Esophageal Cancer Model Description

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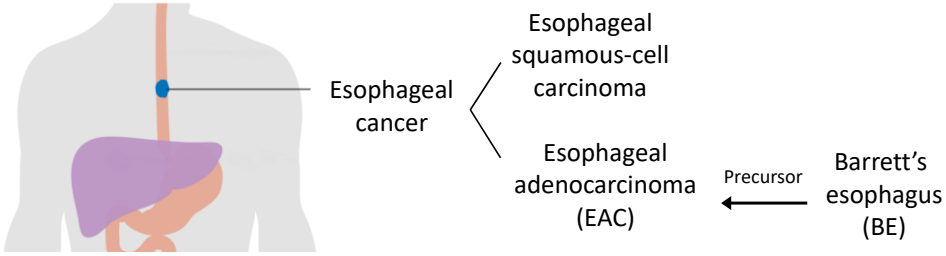
Introduction

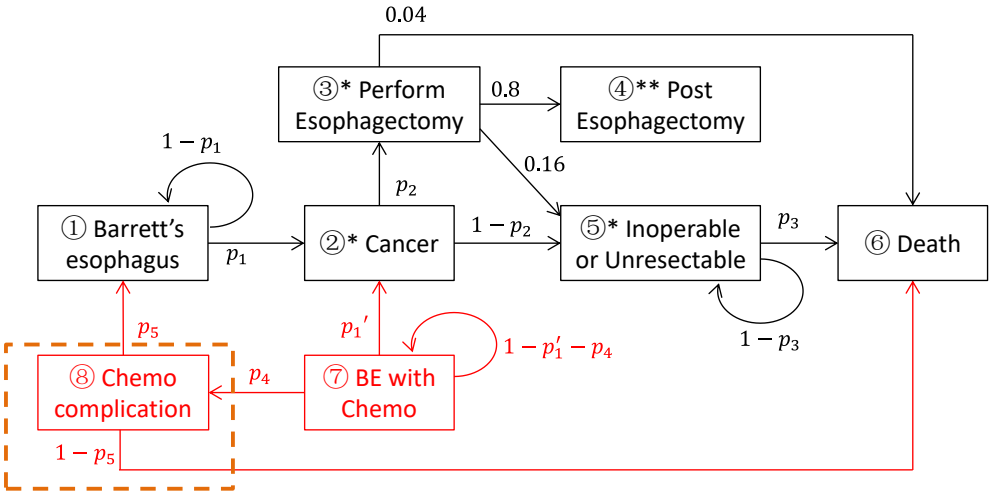
Esophageal adenocarcinoma (EAC) is a main sub-type of esophageal cancer, while Barrett's esophagus (BE) is a precursor to EAC (see the figure below). Recently, chemoprevention has received substantial attention as a method to lower the progression of BE to EAC, and aspirin and statin are two particular drugs that are demonstrated to be effective (Kastelein et al. 2011). For each BE patient, the progression rate to cancer depends on a variety of factors including age, weight, lifestyle habits such as smoking and alcohol use, the grade of dysplasia, etc. In addition, each patient may have a different response to drugs depending on his or her drug resistance and tolerance. Hence, it is conceivable that the best treatment regimen for BE is patient-specific.



Note: Image from Cancer Research UK / Wikimedia Commons, licensed under CC BY-SA 4.0.

This simulation model is adopted from Hur et al. (2004) and Choi et al. (2014), and it simulates the transitions among different health states of a BE patient until death, and the transition diagram of the model is shown and explained as follows.

Main Schematic of the Markov Simulation Model



* 50% quality-of-life factor
** 97% quality-of-life factor

Note:

(1) The simulation starts with a patient with Barrett's esophagus, who is X_1 $(55 \le X_1 \le 80)$ years old, end until he dies.

(2) Time length between state transitions is 1 month.

(3) All numbers on the arrows denote transition probabilities.

