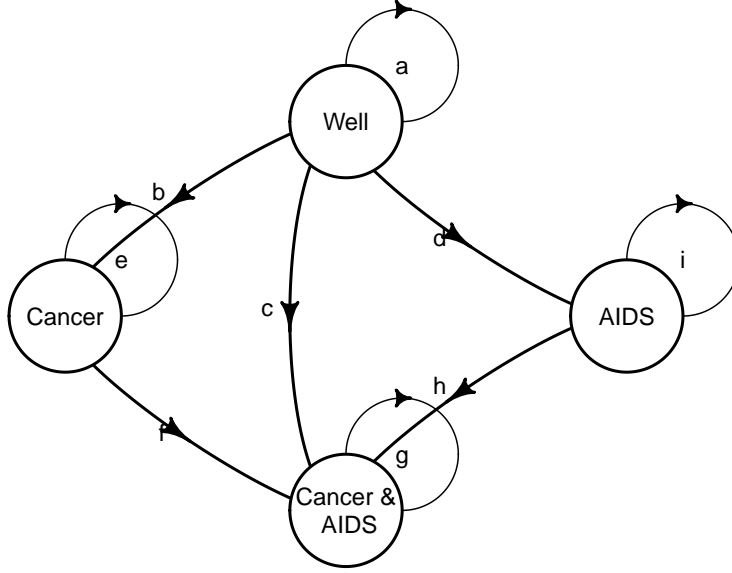
We can rearrange the Markov-cycle tree to closer resemble to Markov model by collapsing the branches into a single cycle and simply combining the probabilities.



C3. Modify the model of C2 to create a One-cycle Markov-cycle tree.

### 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 shown for simplicity).



C4. Create the equivalent discrete-time Markov model.

## 5. Calculate mean QALYs

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:  $R_d = 0$

C5. Calculate cumulative proportion of patient cycles in each state and take product with health utilities for each respectively to obtain expected QALYs.

## 6. Roll back Markov-cycle tree

A neat strength is that we can calculate the mean QALYs 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 QALYs using the one-cycle Markov-cycle tree and value iteration.

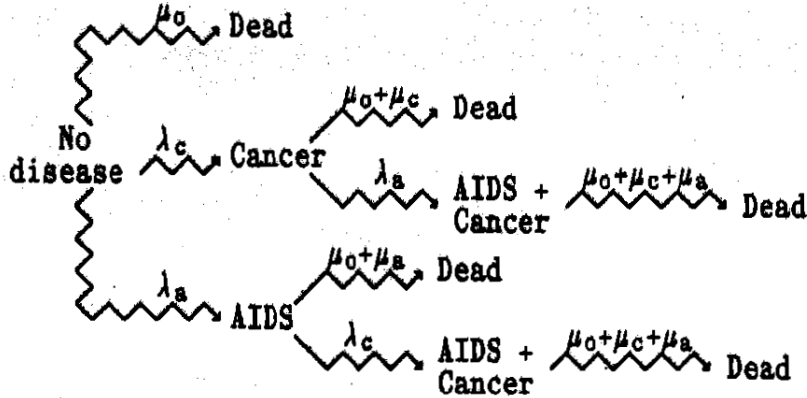
## C7 (BONUS CHALLENGE): Roll back stochastic tree

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 (2014) 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 QALY 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 QALYs using value iteration.

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## References

Hazen, Gordon B. 2014. "Stochastic Trees : A New Technique for Temporal Medical Decision Modeling," no. August 1992. <https://doi.org/10.1177/0272989X9201200302>.