Health Economics

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Week – 09

Lecture 46- Markov modelling and Sensitivity analysis in Healthcare

Welcome to our NPTEL MOOC module on Health Economics. The lecture is on Markov modelling and an introduction to sensitivity analysis. This is in continuation to the previous lecture, where we discussed about costing, discounting and economic evaluation under uncertainties. Some of the things, if you remember, we discussed were related to costing and discounting. Under costing, we discussed top-down and bottom-up approaches. In discounting, we have emphasised cost and health discounting, and we also talked about theories supporting health discounting and economic evaluation with uncertainty. Then, we emphasised decision analysis, incorporating the steps of decision analysis, decision tree, and their limitations. In this lecture, we emphasise Markov modelling and introduce sensitivity analysis, which includes one-way and multi-way. We will also discuss the challenges and different approaches obtained as a solution (as part of the sensitivity analysis).

So, let us introduce the Markov model. This is particularly referred to- as a dynamic model under uncertainty. In the real world, patients are not simply cured or not cured as a result of treatment. Just cure, and not cure should not be the final option. In reality, we may get various possibilities. They (Patients) might have different health states over time.

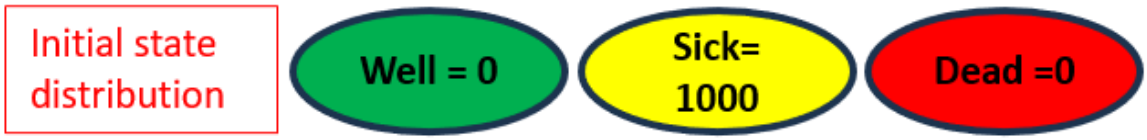
Markov model is a way in which these different health states can be structured and analysed. There are particular assumptions in the Markov model that should be introduced to before explaining the Markov model. The first one is that patients are in specific Markov states, called health states, at any given time. Second, over a specific time period called cycles, they either stay in the same state or move to another state. The probability of moving is called transitional probability. Hence, the third assumption is that as there is uncertainty, transitional probabilities are attached.

Let us use a simple example to understand this 'Markov model' in economic evaluation. We have just cited here the use of the Markov model in some healthcare for disease progression.

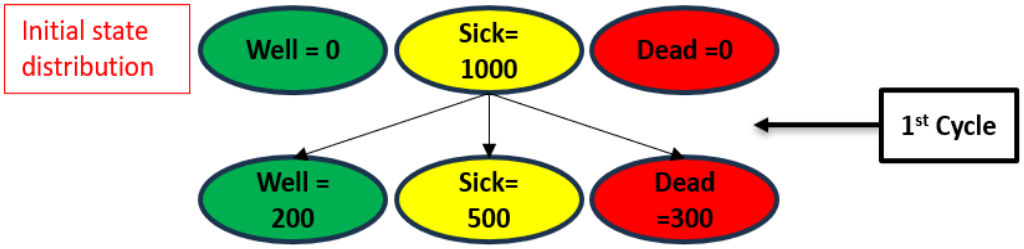
Example: Markov Model in Health Care for Disease Progression
Consider a healthcare scenario where there are **1000** patients with a specific illness→ who can be in one of three states: **'Well,' 'Sick,' or 'Dead**.' A Markov model is employed to analyse the evolution of health states over time.

Consider a healthcare scenario, where there are 1000 patients with specific illness, who can be one of the three states: either 'well', 'sick', or 'dead'. A Markov model is employed to analyse the evolution of health states over time. We will explain the possible options.