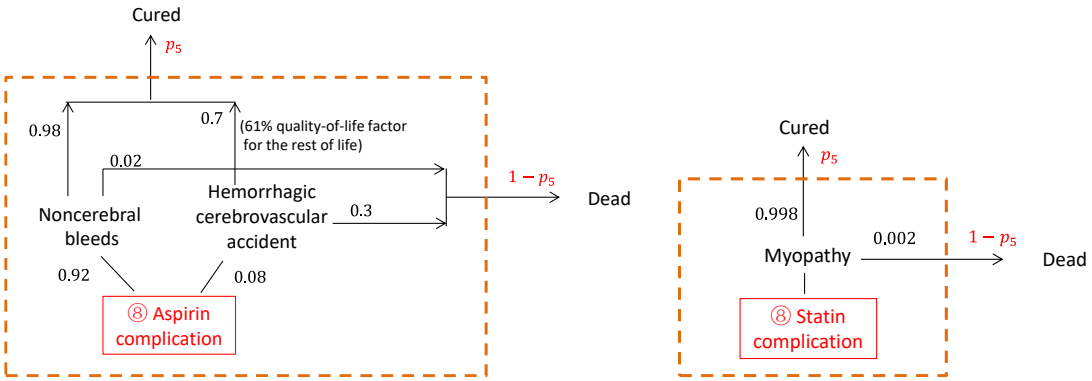
(4) The simulated patients can die from age-related all-cause mortality (Data source: Arias (2015)). Assume in the middle of each year, a patient may die due to other reasons, according to some known probability related to age.

When the Patient Uses No Drug

- The simulation starts from state ①. He will only transit among the states with black color.
- Risk, i.e., $X_2 \in [0,0.1]$, means the *annual* Barrett's esophagus to cancer probability. So,
$$(1-p_1)^{12} = 1 - X_2.$$
- $p_2 = -0.0023 \times \text{current age} + 1.1.35$. For current age, only consider integers, i.e., 55 years old, 56 year old, etc.
- State ⑤ means the patient has esophageal cancer but can't take surgery, he just suffers with cancer. The *annual* esophageal cancer mortality probability is 0.29. So,
$$(1-p_3)^{12} = 1 - 0.29.$$

When the Patient Uses Drug (aspirin or statin)

- The simulation starts from state ⑦. But the drug may give him some complication. If the complication is cured, he will stop using the drug, so goes to state ①.
- The red transition probabilities are different for two drugs.
- $X_3 \in [0,1]$ is the aspirin effect. It means, when using aspirin, the risk is $\text{risk}' = X_2(1-X_3)$.
- $X_4 \in [0,1]$ is the statin effect. It means, when using statin, the risk is $\text{risk}' = X_2(1-X_4)$.
- *Annual* complication probability of aspirin is 2.4×10^{-3}.
- *Annual* complication probability of statin is 1×10^{-3}.
- For each drug, it can be found that, if let $k = \text{risk}'/\text{annual complication probability}$,
$$p_4 = \left[1 - (1 - \text{risk}' - \text{annual complication probability})^{1/12}\right]/(1+k),$$
$$p_1' = kp_4.$$
- The complication also depends on drug, as shown in the following figures.



Note:

(1) The numbers are all probabilities.

(2) For aspirin complication, $p_5 = 0.9576$; for statin complication, $p_5 = 0.998$.

References

Arias, Elizabeth (2015). United States Life Tables, 2011. *National Vital Statistics Reports.* **64**(11). Available from: https://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_11.pdf

Choi, Sung Eun, Katherine E. Perzan, Angela C. Tramontano, Chung Yin Kong, and Chin Hur (2014). Statins and aspirin for chemoprevention in Barrett's esophagus: Results of a cost-effectiveness analysis. *Cancer Prevention Research.* **7**(3), 341-350.

Hur, Chin, Norman S. Nishioka, and G. Scott Gazelle (2004). Cost-effectiveness of aspirin chemoprevention for Barrett's esophagus. *Journal of the National Cancer Institute.* **96**(4), 316-325.

Kastelein, Florine, Manon CW Spaander, Katharina Biermann, Ewout W. Steyerberg, Ernst J. Kuipers, Marco J. Bruno, and Probar-study Group (2011). Nonsteroidal anti-inflammatory drugs and statins have chemopreventative effects in patients with Barrett's esophagus. *Gastroenterology*. **141**(6):2000-2008.