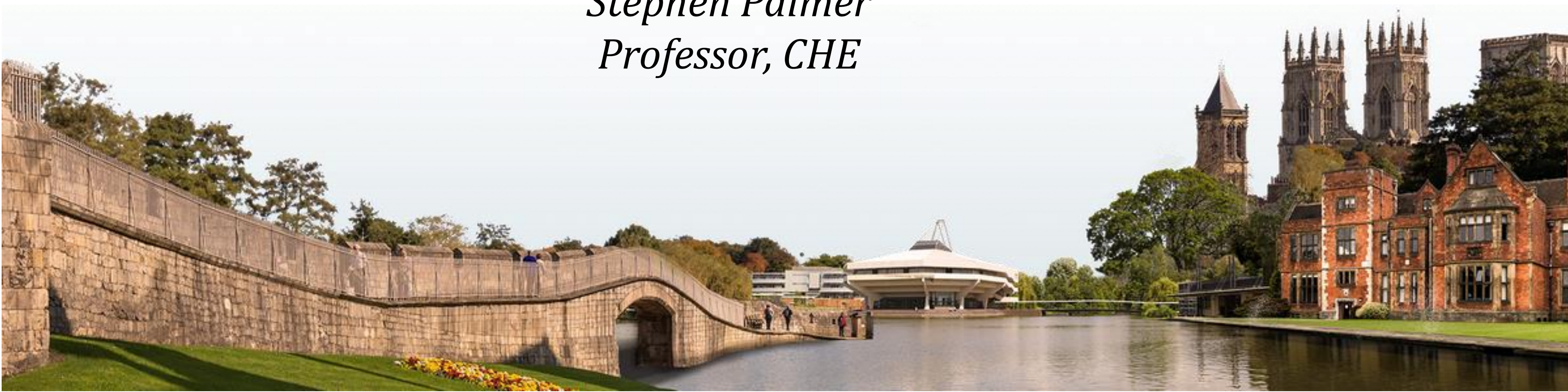
UNIVERSITY of York RESEARCH

CHE Centre For Health Economics

Online Advanced Methods for Cost-Effectiveness Analysis

Presentation 6: Model structure
6.3: Decision trees and Markov models

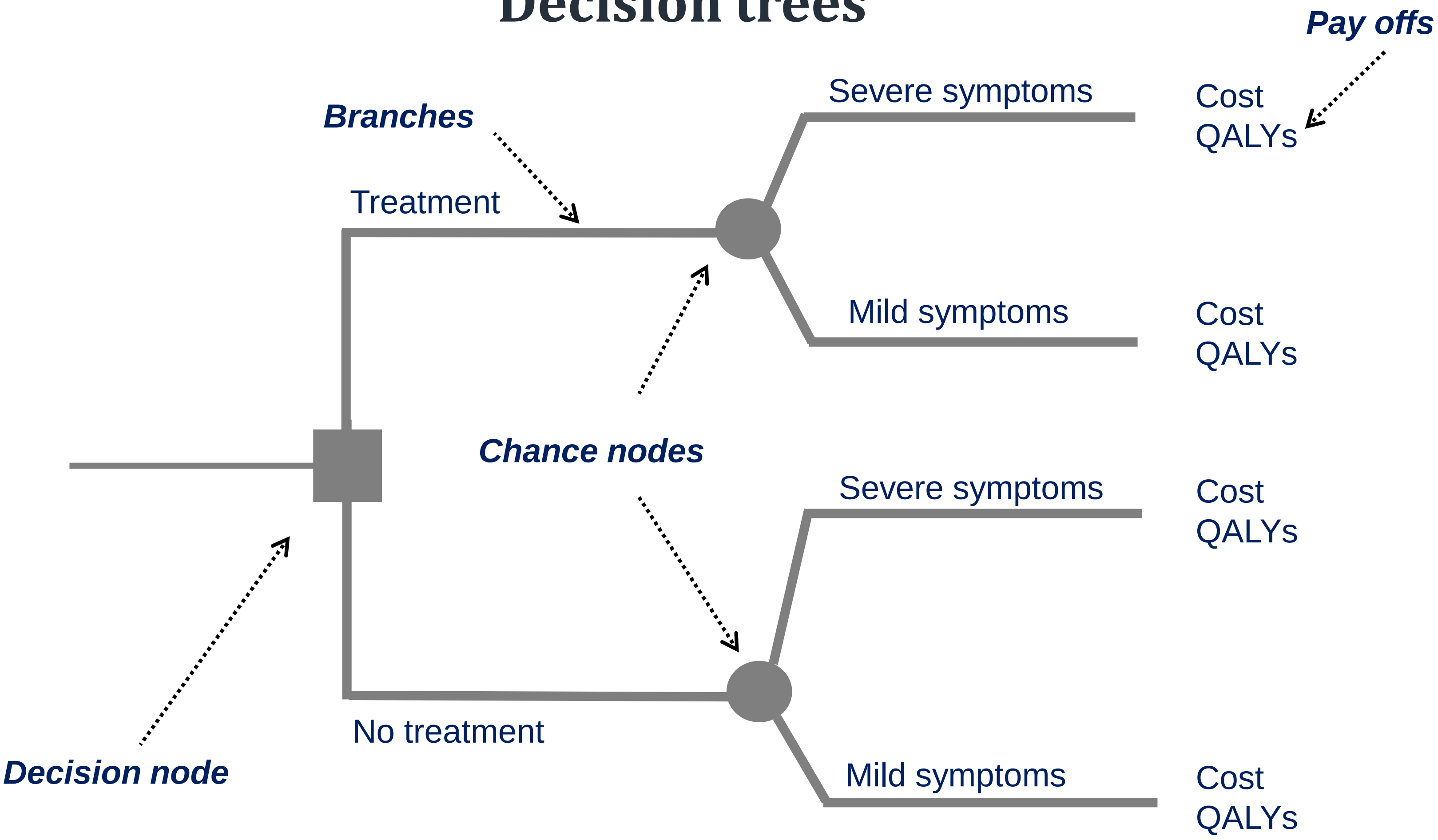
Stephen Palmer
Professor, CHE



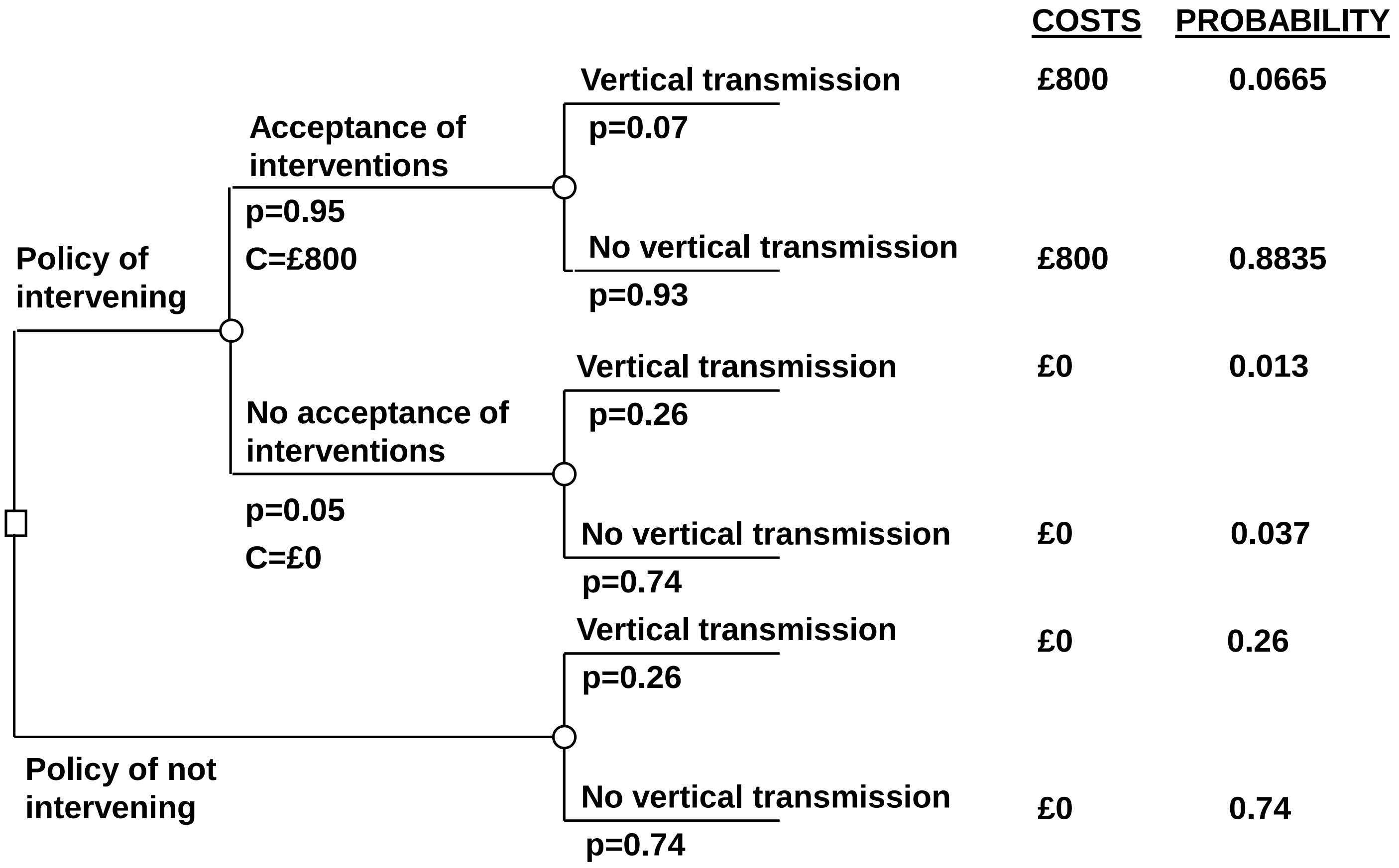
Objectives

- Understand key features of the most common model types
  - Decision trees
  - Markov models
- Appreciate how to evaluate models and the use of cohort simulation
- Explore alternatives ways that Markov models can be used

Decision trees



Example of prevention of vertical transmission of HIV



Adapted from Ratcliffe *et al. AIDS* 1998; 12: 1381-1388

Incremental cost per HIV-infected child avoided

Intervention:

Expected cost: 0.95 x £800 = £760

Risk of vertical transmission:

0.0665 (0.95 x 0.07) + 0.013 (0.05 x 0.26) = 0.0795

No intervention:

Expected cost: £0

Risk of vertical transmission: 0.26

Incremental cost of interventions per HIV-infected child avoided:

$$\frac{\textbf{Differential cost :}\ 760 - 0 = 760}{\textbf{Differential risk :}\ 0.26 - 0.0795 = 0.1805} = £4{,}211$$