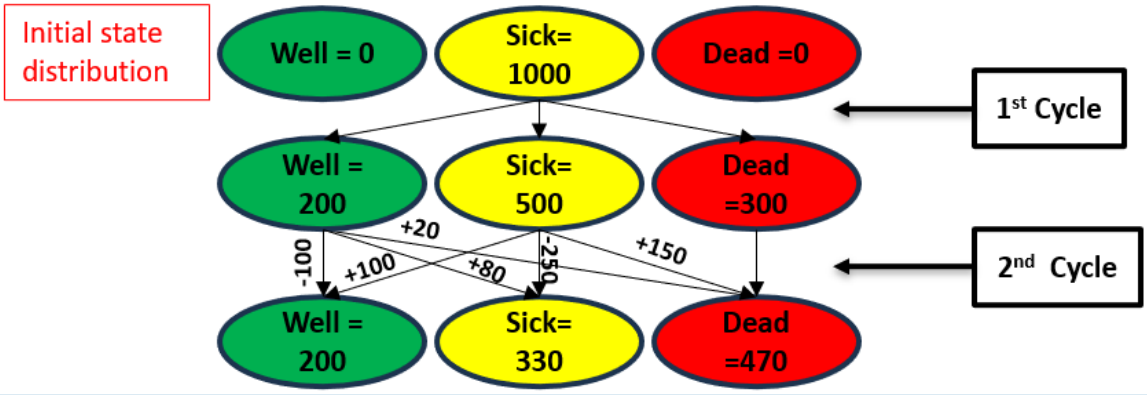
In the very initial state distribution, there might be three options i.e., - Out of all, 1000 might be sick, 0 numbers are well, and 0 dead (since we are saying all 1000s are sick).



During the first cycle, some get well (i.e., 200), let it be 200 out of the 1000 sick people which we have assumed. Let be the case that in the first cycle, 200 are cured and some die (let it be 300), so 500 are remaining as sick.



Hence, it connects to the second cycle. We will just explain here. Among those 'well', there is a possibility that they might also get sick in the next cycle. Hence, in the second cycle, there are little complex possibilities. To start with the 'sick' people, out of 500, some might get cured, i.e., 100 and 150 are dead. So, the remaining who are still sick are 250.



Similarly, from the 'well', those who are cured in the first cycle, might be facing troubles in the second cycle. Hence possibilities are like this, 100 may be cured out of 200, and 80 might be sick. So, 100 (cured), then 80 (sick), then 20 are dead. We are supposed to add all together to find how many are dead and how many are sick, till the end of the second cycle.

The process can be repeated as many times as required. Although in this example, eventually, everyone will be in an absorbing state by the 30th cycle (as mentioned by the author). So, in total, all are absorbed. This is demonstrating Keynes' assertion that in the long run we all are dead, as in the final cycle, all are dead. Hence, present allocation or evaluation really matters. You can just see here we have just presented Morris et al., (2012) work of different cycles-

Cycle	Well	Sick	Dead	Total
0	0	1 000	0	1 000
1	200	500	300	1 000
2	200	330	470	1 000
3	166	245	589	1 000
4	132	189	679	1 000
5	104	147	749	1 000
6	81	115	804	1 000
7	64	90	846	1 000
8	50	71	880	1 000
9	39	55	906	1 000
10	31	43	926	1 000
11	24	34	942	1 000
12	19	26	955	1 000
13	15	21	965	1 000
14	11	16	972	1 000
15	9	13	978	1 000
16	7	10	983	1 000
17	6	8	987	1 000
18	4	6	990	1 000
19	3	5	992	1 000
20	3	4	994	1 000

Source: Morris, S et al. (2012)

How many are well, how many are sick, and how many are dead out of 1000 people. 20 cycles are presented here. There are 10 more cycles, but they have minimal values as most people are dead by the 20th cycle. So, a total of 30 cycles are shown and in last 10 counts, all are dead. There is no further cycle possible.

How can we make this useful for economic evaluation? So let us see. We require further add-ins. We require add-ins of cost or benefits in terms of the utility. So let us say, we assign utility values to our existing example.

Let's say→ we assign utility values to our existing example as→ **being well= 1,** to **being dead= 0,** & to **being sick= 0.6**

Further, let's assume 1 cycle = 1 year

For 'being well'= 1; for 'being dead' = 0; for 'sick' = (let it be) 0.6. Let us assume that 1 cycle is equal to 1 year.

We are supposed to calculate QALY (Quality-adjusted life years). If you remember, we had few figures in our example on the first cycle (500 sick, 200 well, and 300 dead). We are just going to use it further.

