Ry Hafez Hamam.

The use of decision analysis in economic evaluation.

Dr. Rimal Mousa Dr. Eman Hammad

THANKS FOR DANIA AL-HALHOULI, MARAH JEHAD ALI FOR COLLABORATION IN THE LECT WITH THE DOCTOR

Learning outcomes

By the end of this lecture you will be expected :

- To understand the use of modeling as a decision tool in health economics
- To learn about the decision tree
- To learn about Markov model

Us still for the cange & outcome to decrease complications for eg to the chronic chiscases Types of economic evaluation based on the Resource Cost data source (Pros and cons)

- Economic evaluation (EE) alongside observational study study) Stong
 - Enhance the generalisability to clinical practice (External validity) مرابط صرابيل
 - Prone for selection bias
 - TATUNAN Applicable if all the key parameters can be obtained from one source

Economic evaluation alongside randomised controlled trial (RCT)

genializEstimate total cost sand outcomes from one data source (RCT)

- Provide a robust source of data (internal validity)
- Inapplicable to clinical practice (due to the controlled condition during practice conducting the trial)
 - Applicable if all the key parameters can be obtained from one source

Predict from short to long torm (short (Jul)

- - Combining data from different resources when model parameters, i.e. transition probabilities, treatment effect, utility can not be obtained from one data source
 - Extrapolate beyond the time horizon of the trial in order to capture all the events and cost associated with different options especially in chronic diseases.

(Hat in Future) COST 1 vis Age 1 Qis in future

You must nut think in short term, ball on price / eg: Insulin (glargine ve nph) def high hypergravenia Stere bigh hypergraveni Stere bigh hyper

- Mathematical modelling has been used widely in economic evaluations.
- A model is any mathematical structure that simplifies reality to a level that describes the essential consequences and complications of different options for decision-making.
- Decision analysis is a form of modelling. It is a systematic approach to decision-making under conditions of uncertainty

Process of conducting a decision analysis

Identify and structure the research question, and defining the most appropriate model

Identify and obtain cost and clinical evidence

Incremental economic analysis

Sensitivity analysis

Present the results

Identify and structure the research question

- P: Characteristics of the population
- I: Intervention
- C: Comparators
- O: Input and output of the alternatives
- Perspective: Societal/ Provider/Payer
- Time horizon: is the duration over which health outcomes and costs are calculated.

Identify the most appropriate model

- Once the question has been defined, it is also important to define the appropriate type of model to answer this question
- Model should reflect the possible treatment pathways of the disease, i.e. different treatments and subsequent events, therefore final outcome is also important to assess
- Model should balance between representing reality and complexity
 - Reality: reflecting possible events and pathways
 - Complexity: avoid complicating the model, and render it difficult to compute

 Types of decision analytical model دبت العالي العالي المعادين الرول كلما افترامن Cohort model (المودل كلما افترامن) Cohort model (المودل كلما افترامن) Simulating the expected costs an outcomes for a group of patients who share similar characteristics through the model simultaneously (Markov model and decision tree) (Markov model and decision with DH2, ages Avg 70, 50, 50, 50, Patient-level simulation model Simulating the expected costs an outcomes for each patient individually (including discrete event simulation (DES)) (will not covered in this course) لحال

Clinical and economic evidence

- Once the model has been designed, it is also important to identify the clinical and economic outcome needed to populate the model
 These data including
 - Effectiveness
 - Utility
 - Resource use

Either collected alongside RCTs and observational studies, i.e. **Primary** economic evaluation

or collected from published literature from different source, i.e.
Secondary economic evaluation (economic modelling)
Secondary illestre

 Economic & clinical information preferably from RCTs or good observational studies since they provide the robust source of evidence
 However, it is inapplicable to collect all the data from one source, therefore most commonly using modelling to collect data from different sources

Incremental cost analysis

• The cost and outcome collected for each alternative are used to generate the ICER (Base case analysis)

Sensitivity analysis

- As previously mentioned, base case analysis is not enough to determine whether the study conclusion is robust or not
 - It is also important to define whether the conclusion is robust for change in the data source estimate and assumptions

Decision tree (to preduct in the long vin) • Simplast to a

- Simplest type of economic model
- It can be used to reflect the treatment pathways for disease with short time horizon

Decision Tree

- Consist of five components (Se Next Slike)
 - Starting point: define the population
 - Alternatives: defines the intervention and comparator