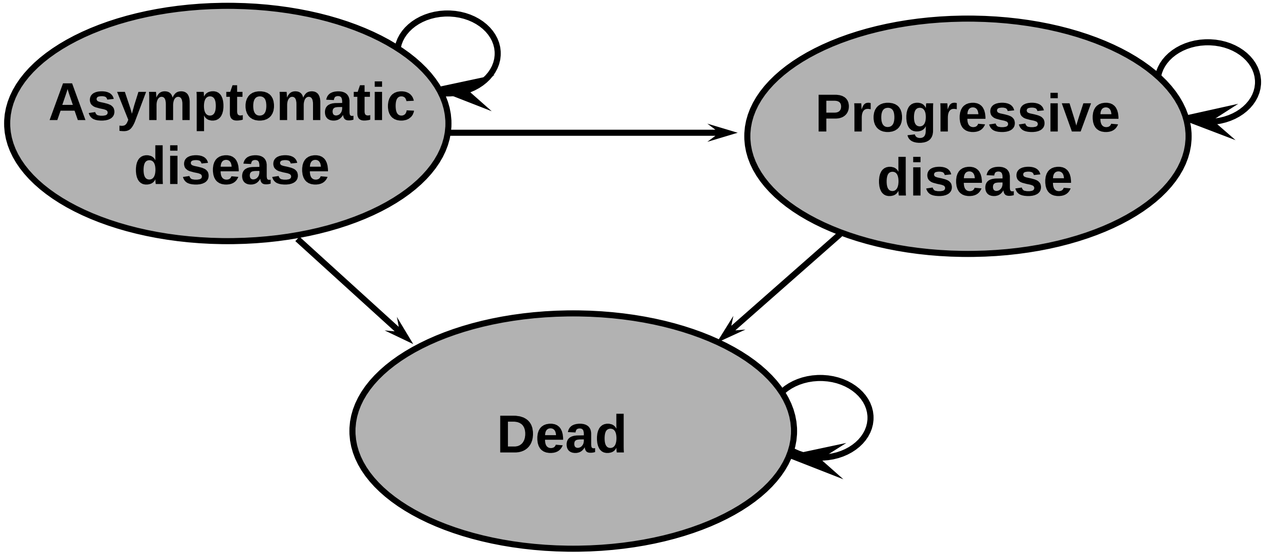
Limitations of the decision tree

- Frequent need to model prognosis
- Decision trees: sequence of events over a particular time period
- Inflexible when events recur over time
- Particular difficulty in modelling chronic diseases: complications, recurrence, remission, mortality
- Decision trees may become excessively ‘bushy’

State-Transition Models – Key Features

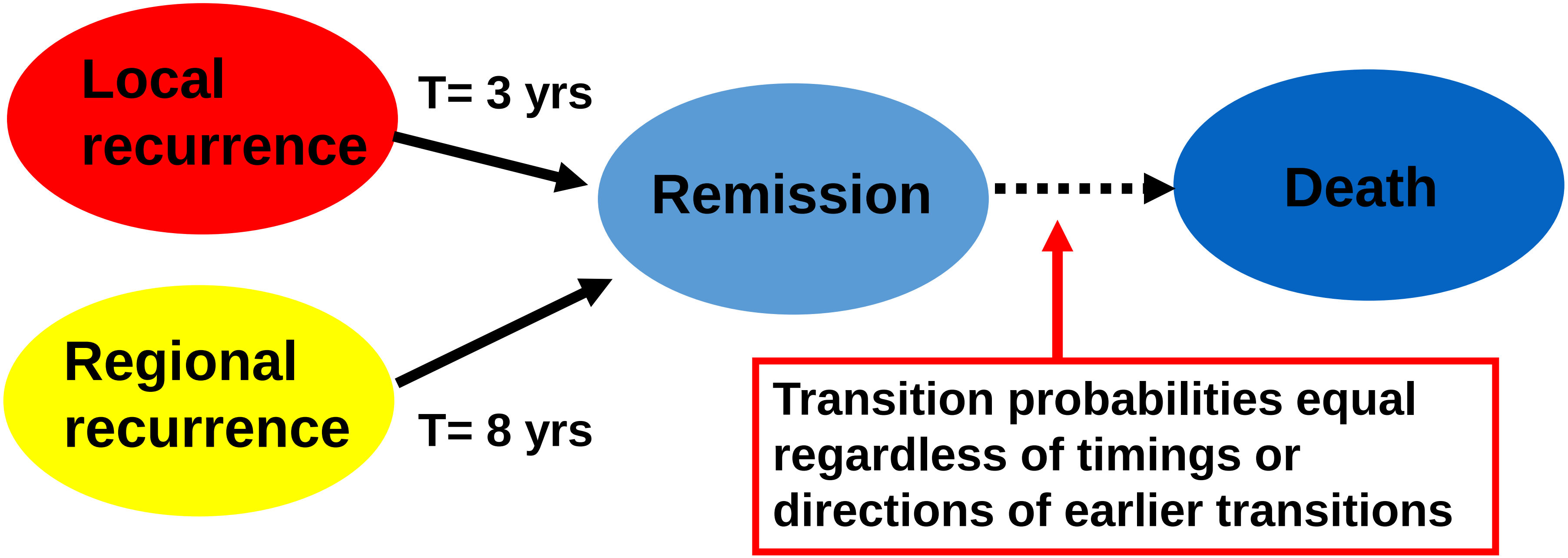
- Simplification of ‘bushy’ decision trees
- Organised around states rather than pathways
  - How individuals move among states (transitions)
  - How likely such moves are (transition probabilities)
- States are mutually exclusive and exhaustive
- Cycle length specifies transition intervals
- State values (costs and health outcomes) assigned
- Most common types:
  - Markov models
  - Area under the curve (AUC) models