❖ **QALY Calculation (Utility Values):**

End of first cycle: 500 * 0.6 + 200 x 1 = 500 QALYs
End of second cycle: 330 * 0.6 + 200 x 1 = 398 QALYs

} Cumulative total = 898 QALYs

In the first cyle , we said that '500 are sick' and their 'probability value is 0.6'; in 'being well' there are '200 people', hence '200 x 1', and 0 (they are dead), so that will be 0 then. In total, there are 500 QALYs on the end of first cycle. Similarly, we use the same approach for 2nd cycle. Based on the number 2nd cycle, you can just see how many are there: 330 and 200 (see from table). So, 330 x 0.6 + 200 x 1 = 398. So, the cumulative QALYs are 898. So, in this way, QALYs accumulate over time, giving the cumulative value of the quality of life.

From the table, we are just presenting the cumulative QALYs:

Cycle	Well	Sick	Dead	Total	Total Utility	Cumulative Utility
0	0	1 000	0	1 000		
1	200	500	300	1 000	500	500
2	200	330	470	1 000	398	898
3	166	245	589	1 000	313	1 211
4	132	189	679	1 000	245	1 456
5	104	147	749	1 000	192	1 648
6	81	115	804	1 000	150	1 799
7	64	90	846	1 000	118	1 917
8	50	71	880	1 000	92	2 009
9	39	55	906	1 000	72	2 081
10	31	43	926	1 000	56	2 138
11	24	34	942	1 000	44	2 182
12	19	26	955	1 000	35	2 216
13	15	21	965	1 000	27	2 243
14	11	16	972	1 000	21	2 265
15	9	13	978	1 000	17	2 281
16	7	10	983	1 000	13	2 294
17	6	8	987	1 000	10	2 304
18	4	6	990	1 000	8	2 312
19	3	5	992	1 000	6	2 319
20	3	4	994	1 000	5	2 324

Initially, it was 500 (which we have already shown you), and then another 398 added. It accounts for this 500 plus 398, so it is a cumulative value of 898. The process continues until all individuals are dead. Most QALYs are accumulated in the earlier years. You can just see, for most of the QALYs, the change is huge value of the QALYs, and these are accumulated in the earlier years. Later on, since we are approaching the later age and

towards the period of death, the QALY returns are very low. So, the total after 20 years is 2324, but 90 percent of this is gained in the very first 10 years. You can see, in first 10 years, 90 percent have already been gained. To compare alternative treatments, assume that different treatments will have different transition probabilities and generate different utilities or costs. Since there are transition probabilities, it will have different utilities.

Now, let us discuss sensitivity analysis. Earlier, we discussed how models, to some extent, deal with uncertainties by assigning probabilities to the events within the model. The other aspects of uncertainty are dealt through sensitivity analysis.

So, what do you mean by sensitivity analysis? This is a set of techniques that essentially seeks to analyse how sensitive results are to uncertainty. In the context of modelling, it analyses how sensitive results are to change in the model. For example, change in the structure of the decision tree or in the data that is contained within, say- a parameter value. There are different forms of sensitivity analysis. One type is using the plausible range method, that are i) 'one-way sensitivity analysis' and other one is ii) 'multi-way sensitivity analysis'.

In the one-way sensitivity analysis, we are looking at how sensitive the results are to the change in one parameter. This can also be discussed with this example of alternative treatments for an illness, such as surgery versus drug therapy, and the sensitivity of the rates, with the assumption about different discount rates in the horizontal axis, is given. So, over time, the rates are discounted.

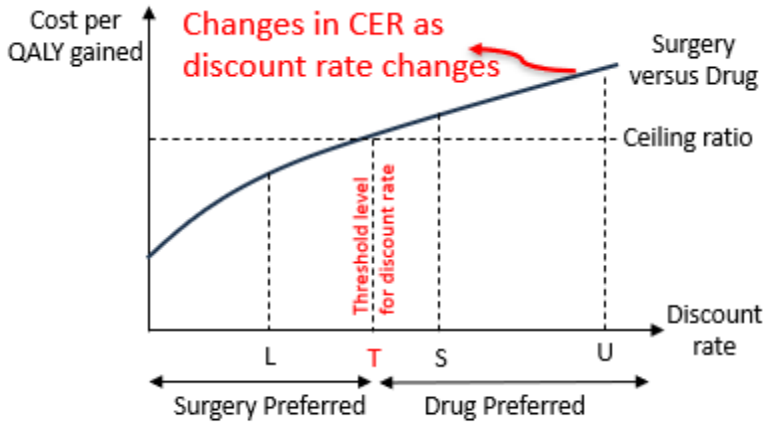


Fig: illustrates One- way sensitivity analysis

In the vertical axis, we measure the incremental cost of surgery against drugs. Hence, the vertical axis measures the incremental cost-effectiveness ratio, called ICER (incremental cost-effectiveness ratio) for surgery versus drug therapy. So, what is this? Basically, it is all about:

