RDS 285
Decision Analysis Methods in Public Health and Medicine
Spring 1 2023

EXAM 1

Due on Friday February 17, 2023
by 11.59pm (midnight) on Canvas

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Instructions

- There are three questions with multiple parts, making up a total of 40 points, plus 2 possible bonus points. Credit for each question is indicated.
- Partial credit will be given for partially completed but well-reasoned answers. Be explicit about any assumptions you make and the reasoning behind your approach to each problem.
- Read each question carefully. Any clarification questions should be emailed to ALL teaching staff, no later than 12pm (noon) on Friday, February 17.
- You may consult any notes, books, articles, and other written material, and can use software (e.g., TreeAge, Excel) to solve the problem or check your answers, but you may not discuss the exam with other students.
- Please submit each question as a separate file, and make sure to show your work. If you use any software to solve the problems, submit all the relevant files (e.g., Excel workbooks, TreeAge models) with your exam.
- Please round your answers to four digits after the decimal. Do not round intermediate calculations.

Note:

- The disease topics included in this exam are simplified. Please do not read into the specific names of diseases or treatments according to your outside knowledge. Please rely on the information provided in the questions and methods demonstrated in class.

Good luck!

Note: this document corrects two typos in the utility weights provided in Question 3

QUESTION 1 [8 points]

Chronic hepatitis B (CHB) is a vaccine-preventable disease caused by the hepatitis B virus (HBV). CHB can lead to severe inflammation and damage in the liver, resulting in cirrhosis and liver failure if left untreated. However, not all who are infected with HBV will exhibit symptoms: HBV carriers have *asymptomatic* infection but can still pass HBV to others and are at higher risk of developing complications, such as liver damage, than a healthy person. Healthy 50-year-old men without hepatitis B have a life expectancy of 26.2 years, while 50-year-old men with symptomatic CHB have a life expectancy of 15.7 years. 50-year-old men who are HBV carriers have a life expectancy of 24.3 years.

a. [3 points] Assuming that you do not have a life table, under an excess mortality model, what is your estimate for the excess mortality rate associated with CHB? What is your estimate for the excess mortality rate for HBV carriers? What assumption(s), if any, did you make?

b. [2 points] Nucleoside analogues (NAs) are a class of antiviral drugs used in the management of symptomatic hepatitis B. NAs reduce the all-cause mortality rate for men with CHB by 14.5%. Assuming NAs do not affect background mortality, by what percentage do NAs reduce the excess mortality rate associated with symptomatic CHB?

c. [2 points] 50-year-old men in the general population (including individuals with and without symptomatic CHB) have a 2% chance of developing cirrhosis in the next 10 years, conditional on surviving to age 60. Individuals with symptomatic CHB, however, have a higher risk of cirrhosis: 50-year-old men with symptomatic CHB have a 25% chance of developing cirrhosis in the next 10 years (again, conditional on surviving to age 60). The prevalence of symptomatic CHB in 50-year-old men is 0.5%. What is the risk ratio of developing cirrhosis in the next 10 years for 50-year-old men with symptomatic CHB compared to those without symptomatic CHB?

d. [1 point] Assuming that the rates of cirrhosis calculated in part (c) are constant over time, what is the risk ratio of developing cirrhosis in the ***next 1 year*** for 50-year-old men with symptomatic CHB compared to those without symptomatic CHB?

QUESTION 2 [12 points]

Public health officials have recently become concerned about an outbreak of a new disease known as Restless Dream Syndrome (RDS). RDS is characterized by three health states: (1) Asymptomatic (with a low risk of death); (2) Symptomatic (with an elevated risk of death); and (3) Dead.

For those with asymptomatic RDS, the annual probability of developing symptoms is 0.04. Also, the annual probability of staying symptomatic for those who have symptoms is 0.75. People who start out asymptomatic live an average of 4 years in the symptomatic state. People who start out symptomatic live 6.25 years on average in the asymptomatic state. Assume that nobody receives treatment, and it is not possible to cure RDS. In thinking about this problem, you can assume that all transitions happen at the end of each year, and that the transition probabilities do not change over time.

a. [6 points] What is the probability that someone who starts out asymptomatic will still be asymptomatic after one year? What is the probability that someone who starts out symptomatic becomes asymptomatic in one year?

b. [2 points] Given your answer to part (a), what is your transition matrix for RDS?

c. [4 points] Asymptomatic patients have a utility of 1 and symptomatic patients have a utility of 0.4. The quality-adjusted life expectancy for a cohort of patients with RDS is estimated to be 15.59 years. What percentage of the starting cohort is symptomatic?

