School of Engineering and Applied Science (SEAS), Ahmedabad University

B.Tech(CSE) Semester IV
Probability and Stochastic Processes (MAT 277)

Group No : SB11

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Project Title:

Neoadjuvant therapy versus upfront surgery for potentially resectable pancreatic cancer using Markov Cohort Analysis.

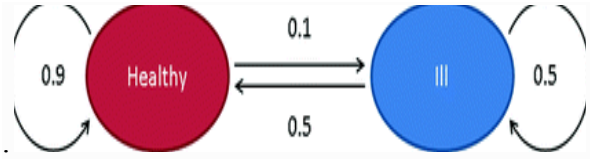
1) Justify how a probabilistic model/PSP concept is used in your project. How uncertainty is modeled?

In this case study, our aim is to find out the best of two given treatments by Markov decision process. In order to understand MDPs, we first need to understand Markov models. Markov models are stochastic processes that undergo transitions from one state to another. Markov models are useful to model environments and problems involving sequential, stochastic decisions over time. They can be examined by an array of tools including linear algebra, cohort simulations, Monte Carlo simulations, etc. We will use Monte Carlo simulations for our study.

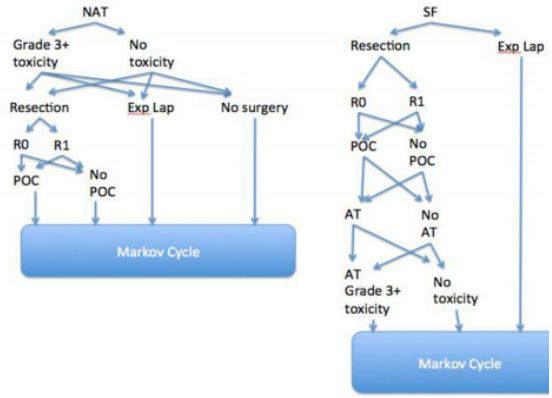
A fundamental property of all Markov models is their memorylessness. They satisfy a first-order Markov property if the probability to move a new state to s_{t+1} only depends on the current state s_t, and not on any previous state, where t is the current time. Said otherwise, given the present state, the future and past states are independent. Formally, a stochastic process has the first order Markov property if the conditional probability distribution of future states of the process depends only upon the present state:

$$P(s_{t+1}|s_1,s_2,\ldots,s_t) = P(s_{t+1}|s_t)$$

Markov chains: The discrete time Markov chain, defined by the tuple {S,T} is the simplest Markov model, where S is a finite set of states and T is a state transition probability matrix, $T(s',s)=P(s_{t+1}=s'|s_t=s)T(s',s)=P(s_{t+1}=s'|s_t=s)$. A Markov chain can be ergodic, if it is possible to go from any state to every other state in finitely many moves. The figure shows a simple example of a Markov Chain.



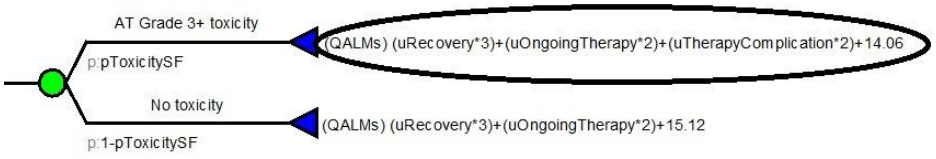
Markov Decision Processes are an extension to Markov chains, which include a control process. They are a powerful and appropriate technique for modelling medical decisions. They are most useful in classes of problems involving complex, stochastic and dynamic decisions like medical treatment decisions, for which they can find optimal solutions. Monte Carlo (MC) simulations are a useful technique to explore and understand phenomena and systems modeled under a Markov model. MC simulation generates pseudo random variables on a computer in order to approximate difficult to estimate quantities. From our study, we have made a markov cohort analysis which is shown below.

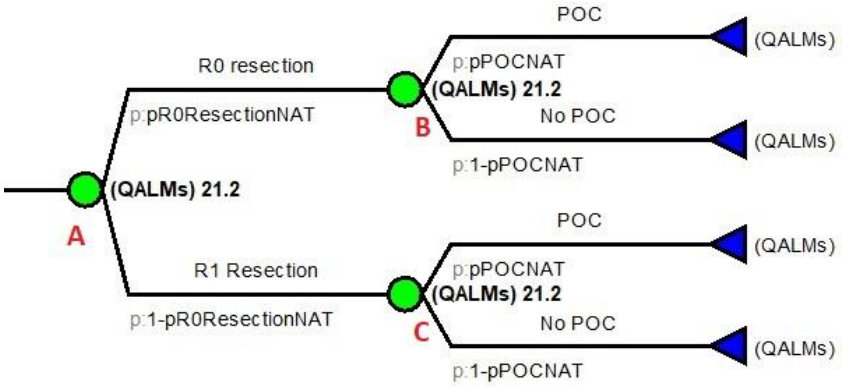


Markov cohort Analysis

2) Clearly enlist the new things done in the coding part, excluding the shared code.