$$(Cost_{surgery} - Costdrug_{\_therapy} / QALYsurgery - QALYdrug_{\_therapy})$$

We have already explained the ICER in our earlier lectures, you can follow that. When ICER is below the ceiling ratio, surgery is preferred. You can just see that surgery is preferred once the ICER is below the ceiling ratio. Once it is above the ceiling ratio, then drug therapy is preferred. From the ceiling ratio onwards, we have already just highlighted that it is drug therapy. And this explains one-way sensitivity analysis.

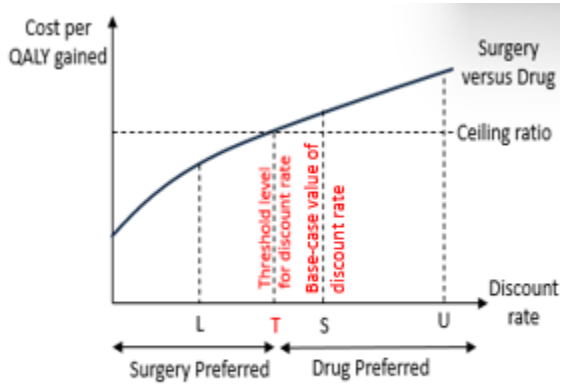


Fig: illustrates One- way sensitivity analysis

In the one-way, if S is taken as the base-case value of the discount rate (i.e., the variable parameter), ranging from upper limit (U) to lower limit (L), and T lies below U and L, it is sensitive. If outside, then of course it is not.

Coming to the multi-way sensitivity analysis, where we vary more than one parameter at the same time. So far, we have only taken one parameter; therefore, our case is presented in two-dimensional space. But if it is more than one, it is relatively complex. Unfortunately, it becomes very cumbersome for more than two or three parameters. Hence, we have shown it just for two variable parameters.

We have taken two variables. The two parameters to understand this sensitivity analysis are- *'discount rate'* (which we already discussed in the previous one-way case) and the second one is the *'proportion of patients that experience adverse events with the drug'* (with the drug, how they experience adverse events). So, each point represents a different combination of the discounted or the adverse event rate. You can see all points where the cost-effectiveness ratio is presented, and we will also mark the threshold. Since we have already taken two variable or two parameter cases, the threshold level itself is the line, not the level. So, the line basically compares these two (surgery and drug therapy), either going for drug adverse events (like the proportion of patients that experience adverse events with the drug) or the discount rate based decisions.

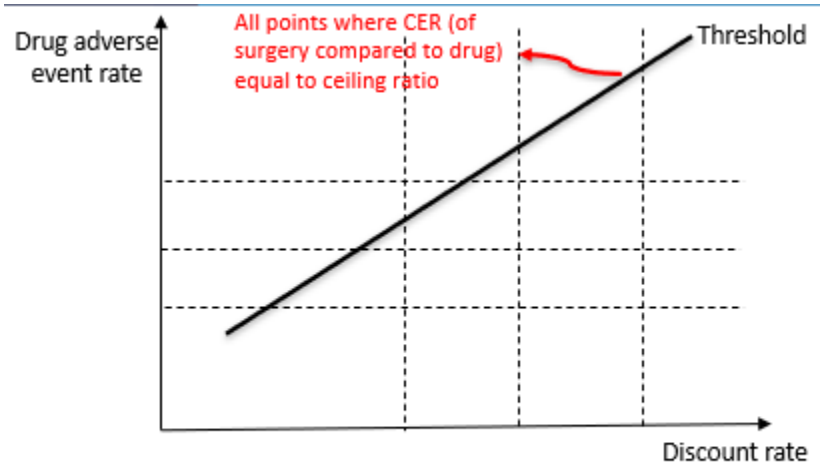


Fig. Illustrates Two-way sensitivity analysis

All points on the threshold line explain a person is indifferent between surgery and drug therapy. So, drug and surgery therapy can be explained through a threshold line that we have already highlighted here. The drugs' adverse effect rate does not impact surgical options directly. But the higher it is, the higher the cost of the drug option. That means it is better relative to the CER of surgery.

