Homework Assignment 9

Submit the link to the GitHub repository where your code is located by 11:59PM, Tuesday, April 10.

Overview: Atrial fibrillation is a major public health problem, as it is the cause of 10-15% of all stokes. It is an irregularity of the heat rhythm that can lead to the formation of small blood clots (emboli) in the circulation. If these clots reach the brain, then a stroke occurs. Several trials have demonstrated that anticoagulation dramatically reduces this risk of stroke. The dilemma is that it also increases the risk of bleeding, the most serious form of which is a bleed into the brain (i.e., a hemorrhagic stroke). Thus, the decision problem is whether the reduced risk of embolic stroke from using anticoagulation is worth the increase risk of bleeding. Clearly, this depends on the risk of emboli – the higher the risk, the greater the payoff from anticoagulation. Note that a stroke or bleed can occur repeatedly during the lifetime of the patient, so we must model the entire uncertain life span of the patient, and allow for repeated uncertain events. Similarly, we must allow for death to occur at any point in time.

Problem 1: Markov Diagram (Weight 1): Draw a Markov diagram with three mutually exclusive health states "Well", "Post-Stroke" and "Stroke Dead" and arrows that represent the following probability transition matrix.

		State of Next Cycle (Year)		
		Well	Post-Stroke	Stroke Dead
State of Current Cycle (Year)	Well	0.75	0.15	0.1
	Post-Stroke	0.0	0.8	0.2
	Dead	0.0	0.0	1.0

The "Well" state represents patients who are asymptomatic but atrial fibrillation continues. Their physical functioning is normal and let's assume they have a normal quality of life despite the increase risk of stroke. The "Post-Stroke" state relates to patients who have survived a stroke. They have a reduced quality of life and an increase probability of further stroke (and hence require treatment with anticoagulation).

Problem 2: Temporary State (Weight 1): Assume that the cost incurred due to a stroke is $5,000. Can you think of a way to incorporate this cost into you model to estimate a patient's total cost during their lifetime? The stroke cost cannot be properly accounted for in this Markov model with only 3 states. Note that in this model a patient who is in "Post-Stroke" state will continue to stay in this state with 90% probability. Now if a patient continues to stay in "Post-Stroke" state, it is not obvious whether the patient has had a stroke in the meantime or if the patient just stayed alive and kept her post-stroke status. Therefore, with only 3 states, we cannot properly count the number of strokes that a patient may experience.

To resolve this problem, we can add a temporary state "Stroke" to model the actual event (here stoke) that causes transition from state to state. This temporary state is characterized by having transitions

from it only to other states and not to itself. Therefore, a patient can stay in this state for one cycle only and must move to another state for the next cycle. The presence of temporary "Stroke" enables the calculation of costs incurred due to stroke episodes.

Update your Markov model diagram to reflect the addition of the temporary state "Stroke". Adding a temporary state will change the transition probability matrix:

		State of Next Cycle (Year)			
		Well	Stroke	Post-Stroke	Stoke Dead
State of Current Cycle (Year)	Well	0.75	0.15	0.0	0.1
	Stroke	0.0	0.0	1.0	0.0
	Post-Stroke	0.0	0.25	0.55	0.2
	Dead	0.0	0.0	0.0	1.0

Note that:

1. We don't have transition from "Well" to "Post-Stroke" and instead a patient who experiences stroke while in state "Well" will move to the temporary state "Stroke".
2. From state "Stroke" one can move only to "Post-Stroke" state (by the way we have constructed the temporary state "Stroke").
3. And the movements out of the state "Post-Stroke" is now more accurately modeled. A patient in this state may experience another stroke with 25% probability or may experience an "event-free" cycle and stays in "Post-Stroke" state with 55% probability.

Problem 3: Markov Model (Weight 5): Develop a Markov model to simulate 2,000 patients over 50 years to estimate the expected life-years of a patient who is in state "Well" at the beginning of the simulation period. Provide 95% confidence intervals for your estimates.

Problem 4: Modeling the effect of anticoagulation (Weight 1): Assume that the anticoagulation relative risk in reducing stroke incidence and stroke death while in "Post-Stroke" is 0.65 and its relative risk in increasing mortality due to bleeding is 1.05. Calculate the transition probability matrix for this scenario where patients will receive anticoagulation while in state "Post-Stroke". Make sure that the sum of probabilities in each row is 1.

Problem 5: Modeling the effect of anticoagulation (Weight 2): Use your model to estimate the life-years of a patient who start in state "Well" and will receive this anticoagulation while in the state "Post-Stroke". Provide 95% confidence intervals.

Problem 6: Survival curves (Weight 2): Estimate the survival curves of a patient who start in state "Well" under both alternatives.

Problem 7: Number of strokes (Weight 2): Estimate the mean and show the histogram of the number of stokes that an individual who start in state "Well" may experience under both alternatives.