The basic Markov chain



	Transition to:		
Transition from:	Asymptomatic	Progressive	Dead
Asymptomatic	0.6	0.3	0.1
Progressive	0	0.8	0.2
Dead	0	0	1

The Markov assumption



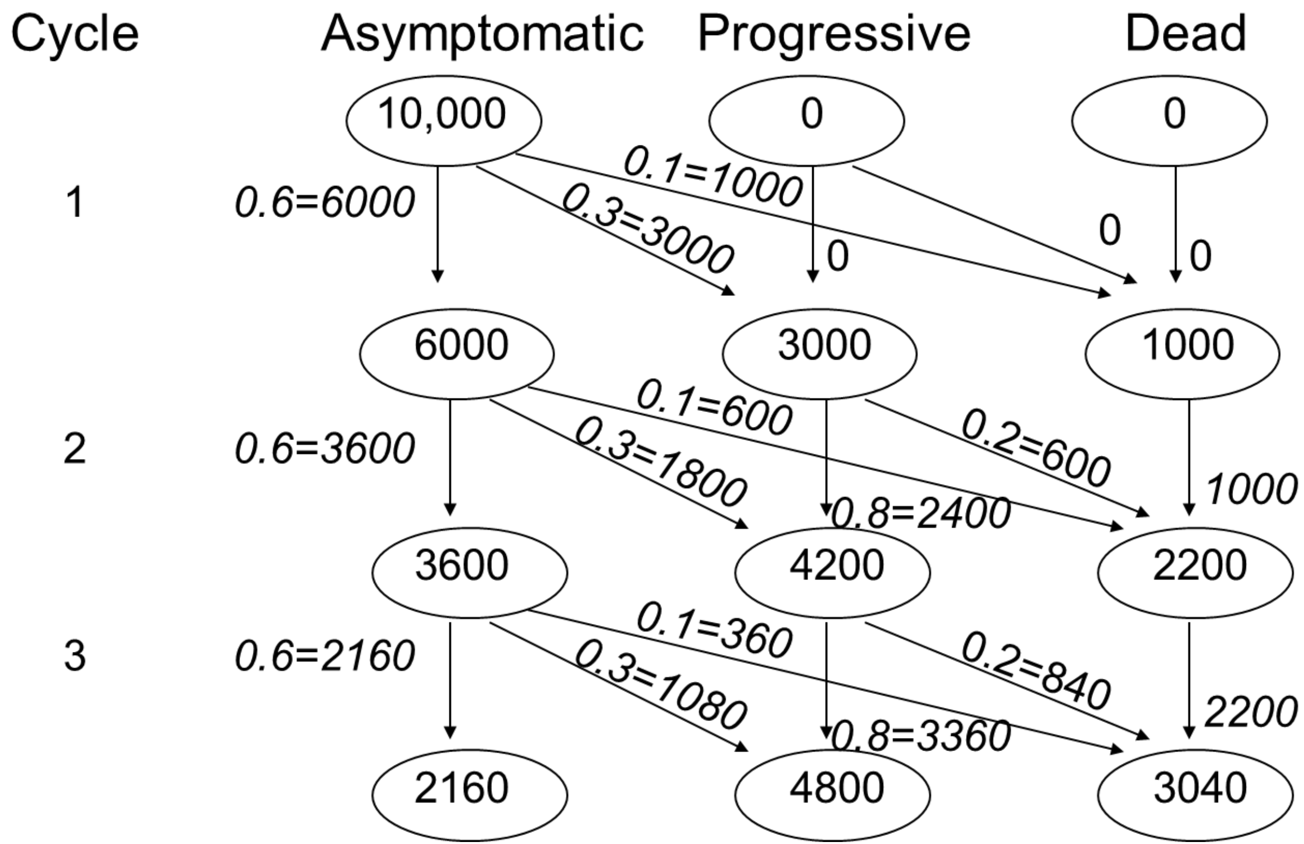
Evaluating Markov chains

- Matrix solution
  - Not possible with discounting
- Cohort simulation
- Individual patient simulation (1st order Monte-Carlo simulation)

