

Practical Health State Transition Model 2A

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2021-08-09

Aim

The aim of this practical assignment is to get you acquainted with the principle of health state transition models (HSTM). This assignment focuses on evaluating the cost-effectiveness of aspirin treatment versus no aspirin treatment for the primary prevention of cardiovascular disease events using a Markov model. During this assignment, you will first define the cohort simulation of both strategies (using transition probabilities, 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).

Instructions

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_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. During the completion of the assignment, answer the questions of this document
- DISCLAIMER: FOR THE FOLLOWING ASSIGNMENT, 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 aspirin 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”.

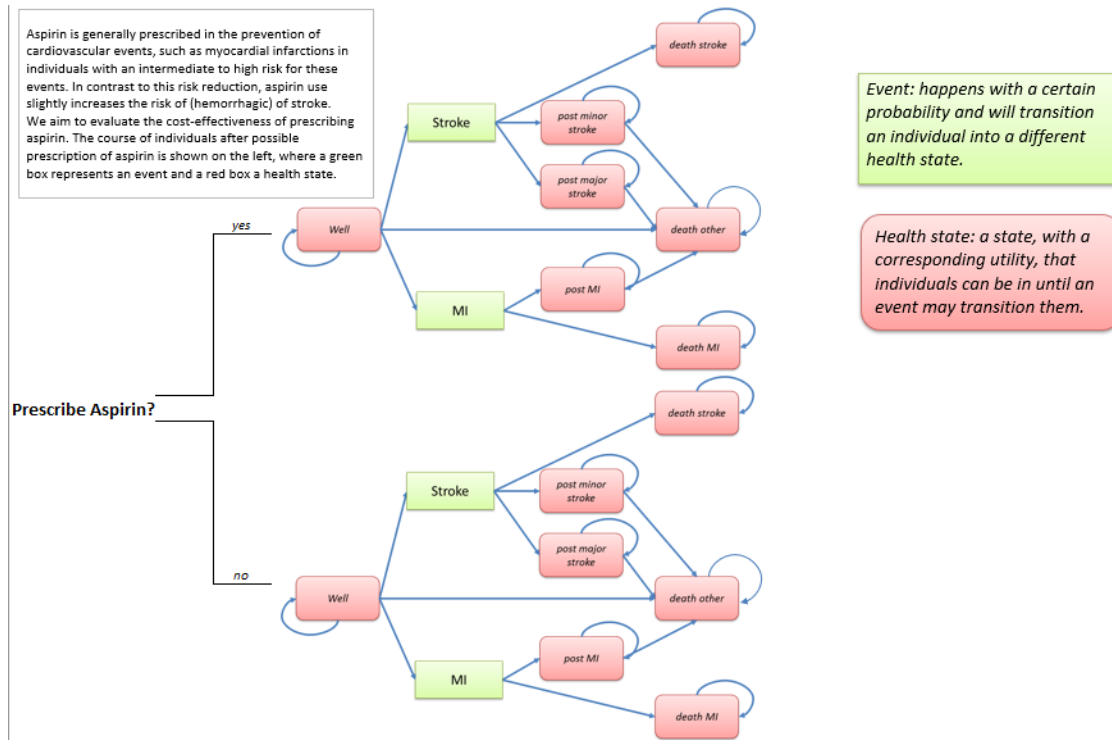


Figure 1: Health state transition model structure

Questions

1. As you can see both strategies (prescribing aspirin or not) have similar diagrams. However, there will be differences in the values of the parameters applied in these strategies. First, we will focus on the course of patients not using aspirin. Have a look at the parameters which are already defined in the `Assignment_start.R` script.
 - 1.a. In making a health economic model we often have to combine evidence from different sources of literature. Assume that there was evidence that 235 out of 1,000 patients **who had a stroke and survived** moved into a post major stroke state (the remaining patients experienced a minor stroke). Based on this evidence, please define the parameter `p_minor_stroke` (probability of transiting to the “post-minor stroke” health state **after having experienced a NON-FATAL stroke** and `p_major_stroke` (probability of transiting to the “post-major stroke” health state **after having experienced a NON-FATAL stroke**.
 - 1.b. From other sources, you found that the incidence rates for myocardial infarction (MI), stroke, and death from other causes were respectively **400, 50, and 650 per 100,000 person-years**. Calculate the yearly incidence rates of MI, stroke, and death from other causes than MI and stroke in the placeholder of parameters `r_inc_mi`, `r_inc_stroke`, and `r_mort`.
2. Based on the parameter values, determine the transition matrix of the “No aspirin” strategy, and call it `m_tp_comp` (for matrix transition probabilities of the comparator). Assume here that `r_mort` can be used to approximate the probability of ‘Death other’.

HINT: To do so, create a matrix of 7 by 7, and use the evidence `p_` and `r_` parameters to fill it in. Use the model structure to fill in the transition matrix. Once an individual dies, that person remains in that health state. The transition probabilities to the post-minor stroke health states are the product of experiencing a non-fatal stroke and of the consequences being minor or major.

 - 2.a. Check whether the sum of all rows equals 1.
3. Assume all 100,000 individuals (defined as the `n_ind` object) start in the “Well” health state (as defined in the `v_start_hs` vector), and perform the cohort simulation for the “No aspirin” group using the transition matrix `m_tp_comp`. Remember from previous assignment that you need the following elements to perform the matrix multiplication needed to perform the cohort simulation. Most of these elements are already defined in the `Assignment_start.R` script:
 - `n_cycles`: the number of cycles to simulate, assume 10 years (yearly cycles)
 - `n_ind`: the number of individuals to simulate, assume 100,000
 - `m_hs_comp`: a matrix to store the number of individuals in each health state during each cycle for the comparator. This matrix has `n_cycles + 1` row (because we need to account for the start position), and as much columns as health states (75). Numerate the rows from 0 to `n_cycles` and name the column with the names of the health states (“Well”, “Post-minor_stroke”, “Post-major_stroke”, “Post-MI”, “Death_stroke”, “Death_MI”, “Death_other”).
 - `v_start_hs`: a vector determining the starting position of the individuals over the different cycles (assume all individuals start in the “Well” health state)Once you have determined these parameters, use `v_start_hs` to determine the starting position of the individuals in the simulation.
 - 3.a. Check whether all rows sum up to 100,000 to ensure you do not ‘lose’ or ‘add’ any person to the cohort simulation. Sometimes, due to rounding errors, you may seem that the sum does not exactly match the number of individuals, so round your sums to 5 decimals.
4. 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).

4.a. Calculate the life years of this strategy, 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 a vector `v_ly_comp` of 7 values which determine the number of life years gained by an individual in a health state during a single (for health state were individuals are alive, this should 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 a vector called `v_t_ly_comp`, calculate the cumulative number of life years over the cycles (`v_cum_ly_comp`, using the `cumsum()` function) and calculate the total number of life years as the sum of this vector (`n_t_ly_comp`). The calculations for the life years are provided in the `Assignment_start.R` file, use this example for performing 4.b. and 4.c.

4.b. Using the utilities defined in the `Assignment_start.R` file, calculate the total quality adjusted life-years (QALYs) 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. Also calculate the cumulative amount.

Assumption: Individuals in the “Well” health state have a utility value equal `tu_healthy` 4.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. Also calculate the cumulative amount.

Assumption: Individuals in the “Well” health state do not incur any costs (as well as dead individuals).

4.d. Calculate the mean outcomes (life years, QALYs, costs) per individual.

5. 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 per individual.

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.