Practical Health State Transition Model 2B

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Aim

This assignmment still focuses on evaluating the cost-effectiveness of aspirin treatment versus no aspirin treatment for the primary prevention of cardiovascular disease events using a health state transition model (HSTM).The aim of this practical assignment is to get improve the health state transition model (HSTM) you have built during 2A with age-dependent mortality values since we only used a mean estimate for all age in assignment 2A. Furthermore, you will include the "Aspirin" strategy to the model you have performed in the previous assignment. During this assignment, you will first define the cohort simulations of both strategies (using (age-dependent) transition probabilities, a three-dimentional array, and matrix multiplication) and then calculate the outcomes (quality-adjusted life years, costs). First, familiarise yourself with the model structure. on the next page.
The method described in this practical is more extensively described in Alarid-Escudero et al. (2020).

Instuctions

1. Download the folder `Practical_HSTM_2` from the Canvas page and save it on your computer

2. Before performing the assignment, have a look at how the model structure looks like on the next page

3. Open the `Assignment_2B_start.R` file and follow the instructions of this document and in the R file. Use the model structure on the next page to perform the assignment.
4. Start the assignment by loading the inputs for the model from the `data_HSTM_2A.RData` file. The model inputs are the same as in the previous assignment.

5. During the completion of the assignment, answer the questions of this document
   DISCLAIMER: FOR THE FOLLOWING AASIGNMENT, ASSUME THAT PROBABILITIES ARE THE SAME. SEE Fleurence and Hollenbeak (2007) FOR AN EXPLANATION OF THE DIFFERENCES BETWEEN RATES AND PROBABILITIES AND REMEMBER THAT WE USUALLY USE PROBABILITIES IN HEALTH ECONOMIC MODELLING

Model structure

In this HSTM, individuals either receive aspriring or not (the two strategies we compare). These individuals may remain "Well", or they can experience a stroke or a myocardial infarction (MI). These two events may be fatal or individuals may remain in the "Post-minor stroke", "Post-major stroke", or "Post-MI" health states if they survive these events. From all health states, individuals may die from general causes of death to "Death other".