- We have tried to make a python simulator by taking the references from the AMUA software provided by TA and the probabilities mentioned in the research article. The output specifies the QALMs of the NAT and SF process by the calculations using :
    - QALM at terminal Terminal Node = (Utility of the survival state * No. of months patient stayed in that month) + Observed QALM
    - QALM value at Node A = (Probability at Node B * QALM at Node B) + (Probability at Node C * QALM at Node C)





- There is a slight difference between the QALMs calculated at every node between the python code and the AMUA simulator , the QALM calculated at every node is not rounded to 1 decimal digit in our code but AMUA software rounds it at every node which generates a difference of ± 0.2 .

3) Contribution of team members

- *Technical contribution of all team members*

Enlist the technical contribution of members in the table. Redefine the tasks (e.g Task-1 as simulation of fig.1 and so on)

Task	Neel Popat	Krunal Savaj	Kashish Jivani	Axay Ghoghari	Yashvi Navadia	Hinanshi Suthar	Mikita Vyas
AMUA software implementation in python	1	1			1	1	
Markov Cycle for specific cycles		1	1			1	
Analysis from the output of the several cycles			1		1		1
Graph plotting using python libraries	1			1			

- *Non-Technical contribution of all team members*

Enlist the non-technical contribution of members in the table. Redefine the tasks (e.g Task-1 as report writing etc.)

Task	Neel Popat	Krunal Savaj	Kashish Jivani	Axay Ghoghari	Yashvi Navadia	Hinanshi Suthar	Mikita Vyas
Concept Map v1	1	1	1	1	1	1	1
Concept Map v2	1	1	1	1	1	1	
Miro Board explanation of base article	1	1	1	1	1	1	1
Report	1	1	1	1	1	1	
Handwritten Analysis		1					

4) Any innovation done considering the society/neighborhood problem?

- Our problem specifically describes deciding the paths for choosing the therapy in order to cure pancreatic cancer.
- The code could be helpful for the doctors in order to decide the treatment by considering the utilities and the probabilities from the default values provided or their own specific values statistically observed from the patient database.
- We have created a process and code which can compare the total cost effectiveness and QALMs of the two pathways and patients can have a way to analyse the cost and QALMs beforehand.

- Assuming number of cycles = 20, total states =7 and number of patients = 2000, we created a transition probability matrix (we assumed values as we didn't have the real data) and using it, we got the number of patients in each survival state.

- The cost required in each survival state, QALMs for each state and total patients in each state gives us the values of cost and QALMs for each iteration and so we get 20 values of cost and QALMs for 20 cycles.

- Then averaging the costs and QALMs for both SF and NAT, we get the final costs and QALMs of a patient for both the pathways.

5) Enumerate the inferences derived from a user-centric perspective.

We have considered the parameter of QALMs as the output result for getting the inference from the code.

1. The QALMs of processes according to **one way deterministic analysis** are as follows.

   For pResectionNAT (0.26-0.70) and pATSF(0.30-0.90) if we take the case of :

- If pResectionNAT>0.54 and pATSF in the given range we can infer that the QALMs of NAT will be higher than the QALMs of SF according to our outcome ,NAT is a preferable pathway as compared to SF.
- If pResectionNAT<0.54 and pATSF in the given range we can infer that the QALMs of SF will be higher than the QALMs of NAT according to our outcome ,SF is a preferable pathway as compared to NAT.

2. **Two way deterministic analysis** states that the treatment superiority depends upon receiving multimodal treatment by altering the parameters of two variables simultaneously.

3. According to **probabilistic sensitivity analysis**, the best fit is the Anderson darling statistics which uses Monte Carlo simulations i.e. running 10,000 patient cycles and concludes that SF is superior than NAT. The results are as follows:

   The QALM for SF = 19.72, range (5.57-22.95),
   SVD-2.68 Variance -7.17
   The QALM for NAT = 17.16, range (16.50-17.38),
   SVD-0.19 Variance - 0.04

4. According to the **statistical analysis**, which uses the weighted estimate of median survival months, NAT is superior than SF. The results are as follows:
   Total QALM Months for NAT = 21.25
   Total QALM Months for SF = 18.51

5. According to **intention to treat basis**, which uses Markov decision analysis, SF is superior than NAT.
   Total QALM Months for NAT = 16.26
   Total QALM Months for SF = 18.51

References

1. (Base Article)

   B. A. V. D. M. R; “Neoadjuvant therapy versus upfront surgery for potentially resectable pancreatic cancer: A Markov decision analysis,” *PloS one*. [Online]. Available: https://pubmed.ncbi.nlm.nih.gov/30817807/ [Accessed: 05-Apr-2021].

2. *Simple Markov cohort model*, 17-Feb-2021. [Online]. Available: https://cran.r-project.org/web/packages/hesim/vignettes/markov-cohort.html [Accessed: 05-Apr-2021].
3. Komorowski, M. and Raffa, J., 2021. *Markov Models and Cost Effectiveness Analysis: Applications in Medical Research*. https://link.springer.com/chapter/10.1007/978-3-319-43742-2_24