QUESTION 3 [20 points]

Patients with chronic kidney disease (CKD) experience gradual loss of kidney function over time. As the disease worsens, the extent of kidney damage results in complications such as difficulty urinating, high blood pressure, anemia, malnutrition, nerve damage, and decreased mental sharpness. In End-stage CKD, patients experience kidney failure and face high mortality rates. Therefore, CKD can impact both survival and quality of life.

For a hypothetical cohort of 60-year-old U.S. men with CKD, the stages of CKD are categorized into three health states: Mild, Moderate, and End-stage (Note: CKD is usually classified into five stages, but we have simplified it for this question). We assume that patients can never return to a state of perfect health once they have developed CKD.

All patients in this hypothetical cohort begin with a new diagnosis of CKD in the Moderate state which has a utility weight of 0.67. Each year, conditional on surviving background mortality, patients in the Moderate state receive standard of care and have a 14% probability of progressing to the End-stage state and an 6% probability of regressing back to the Mild state. For patients in the Mild state, if they survive background mortality, 30% of them can progress to the Moderate state under standard of care.

Individuals in the Mild state have a utility of 0.85. For patients in the End-stage state, if they survive background mortality, they have a 20% probability of dying directly from kidney failure and they cannot regress to other disease states.

Individuals in the End-stage state have a utility of 0.55. Individuals in Mild and Moderate states are assumed to experience no CKD-specific mortality unless they progress to the End-stage state.

For this question, use an annual cycle length and apply a termination criterion of 100 cycles. Apply the half-cycle correction for all calculations. You are given the 2012 U.S. life tables to inform the values of age-specific background mortality rates.

a) [5 points] Estimate the (undiscounted) quality-adjusted life expectancy (QALE) for a cohort of 60-year-old U.S. men who have been diagnosed with Moderate state CKD.

b) [2 points] What is the probability that a U.S. man who is in the Mild state at 70 years old will be in that state four years later? The individual may transition between model states during this time.

c) [3 points] New evidence suggests that individuals in the Moderate state face an excess mortality of 0.005 deaths per person-year. The probability of progression to the End-stage state remains at 14% and the probability of regression to the Mild state remains at 6% (conditional on surviving background and CKD-specific mortality). Under this assumption, what is the undiscounted QALE for a cohort of 60-year-old U.S. men who have just been diagnosed in Moderate state CKD?

For the following sections, use the model you developed for parts a)-b). Do not use the assumption from part c).

Two RCTs (randomized controlled trials) have just been published that each compared one new treatment to standard of care and showed promising results in slowing progression from the Moderate state to End-stage state. Both treatments are only used for CKD patients in the Moderate state. Therefore, individuals in the Moderate state would stop receiving treatment upon progression.

In the first RCT (for Treatment A), researchers reported that individuals with Moderate CKD receiving Treatment A experienced a hazard ratio of 0.6 for progression from the Moderate state to the End-stage state, as compared to individuals receiving the standard of care, conditional on surviving background mortality. Side effects from Treatment A lower the utility weight of the Moderate state to ~~0.82~~ **0.64** **[this value has been corrected]**.

The second RCT compared Treatment B to standard of care and reported a one-year risk ratio of 0.55 for the progression from the Moderate state to the End-stage state, conditional on surviving background mortality. Side effects from Treatment B lower the utility weight of the Moderate state to ~~0.78~~ **0.60** **[this value has been corrected]**.

Given these RCT results, you are interested in evaluating the long-term impact on patients under these two treatments.

d) [5 points] Estimate the <u>discounted</u> quality-adjusted life expectancy for a cohort with a new diagnosis of Moderate CKD who receive Treatment A. Estimate the discounted QALE for a cohort with a new diagnosis of Moderate CKD who receive Treatment B. Apply an annual discount rate of 3%.

e) [3 points] What is the probability that a patient with a new diagnosis of Moderate CKD will be in the End-stage state after six years if given Treatment A? Treatment B?

f) [2 points] You did a literature review and found that a few more RCTs in recent years have compared Treatment B to standard of care. However, these studies reported different values for the risk ratio of progression from Moderate CKD to the End-stage state with Treatment B. Given the uncertainty about the correct value for this risk ratio, what is the risk ratio at which the discounted QALE for someone treated with Treatment B would be the same as the QALE for someone treated with Treatment A?

BONUS QUESTION [2 points]

A study reports a risk ratio of developing disease that is relevant for your modelling analysis. This risk ratio describes incidence for individuals with a certain risk factor to those without it. However, the study was conducted in a setting with extremely high incidence rates. What concerns might you have about using this risk ratio estimate for your analysis, which models outcomes in a lower incidence population? Describe your concerns, as well as the direction of any bias that might be introduced by using this value directly in your study.