 - Chance nodes **O**: The probabilities of outcomes to occur (all events 'probabilities stemmed from the same chance node should be summed to one)
 - Probabilities are restricted from zero to one
 - Terminal node : represents the final outcome



Starting Point: Patient diagnosed with MDD (Major depressive disorder)

Alternatives: **TCA and SSRI (Tricyclic antidepressant vs selective serotonin** reuptake inhibitors)

Decision Node: SSRI or TCA [policy decision]

Chance Nodes: Withdrawal due to intolerance Withdrawal due to lack of efficacy Relapse of MDD symptoms

Final Outcome/Time Horizon: **one year**

Successfully treated patient: Drug effective as episodic treatment and no relapse or hospital admission in 1st year

Limitation



- Unsuitable to model chronic disease with recurrent events
 - Become very bushy to analyze
 - Allow one-way progression of the patients through the model, does not allow movement back and forth between disease state









The expected value (EV) for each strategy (from decision node is the sum of products of the estimates of probability of events and their outcomes (payoff)

Example of decision tree for cancer screening for cally detect Probabilities

Parameter	Base case	Low	High
Sensitivity	0.829	0.744	0.897
Specificity	0.855	0.839	0.901
Prevalence	0.004	0.002	0.006



Payoffs

Outcome	Cost	Utility
True positive	£4974	0.48
False negative	£9108	0.45
False positive	£96	0.79
True negative	£12	0.94
Cancer	£9096	0.48
No cancer	£0	0.89



Example cont ...

Cost Effectiveness Analysis

Strategy	Cost	Incr Cost	Effect	Incr Effect	C/E	ICER	
No screening	£36.38		0.8882		£41		
Screening	£47	£10.42	0.9165	0.0281	£51	£370/10	hy
امممم ح إذا اقل: <u>E</u>	الح (م) معرفة العلي ا منه أو أعلى ا	J Mare (1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1) 1)	معنی میں المیں زشوبف المل	<u>(</u> E? U (Strue	۵۵ * ۲۹) بسبب اری ن	المعام المعام المعام المعام 1933	کل سنا الت

Markov model ((hech /21)

- Markov simulate the natural history of the chronic disease where multiple events could occur during the clinical course of the disease.
 - Example: Patients diagnosed with early stage breast cancer could experience different events during their clinical course (treatment pathways) following receiving the surgical treatment such as remaining disease free, having recurrence, or death. These multiple recurrent events are best represented by Markov model
- It comprise a set of infinite health states where group of patients (Markov cohort) can be only in one health state during a given time interval (cycle)

Steps to construct a Markov model

- Identify the structure of the model by defining the health states (depending on by full hang)
- Identify the starting probabilities
- Determine the transition probabilities
- Decide the cycle length
- Set the time horizon and stopping rule
- Assign, life year gained, cost, and utilities for each health state
- Discounting
- Incremental analysis
- Sensitivity analysis

Selecting health states

- Mutually exclusive (patients cannot be in more than one health states in the same time)
- Represent the most clinically and economically important events during the clinical course of the disease
- Separate states are required to represent any difference in prognosis, utility or cost
- Death is the absorbing state (i.e. once the individuals are in this health state, they remain in it)

Continue

- Health states are represented by oval
- Arrows represent the transition from one state to another
- Arrows pointing back in the state from which it begin represent patients remaining in the health states for more than one cycle
- Patients transit from one health states to another based on certain probabilities (transition probabilities)



• What are the possible transition?

- Disease free to disease free, recurrence and death
- Recurrence to recurrence, disease free, or death

Transition probabilities

- Determine how patients move from one state to another state
- Transition probabilities for each state must sum to one
 - For example: probabilities of transition from disease free to disease free, recurrence, and death should sum to one.
- Probabilities derived from data source or published literature

For example: A patient is disease free after a cancer surgery But it is expected for that the cancer will recur (come back or recurrence) after 2 years or more So how long is the cycle length? ~2 years.

all the boxes written in this page are clarifications from From Dania 🙏

For eg: 20% represents the transition probability of changing from one health sate to another But this change happens or transition happens

aninimum amount of time needed to leave a certain health state and go to another is called the cycle length

- Represent the minimum amount of time the patients will spend in a state before transition to another state
- Determination of cycle length depend on the frequency of event
 - For example: one year cycle used for patients with low frequency clinical events, 1 month can be used for disease with high frequency clinical events
- Cycle length remain fixed during the model period
- Each cycle require annual transition probabilities, cost, and utilities
- Cycle length should be short enough to represent the frequency of clinical events Sto not Underestimate