For any value below this threshold line, the drug is preferred. Then above the threshold line, the surgery is preferred. However, as we said earlier, the degree of sensitivity lies between the range of the base-case values. If X is chosen as the base-case value of both discounted and the drug adverse event rate with different upper and lower ranges of each. Then, the separate one-way analysis would then indicate results as not sensitive, if lines pass through the base-case and cross outside the possible range. All the possible range of that X which I have just highlighted here, if the line passes through that base-case, then it has better interpretation through the two analysis.

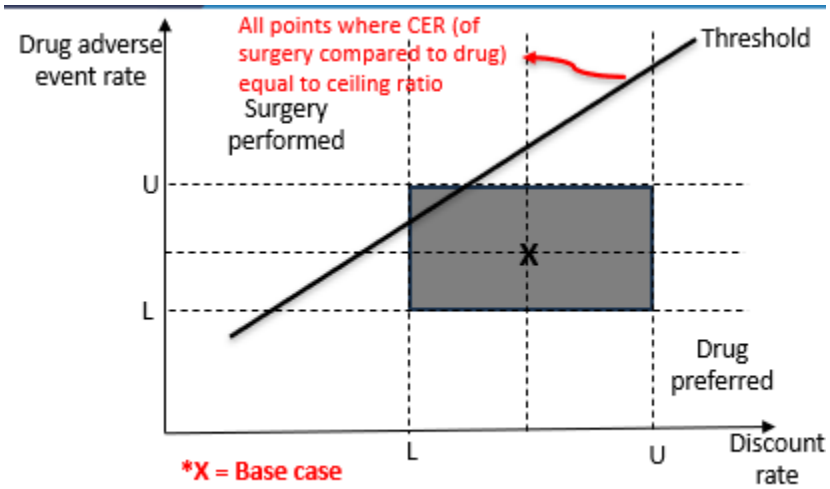


Fig. Illustrates Two-way sensitivity analysis

Like, in this case, we will take the combination of these two aspects. So, in that case, results are sensitive since the threshold line partly passes through the area of sensitivity, which we have highlighted in the grey box, indicating the inefficiency of one-way analysis.

The limitations of sensitivity analysis using plausible range methods are here. Their basis for selecting upper and lower ranges is unclear and not testable. To solve this, probability sensitivity analysis using decision analysis is required. It regards base-case value as a point estimate of cost-effectiveness and uses sensitivity analysis to provide interval estimates or confidence intervals.

