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

EXAM 2
Due on Saturday, March 11, 2023
at 11:59 pm Eastern via Canvas

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Instructions
The exam comprises two parts with multiple questions [40 points total], plus two bonus questions [4 possible bonus points].

- Read each question carefully. Any **clarification questions should be emailed to ALL teaching staff, no later than 5pm on Friday, March 10**. If there is a delay in us getting back to you, please state any assumptions you feel need to be made and move forward.
- You will need the accompanying TreeAge "exam2_tree_2023_bug.trex" file found on Canvas.
- Please use the checklist on the next page to keep track of the files you need to submit. Name your files as shown on the checklist.
- 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.
- 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 anyone apart from the teaching team.
- **Please round your answers to four digits after the decimal.** Do not round intermediate calculations.

Note:
The disease topics included in this exam are fictional or simplified/modified for the purposes of this exam. Please do not read anything into the specific names of diseases or treatments according to your outside knowledge. Rely on the information provided in the questions and methods demonstrated in class.

Good luck!

RDS 285 Exam 2 File Submission Checklist

<<< You do NOT need to submit this checklist>>>

Question	Files to submit	File names*	Self-check
Part I	Answers to Part I Q1-3	Lastname_Exam2_Part_I.pdf	
	Revised TreeAge tree for Part I Q3	Lastname_Exam2_Q3.trex	
Part II	Answers to Part II Q5-8	Lastname_Exam2_Part_II.pdf	
	TreeAge tree for Part II Q4	Lastname_Exam2_Q4.trex	
	TreeAge tree for Part II Q6	Lastname_Exam2_Q6.trex	
	TreeAge tree for Part II Q7	Lastname_Exam2_Q7.trex	
	TreeAge tree for Part II Q8	Lastname_Exam2_Q8.trex	
Bonus Questions	Answers to Bonus Questions	Lastname_Exam2_Bonus.pdf	

* Lastname, please insert your last name. For example, Santa Claus will submit the first file as "Claus_Exam2_Part_I.pdf".

CASE

You are part of a research team investigating the epidemic of "Markov Pain Horror" (MPH) in the United States. MPH is characterized by physical pain at different locations of the body depending on the patient's emotional status at the moment. MPH has two stages: a mild first stage (Stage I), and a severe second stage (Stage II).

Both stages of MPH are associated with reduced quality of life. Stage I MPH has a utility weight of 0.8 and Stage II MPH has a utility weight of 0.5. Individuals without MPH have a utility weight of 1.0.

In a cohort study of healthy 18-year-old men and women, the 9-month cumulative incidence of Stage I disease was 11%. There were no deaths in the study cohort over the 9-month follow-up period.

The annual probability of progression from Stage 1 to Stage II MPH is 0.1 among those who survive background mortality. Individuals with Stage II MPH regress to Stage I MPH at a hazard rate of 0.03 per person-year. Individuals with Stage I MPH can also become well again, but individuals with Stage II MPH cannot directly become well without passing through Stage I MPH first. The annual regression probability from Stage I MPH to Well has been estimated to be 0.06 for those who survive background mortality. Individuals who become well after having developed MPH face the same risk of developing MPH again as those who have never had MPH.

There is also excess mortality from Stage II MPH. An observational study that followed 25-year-old individuals with Stage II MPH found that one-year survival was 95.7783%.

TREEAGE TREE

The TreeAge file "exam2_tree_2023_bug.trex" represents the natural history model of MPH (i.e. no treatment) for a cohort of healthy 18-year old individuals in the United States. Utilities are NOT included in this tree. An annual cycle length is used. The calculation method is set to "Cost-Effectiveness." Payoff 1 is designated for Costs, and Payoff 2 is designated for Effectiveness. The tree contains one table: a "muALL" table that contains annual mortality rates for the total US population (men + women) derived from the 2018 U.S. life tables.

PART I. QUESTIONS [18 points]

1. [3 points] The annual risk of developing Stage I MPH among those who are healthy is estimated to be 0.143909. This value is already entered into the TreeAge model. Describe step-by-step how this estimate was calculated, and state at least one assumption that is required for this calculation.

2. [3 points] The excess mortality rate associated with Stage II MPH is estimated to be 0.042054. This value is already entered into the TreeAge model. Describe step-by-step how this estimate was calculated, and state at least one assumption that is required for this calculation.

3. [12 points] There are **six** errors ("bugs") in the model (exam2_tree_2023_bug.trex) provided for a cohort of 18-year-old health individuals in the U.S. List all six of these bugs in your response to the question. **Fix the bugs in the .trex file and submit the revised tree using the naming convention described on the checklist/cover page**.

   Hints:

   - There is no error in the values entered in the life table muALL or the settings of the life table.
   - There is no error in the initial state vector.
   - No interventions nor costs nor utilities are included in this tree (i.e., you shouldn't consider this exclusion a bug).
   - The undiscounted life expectancy for a **38-year-old with Stage I MPH** should be 29.522664 if all bugs are fixed.

