Instructions: This question is designed to test your programming skills using a stylized disease simulation model. If you have questions on any modeling concepts (e.g., cost-effectiveness acceptability curves), you may email Jinyi for guidance. No guidance will be provided on how to operationalize this simulation model in Python. Please submit your response through email as a pdf (with necessary text response and figures) along with your code by **11:59pm Monday 6/26**. Email Ashley and Jinyi if you need extra time.

TB or not TB*

**The disease is real, but the details in this question are only approximate. You do not need to use outside subject matter knowledge to answer this question*.

TB is an infectious lung disease, characterized by latent and active disease stages. Individuals with latent TB have no signs or symptoms indicating infection, but progress to active TB at a monthly probability of 0.0000833 (though this is highly uncertain). Individuals who progress to active disease experience chronic cough, night sweats, and elevated mortality. If an individual develops active TB, they have a monthly probability of 0.156 of being identified and initiated on treatment, with a TB-specific mortality probability of 0.0328 per month during that period. After treatment, they return to the latent state (you can assume treatment is instantaneous). In this population, the background monthly mortality probability can be approximated as: $1 - e^{(-e^{\left(-8+\frac{t}{20}\right)}.\frac{1}{12})}$, where t is an individual's age in years. (Note: This formula essentially assumes a parametric background mortality function that increases with age.)

In your research you follow a cohort of newborn infants (i.e., initially uninfected). They live in a setting where the force of infection for TB (the monthly probability of acquisition of TB infection) is 0.00167. You can assume that this probability is constant in age and time. You are looking to institute a program to diagnose and treat latent infection, but the tests for latent infection are imperfect. The TST test has a sensitivity of 80% and specificity of 95%. Treatment of latent infection can reduce the risk of developing active TB, with individuals shifting back to the uninfected state.

The program will test individuals once in their lifetime, but you must choose the optimal age for testing to occur.

(a) Considering every 5 years from age 0 to age 50 (i.e., age 0, 5, 10, 15, 20, etc.), what is the age at which a one-time screen will maximize life expectancy, and what is the life expectancy gain compared to no program?

(b) Assuming testing costs of $10 and treatment costs of $200, report the incremental cost-effectiveness of non-dominated strategies (assume no discounting, and a lifetime analytic horizon). For a WTP of $1000 per life-year (LY) saved, what is the optimal strategy based on the information given? (Note, it is also an option to have no program).

(c) Revise your analysis to include uncertainty in the following variables (note that these priors have the same mean as the original point estimates):

Parameter	**Original point estimate**	**Functional form for prior distribution**	**Parameters for prior distribution**
Monthly probability of acquisition of TB infection	0.00167	Beta	Alpha=10, Beta = 6000
Monthly progression probability for individuals with latent infection	0.0000833	Beta	Alpha=0.7708, Beta = 9253
Monthly probability of treatment initiation for individuals with active disease	0.156	Beta	Alpha=20.78, Beta = 112.45
Monthly TB mortality probability	0.0328	Beta	Alpha=20, Beta = 590
TST sensitivity	0.8	Beta	Alpha=40, Beta = 10
TST specificity	0.95	Beta	Alpha=38, Beta = 2
Test costs	10	Gamma	Shape = 40, Scale = 0.25
Treatment costs	200	Gamma	Shape = 200, Scale = 1

Based on these prior distributions, report a mean estimate and a 95% uncertainty interval for the life expectancy gain calculated in part (a). Does the mean equal the point estimate calculated in (a)? Why/why not?

(d) Report the uncertainty in your cost-effectiveness results as a cost-effectiveness acceptability curve. At a WTP of $1000 per LY saved, what is the probability that the strategy identified in (b) is optimal?

Tips:
There are four health states in this TB model: S (Susceptible), E (Latent TB), I (Active TB), and Dead. The transition diagrams (with and without the screening test) are shown in Figures 1 and 2. The only difference is that the diagram with TST would allow transition from Latent TB back to Susceptible.

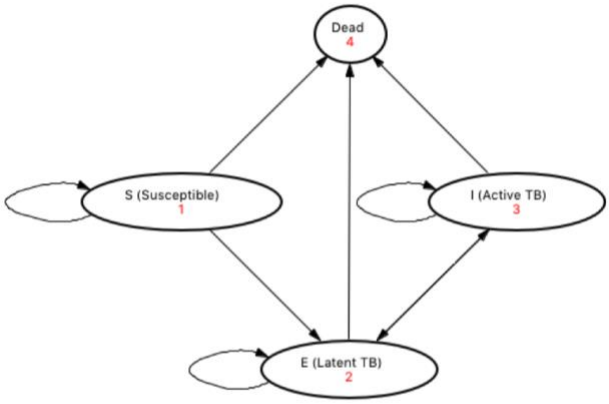

Figure 1: Transition Diagram (without TST)

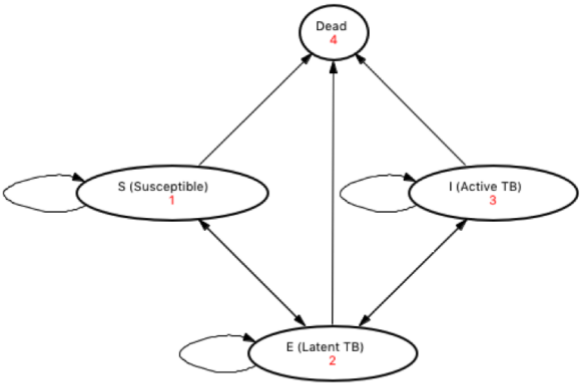

Figure 2: Transition Diagram (with TST)

Here are some reasonable assumptions you can make:

1. Cycle length can be set at 1 month because a yearly cycle length may not be precise enough to capture the rapid disease progression.
2. Since the question cares mainly about different TST test strategies, the treatment for active TB does not vary across strategies, even in the "no program" option. That is, it is not an option to not treat active TB.
3. The treatment for latent TB is the same as the treatment for active TB, i.e., the costs are both equal to "Treatment costs" in the parameter table (on average, $200).
4. For those who are in the susceptible or latent TB state, if they get TST and they are TST positive, they would get the treatment and have no chance of progressing to the next disease stage in this particular cycle; But if they get a negative test result and are thus not treated, they are still subject to the risk of progressing to the next stage of disease. That is, susceptible individuals can still be infected, and latent TB patients can still develop active TB if no treatment is provided.