Cohort simulation

- Simulates a cohort moving through a model
- A proportion of the cohort in each state/passing down a pathway at a given point in time
- Expected values worked out by weighting these proportions by costs/outcome values
- Focus on expected values: size of cohort irrelevant

Cohort simulation
The concept



Cohort simulation
Calculating expected costs

Cycle no.	Numbers in state (total 1000)			Costs	
	Asymptomatic	Progressive	Dead	Per cycle	Cumulative
0	1000				
1	600	300	100	£30,000	£30,000
2	360	420	220	£42,000	£72,000
3	216	444	340	£44,400	£116,400
4	130	420	450	£42,000	£158,400
5	78	375	547	£37,488	£195,888
6	47	323	630	£32,323	£228,211
7	28	273	699	£27,258	£255,469
8	17	226	757	£22,646	£278,116
9	10	186	804	£18,621	£296,737
10	6	152	842	£15,199	£311,936
11	4	123	873	£12,341	£324,277
12	2	100	898	£9,981	£334,258
13	1	81	918	£8,050	£342,309
14	1	65	934	£6,480	£348,788
15	0	52	947	£5,207	£353,995
16	0	42	958	£4,180	£358,175
17	0	34	966	£3,352	£361,527
18	0	27	973	£2,687	£364,214
19	0	22	978	£2,153	£366,367
20	0	17	983	£1,724	£368,091
21	0	14	986	£1,380	£369,471
22	0	11	989	£1,105	£370,576
23	0	9	991	£884	£371,460
24	0	7	993	£708	£372,168
Expected cost/patient over 24 cycles = £372,168 /1000 = £372.17					

<u>Cost assumptions/cycle</u>

Asymptomatic: £0

Progressive: £100

Dead: £0

Correctly estimating transition probabilities (TPs)

- TPs should be estimated to reflect the cycle length. This can be estimated using the rate (*r*) of the event
- Conversion of probability (*p*) to *r* when *p* is reported for time t_{rep}

$$r = -\frac{\ln(1-p)}{t_{rep}}$$

- Conversion of resulting rate to probability for cycle length, *l*

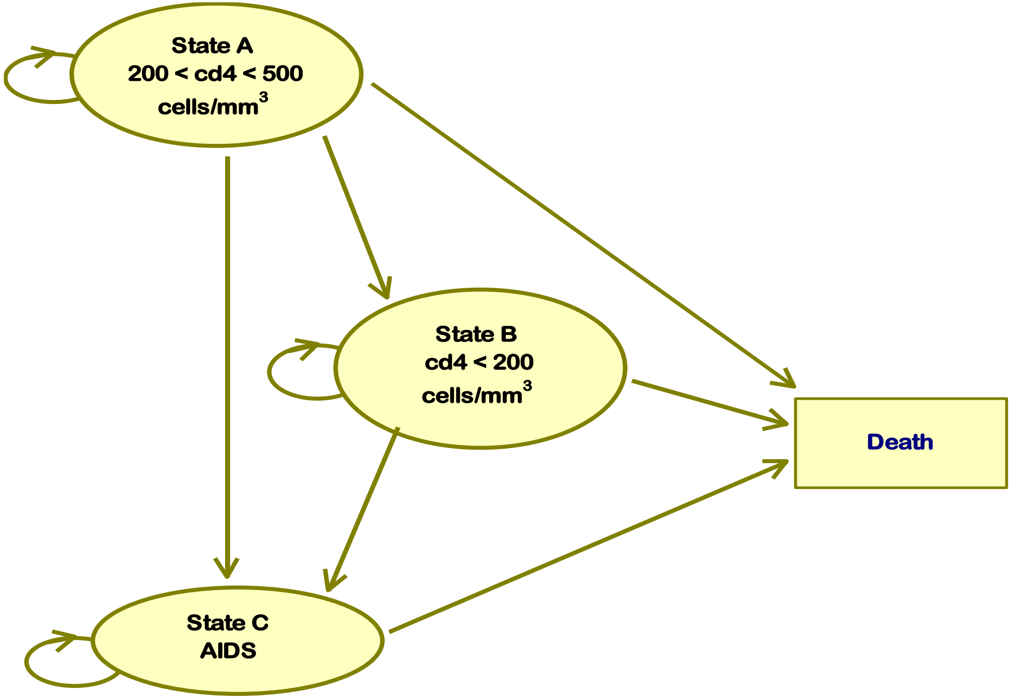
$$p = 1 - \exp(-r.l)$$

- Example: convert 5 year probability of 20% to a 1 year probability
  - Rate = $-\frac{\ln(1-0.20)}{5} = 0.04463$
  - 1-year probability = $1 - \exp(-0.04463\ x\ 1)$ = 0.043648