PART II. COST-EFFECTIVENESS OF TREATMENT [22 points]

The standard of care for MPH is to treat both stages of MPH with the "DRP" (Daily Relief Pill):

- DRP increases the probability of regression from Stage I to Well and the probability of regression from Stage II to Stage I.
    - One RCT studying the effect of DRP on Stage I patients reported that the *hazard* ratio for transitioning from Stage I to Well for patients taking DRP is 1.6, relative to untreated patients.
    - Another RCT studying the effect of DRP on Stage II patients reported that the *risk* ratio for transitioning from Stage II to Stage I for patients taking DRP is 2.8, relative to untreated patients.
- DRP costs $8,500 per year. You can assume that all treated patients are 100% adherent to the treatment.

4. [8 points] Off the blue decision node of the revised tree from Part I-3, modify the model and build the DRP treatment strategy described above, including costs and utilities. Name this strategy 'Treat with DRP'. Assume that people get treated with DRP as soon as they have Stage I MPH and continue treatment as long as they have either Stage I or Stage II MPH. Assume that the cost for the 'No Treatment' strategy is zero and the discount rate is 2.5% per year for both costs and benefits. **Save and submit this tree using the naming convention described on the checklist/cover page.**

5. [3 points] Starting with an initially healthy cohort of 25-year-old men and women, what is the incremental cost-effectiveness ratio associated with the standard-of-care treatment with DRP, as compared to no treatment? Given a willingness-to-pay (WTP) threshold of $50,000 per quality-adjusted life year (QALY), is treatment with DRP cost-effective? Is DRP cost-effective at a WTP threshold of $100,000 per QALY?

Scientists have discovered a new treatment for MPH (both stages), called "Markov Happy Days" (MHD). MHD reduces the severity of symptoms from MPH and therefore increases the utility for Stage I MPH to 0.9 and the utility for Stage II MPH to 0.6. Unlike DRP, it does not have an impact on regression from Stage II to Stage I nor from Stage I to Well. MHD therapy costs $4,900 per year. As with DRP treatment, patients treated with MHD receive the drug only when they are in Stage I or Stage II disease and discontinue the drug if they return to the Well state. Due to drug-drug interaction, patients cannot be given both MHD and DRP.

6. [4 points] For an initially healthy cohort of 25-year-old men and women, conduct a cost-effectiveness analysis evaluating the three treatment strategies: (1) No Treatment, (2) Treat with DRP, (3) Treat with MHD. Given a willingness-to-pay (WTP) threshold of $50,000 per quality-adjusted life year (QALY), what is the optimal treatment strategy? How about a WTP threshold of $100,000 per QALY? Justify your choice. **Save and submit this tree using the naming convention described on the checklist/cover page.**

7. [3 points] A new RCT of the MHD therapy revealed that the effect of the therapy on the utility for Stage II MPH is not constant by age. For those treated with MHD, the utility weight for Stage II MPH remains constant at 0.6 when the Stage II MPH patient is between 18 and 30 years of age (inclusive), but then decreases by an absolute 0.005 per year starting from age 31 until death. You should assume that the treatment strategy for MHD stays the same (i.e. everyone in Stage I and Stage II disease receives MDH treatment, regardless of age). You can assume that the utility weight for Stage I MPH with MHD remains constant over time (0.9).

   Update your cost-effectiveness analysis in Question 6 with this new piece of evidence. Report your CEA results and the optimal strategy under the two WTP thresholds ($50,000/QALY & $100,000/QALY). **Save and submit this tree using the naming convention described on the checklist/cover page.**

8. [4 points] There is uncertainty about the effect of DRP on the risk ratio for regressing from Stage II to Stage I, since our point estimate is derived from one RCT. Using the completed tree from Part 2 Question 5, perform a 2nd-order Monte Carlo simulation (probabilistic sensitivity analysis) using 10,000 parameter sets to understand the implications of this uncertainty for the choice between the No Treatment strategy and the DRP Treatment strategy, for the cohort of healthy 25-year-olds. To do so, specify a LogNormal distribution for the risk ratio associated with DRP treatment, with a mean of 2.8 and median of 2.4. **Save and submit this tree using the naming convention described on the checklist/cover page.**

   Report the 95% uncertainty intervals for discounted costs and discounted quality-adjusted life expectancy for the DRP treatment strategy. Please round your answer to two digits after the decimal.

   Provide a Cost-Effectiveness Acceptability Curve (CEAC) for the WTP ranging from $10,000 to $200,000 per QALY saved (set the WTP Intervals option to 100) and interpret the CEAC to describe the decision uncertainty.

BONUS

9. [2 bonus points!] You are working on a cost-effectiveness analysis with a collaborator. They estimate the ICER for the intervention you are studying and find that it is negative. Is this intervention cost-effective? Justify your answer.

10. [2 bonus points!] Can the expected value of perfect information (EVPI) ever be negative, or zero? Explain your answer.