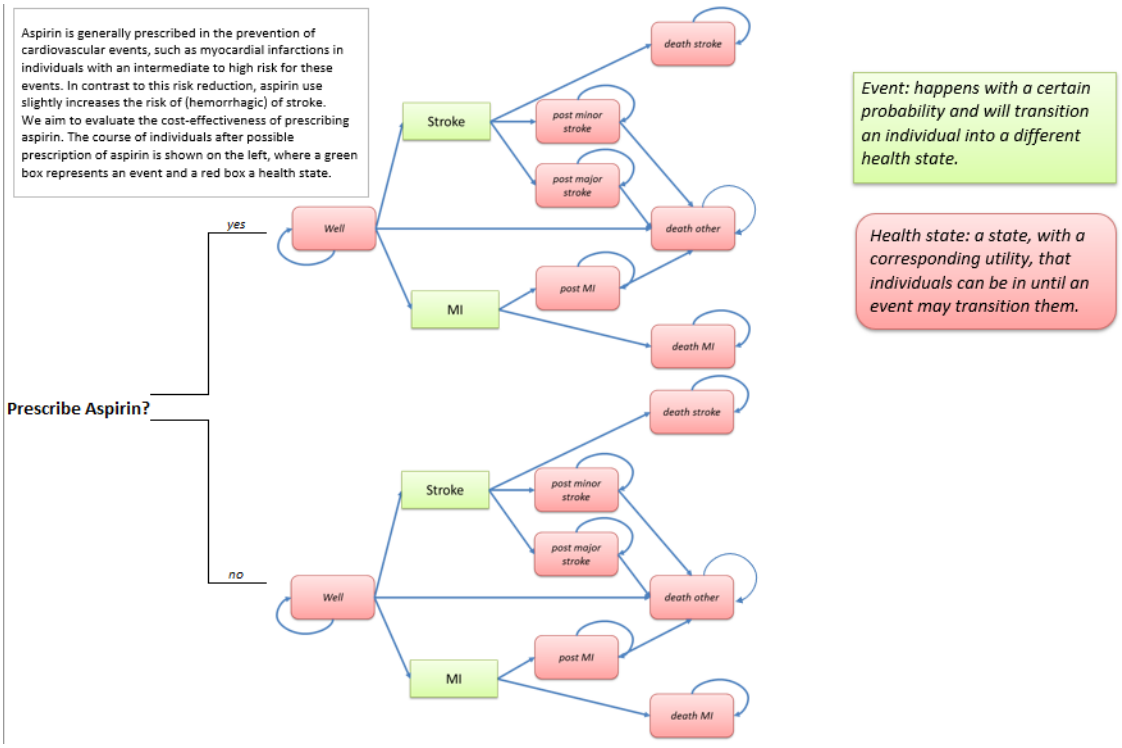

Figure 1: Health state transition model structure

Instructions and questions

Question 1 & 2 are already performed in the `Assignment_2B_start.R` file, please read the instruction and complete the asssignement. 1. In the previous exercise we have used one average mortality rate for all ages. Since this is not realistic, we will now make the mortality rate age-dependent.
1.a. Once loaded, have a look at the inputs. You can see that there is a dataframe `df_mort` added to the model inputs. This dataframe contains the probability of death of individuals for each age. Inspect this dataframe, it contains 2 columns: `Age` = age of an individual (between 20 and 115) and `p_mort` = mortality probability for each age (the data in this assignment is fake, in reality, we would use probabilities based on national statistics estimates!).
1.b. To include these age-dependent transition probabilities in the model, we have to use 3-dimentional (3D) arrays instead of fixed transition matrices. The use of these 3D arrays allow to select a different transition matrix (containing different transition probabilities) for each cycle of the model. Arrays are defined through the `array()` function.
1.b.i. Define empty arrays for the "No aspirin" group (called `a_tp_comp`) with `n_hs` columns, `n_hs` rows, and a depth of `n_cycles`. Inspect this array. As you can see, there are now 10 empty transition matrix when you inspect that object.
1.b.ii. Define the start age of the cohort (`n_start_age`), which is 45 years old. 1.b.iii. Define a vector (of 10 values) of mortality probabilities containing the transition probabilities from `n_start_age` to `n_start_age` + 9.
1.b.iv. Fill in the array with the (time-dependent) transition probabilities, using the transition probabilities from assignment 2A, and the age-dependent mortality probability `v_p_mort` for the "No aspirin" group.
NOTE: elements in a array are called by the number of dimension of the array. Thus, a single element of a 3D array is called via a x, y, and z dimension. If only the x and y coordinates are provided, the vector of elements with the coordinates x and y is returned. In this case, the third dimension (the 'z') represents the cycle number while the rows and columns represent the same as in the transition matrix (transition from - to).
2. Fill the cohort simulation for the "No aspirin" group using the 3D array. To do so, create a matrix to store the cohort simulation (`m_hs_comp`) of 7 columns (number of health states) and 11 rows (`n_cycles` + 1), define the start position of individuals (all in "well", `v_start_hs`), and perform the matrix multiplication using the 3D array to fill the `m_hs_comp` matrix. You have to loop over the elements of the array to ensure that the time dependent mortality probability are used.
3. Fill the 3D array for the "Aspirin" group.
3.a. Make a copy of `a_tp_comp` and call it `a_tp_int`. This will be the transition array we will use for the "Aspirin" group.
3.b. Aspirin has an effect on the probability of experiencing an MI (object `eff_mi`) and stroke (object `eff_stroke`). Use these two input parameters to adjust the probabilities to experience these (non-)fatal cardiovascular events in the `a_tp_int` array. Again you may use the rates as probabilities when calculating the transitions. Assume that once individuals had an event they will no longer use aspirin.
3.b.ii. And what is the probability of an individual on aspirin treatment to have a stroke?
4. Fill the cohort simulation for the "No aspirin" group (`m_hs_int`) using the 3D array `m_tp_int` and the same method has shown in step 2.
5. Now that we know the life course of the hypothetical individuals we can calculate the (undiscounted) costs and effects over time. For convenience, account for state membership at the end of the year (i.e., not all 100,000 individuals are considered to be "Well" at the start of year 1 and you do not have to use a half-cycle correction). Practically, it means that you do not account for the state membership at cycle 0, the starting position.
5.a. Calculate the life years of both strategies, i.e. the number of individuals alive each year, and the cumulative life years over the 10 years of the model. To do so, define two vectors (`v_ly_comp` & `v_ly_int`) of 7 values which determine the number of life years gained by an individual in each health state during a single cycle. These vectors are called the "rewards" vectors, and the vector of rewards should be ordered as the health states in the `m_hs_comp` & `m_hs_int` cohort simulation. For health state were individuals are alive, the reward should thus be 1, and 0 for the "Death" health state. Use matrix multiplication to multiply these health state rewards by the membership of individuals over the cycles (from row 2 onwards!). Store these