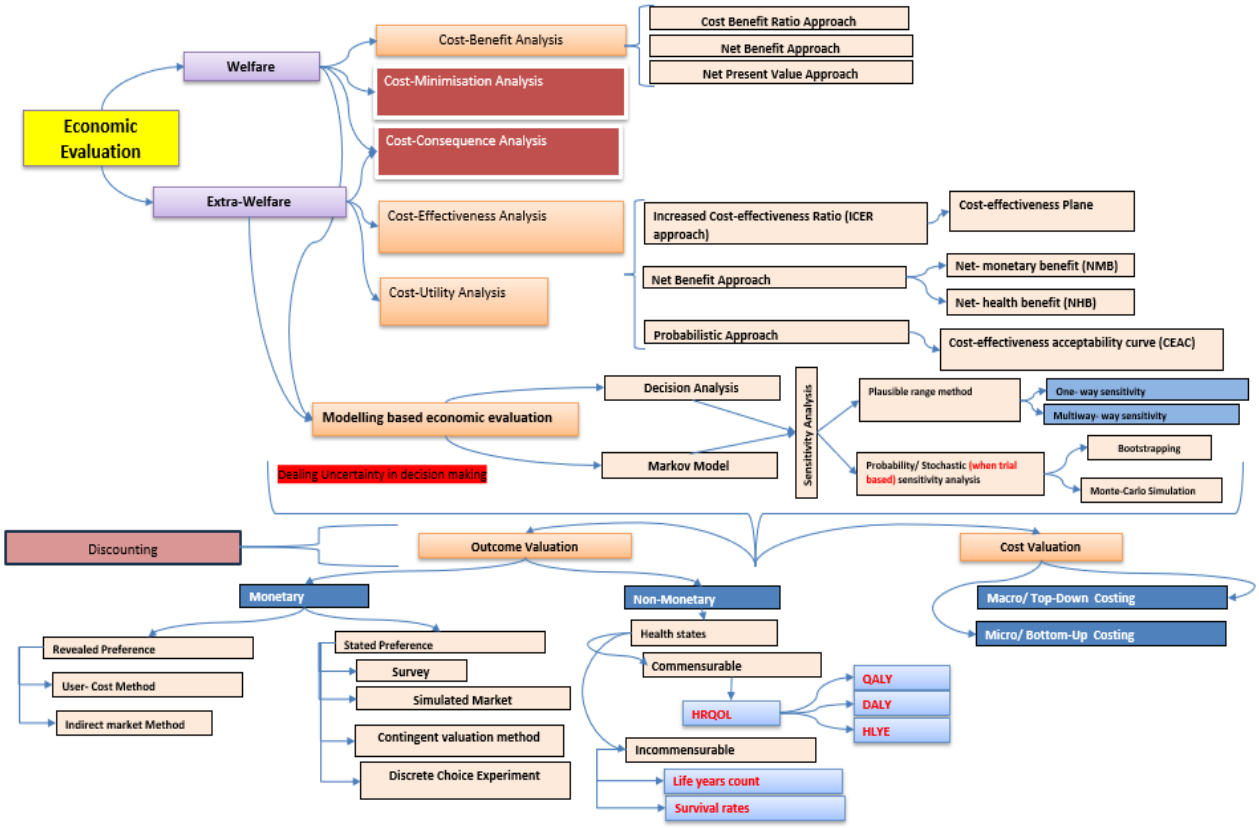
Probability sensitivity analysis is also called stochastic cost-effectiveness analysis when it is part of a trial-based analysis like RCT (Randomized Control Trial). Here, we use methods, such as 'bootstrapping', where the CER distribution is generated by repeated sampling from the data. In the context of modeling, Monte Carlo simulation is also useful, where a distribution is assumed for each of the parameters, and sample is taken for those parameters to calculate CER. When it is repeated many times, this generates an empirical distribution of CERS.

There are challenges with the stochastic sensitivity analysis, such as the fact that it is possible to include both positive and negative values of CER, making no sense to include them in the same confidence interval.

To solve this, NBA, that is, the net benefit approach (which we discuss in lecture number 8.4), and cost-effectiveness acceptability curve, that is CEAC (introduced in lecture number 8.6) are used. Both are based on a critical ceiling ratio or threshold, defining the cost-effectiveness that a treatment must achieve to be acceptable.

Note that, the NBA gives a single number instead of ratio, and is more straightforward to compute the confidence interval of this CER. Whereas, CEAC (cost-effectiveness acceptability curve) retains CER, but replaces the concept of confidence interval, which enables the probability calculation that a treatment is acceptable given a ceiling ratio plotted against its probability.

We have discussed so many directions in the entire sections on economic evaluation and healthcare. These are all the schematic presentation or the systematic presentation of our two units on economic evaluation and healthcare:-



We discussed all possibilities such as- welfarism and extra-welfarism cases. We discussed about their different approaches. Today, we just touched on the Markov model, then sensitivity analysis, etc. So, these are mentioned here, and you can just follow them on your own, I am sure.

Even, just to mention that we discussed about QALY, DALY, HLYE, etc. So please follow this, and if you are still somewhere stuck, please do not hesitate. We are trying our best to clarify in the query lecture. So, in the next lecture, we will introduce you to efficiency analysis in healthcare. The entire week is coming-up with efficiency, productivity, and efficiency analysis in healthcare.

Here are the readings. I think it will be useful, if you are gearing up for taking up the research. So, that is all for today. Thank you.