Stopping rules

- The model keep running (for several cycles) for the period of time horizon
- If the model contain an absorbing state (death), the model is run until all patients reach the absorbing state
- Majorities of the chronic disease were run for the life expectancy of the patients or until 99% of the cohort died
- Time horizon should be long enough to capture all the long term clinical outcomes and costs

الدكتون وقعت المحاضة لمين بجوز الس معادة فوت الو شرعت منسبيًا في ورعة العل من Assigning costs and outcomes

- Markov models are run through a cycle of series
- Each health state associated with certain cost, outcome and utilities and those are weighted by the transition probabilities within each cycle (proportion of patients transiting to each health state within an one-year time), and then summed up across all the heath states to derive the aggregated costs and QALYs in a yearly cycle.
- The mean costs and QALYs were continuously calculated in each yearly cycle until a terminating condition is met (99% of patients died).

Discounting

Discounting for costs and outcomes occur within each cycle

Markov model: Simple example

- Stroke prevention model
 - Atrial fibrillation is a chronic heart arrhythmia which increases the risk of stroke (ischaemic)
 - Therapy available to reduce the risk of stroke e.g. warfarin
 - Disabling stroke incurs costs over a long period of time and reduces quality of life
 - A Markov model is designed to evaluate the costeffectiveness of treatments to prevent stroke in AF
 - Following example will concentrate on model structure

Markov states

- Patients are classified in one of three states
 - Well with atrial fibrillation (AF) (Health state 1)
 - Disabled from stroke (Health state 2)
 - Dead (Health state 3)

Stroke prevention: Markov states



Define transition probabilities

Transitions From time t to time t+1	Well (1)	Stroke (2)	Dead (3)
Well (1)	P11 (=1-P12-P13=0.92)	P12=0.07	P13=0.01
Stroke (2)	0	P22 (=1-P23=0.75)	P23=0.25
Dead (3)	0	0	1

Attach costs and utilities to states

Each health state has a cost and utility attached

Markov state	Cost	Utility
Well, AF	£150	1
(on treatment)		
Disabling stroke	£10,000	0.40
Death	0	0

Stroke prevention: cohort analysis

Cycle	Well, AF	Disabled stroke	Dead	Total
Start	1000	0	0	1000
1	920	70	10	
	(1000 x 0.92)	(1000 x 0.07)	(1000 x 0.01)	1000
2	846	117	37	1000
		(920 x 0 07) +	$10+(920 \times 0.01)+$	1000
	(920 x 0.92)	(70 x 0.75)	(70 x 0.25)	
3	778	147	75	1000
	(846 x 0.92)	(846 x 0.07) + (117 x 0.75)	37+ (846 x 0.01) + (117 x 0.25)	
4	716	165	119	
	(778x 0.92)	(778 x 0.07) + (147 x 0.75)	75+ (778 x 0.01) + (147 x 0.25)	1000

	Cycle	Well, AF	Disabled stroke	Dead	Total cost
S S S S S S S S S S S S S S S S S S S	Start	1 (1*150)	0	0	150
	1	138 (0.92*150)	700 (0.07*10000)	0 (0.01*0)	838
	2	126 (0.84*150)	1170 (0.117*10000)	0 (0.037*0)	1296
	3	117 (0.778*150)	1470 (0.147*10000)	0 (0.075*0)	1587
	4	107 (0.716*150)	1650 (0.165*10000)	0 (0.119*0)	1757

Limitations of Markov models

- Memoryless of feature of Markov model (Not account taken for history)
 - The transition probabilities of patients depend only on the current health state and not on the previous health state
 - May overcome these limitations by using a larger number of states
- Assumes uniform population and equal and constant risk (
 - Did not consider variation between individuals
- Alternatively use other methods (Individual sampling models, discrete event simulation)

Decision tree versus Markov model

Model type	General description	Type of decision best suited for
Decision tree	Diagram the risk of events and health state over a fixed time horizon	Intervention for which the relevant time horizon is short and fixed
Markov model	Simulate a hypothetical cohort of individuals through a set of health state overtime	Modelling interventions for diseases or conditions that involve risk over a longtime horizon and/or recurrent events

Summary

- Economic evaluation based on decision modeling is most commonly used in decision maker since it allows combining data from different source and extrapolation behind time horizon
- Markov model has an advantage over the decision tree in that it allows modelling chronic disease with recurrent events