results in vectors called `v_t_ly_comp` & `v_t_ly_int`, calculate the cumulative number of life years over the cycles (`v_cum_ly_comp` & `v_cum_ly_int`, using the cumsum () function) and calculate the total number of life years for each strategy as the sum of these vectors (`n_t_ly_comp` & `n_t_ly_int`). The calculations for the life years are provided in the `Assignment_2B_start.R` file, use this example for performing 4.b. and 4.c.
5.b. Using the utilities defined in the `Assignment_2B_start.R` file, calculate the total quality adjusted life-years (QALYs) in each year for the 100,000 hypothetical individuals in each group. Use the same approach as for the life years calculations, expect that the state rewards are different. Calculate also the cumulative and total QALY gained.
Assmuptions: Individuals in the "Well" health state have a utility value equal to`u_healthy` in the "No Aspirin" group, while in the "Aspirin" group, they have the utility associated with use of Aspirin. Assume that after a MI or stroke, individuals stop with aspirin. Individuals in the "Death" health states do not accrue QALYs. 5.c. Using the annual costs for health state defined in the `Assignment_start.R` file, calculate the total costs in each year for the 100,000 hypothetical individuals. Use the same approach as for the life years calculation, expect that the state rewards are different. Calculate also the cumulative and total costs.
Assmuptions: Individuals in the "Well" health state do not incur any costs in the "No aspirin" group. However, in the "Apsirin" group, individuals in the "Well" health state incur the costs associated with aspirin use. Assume that after a MI or stroke, individuals stop with aspirin.Individuals in the "Death" health states do not incur any costs.
5.d. Calculate the mean outcomes (life years, QALYs, costs) per individual for each strategy. Calculate the incremental QALYs and costs of the "Aspirin" versus "No aspirin" group and calculate the incremental cost-effectiveness ratio (incremental costs/incremental QALYs).
6. Calculate the discounted results. To do so, define a vector of length `n_cycles`, which contain the discount weights for each cycle, and use matrix multiplication of the vector of total health effects (or costs) by the vector of discount weights. Name the discount weights vector for health effects `v_dw_e` and for costs `v_dw_c`. The yearly discount rates for health effects and costs are provided under the objects `r_d_effects` and `r_d_costs`. The calculations are performed for discounted life years, use that example to perform discounting of QALY's and costs. Calculate the mean discounted outcomes (life years, QALYs, costs) per individual for each strategy. Calculate the incremental QALYs and costs of the "Aspirin" versus "No aspirin" group and calculate the incremental cost-effectiveness ratio (incremental costs/incremental QALYs).
7. Have a look at the expected life-years, costs, and effects of both strategies.
7.a. Which strategy is cheapest?
7.b. Which strategy gives most effects in terms of life years? And which one in terms of QALYs?
7.c. What is your conclusion when looking at the discounted ICER?
7.d. What is the difference between the undiscounted and discounted results? Do you understand this difference?
QUESTION 7.e. - 8.b. can be performed using the R shiny app, you can also modify your own model to answer these questions.
To access the shiny app for the following assignment, use the following command in your R session and select the tab "Assignment HSTM 2B".

```
runGitHub("Teaching", "Xa4P", subdir = "Basics/shiny_app_cea/", ref = "main")
```

7.e. What happens to the costs and effects over the time horizon when the discounting rate of both costs and effects is increased to 6%? And what if it is only 0.5%? How does this affect the ICER of aspirin?
8. Set the discounting rate back to 4% for costs and 1.5% for effects.
8.a. Change the starting age to 65. What do you expect will happen to the costs and effects? And how does it affect the ICER?
8.b. Change the starting age to 95. What do you think will now happen to the effects? How do you explain these results? How does this affect the ICER?

Reference

Alarid-Escudero, Fernando, Eline M. Krijkamp, Eva A. Enns, Alan Yang, M. G. Myriam Hunink, Petros Pechlivanoglou, and Hawre Jalal. 2020. "Cohort State-Transition Models in R: A Tutorial." http://arxiv.org/abs/2001.07824.

Fleurence, Rachael L, and Christopher S Hollenbeak. 2007. "Rates and Probabilities in Economic Modelling." *Pharmacoeconomics* 25 (1): 3–6.