Uses of Markov models

- Estimating costs and effects for comparative interventions
  - Two sets of transition probabilities
  - Often applying a relative treatment effect to baseline transitions
- Extrapolation from trial results assuming no continued treatment effect
  - Trial estimate of treatment effect, Markov estimates the implications
  - Could be decision tree to estimate the effect (e.g. screening)

Example of Markov used for direct comparison
Model structure



Source: Chancellor *et al. PharmacoEconomics* 1997; 12: 54-66

Example of Markov used for direct comparison
Baseline transition probabilities

(a) Transition probabilities - monotherapy

	Transition to:			
Transition from:	State A	State B	State C	State D
State A	0.721	0.202	0.067	0.01
State B	0	0.581	0.407	0.012
State C	0	0	0.75	0.25
State D	0	0	0	1

Assumed a relative effect of combination therapy of 0.509. This was assumed to slow progression between all states. It was applied by reducing the yearly transitions to all worse states

Source: Chancellor *et al. PharmacoEconomics* 1997; 12: 54-66

Example of Markov used for direct comparison

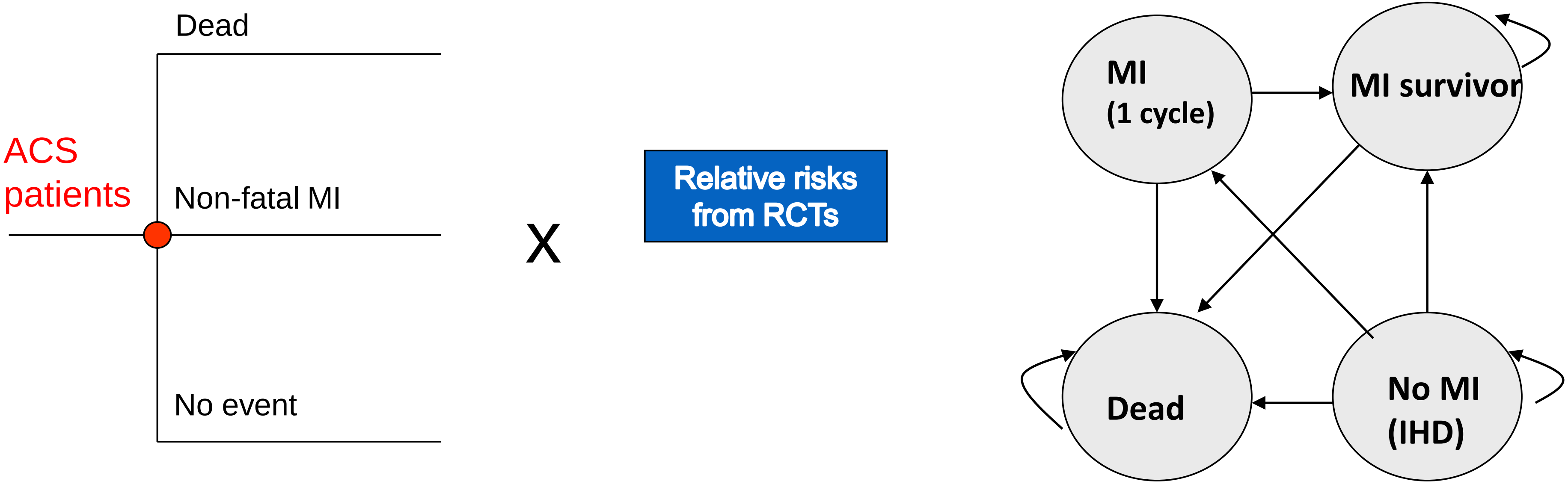
Applying the treatment effect

(b) Transition probabilities – combination therapy

	Transition to:			
Transition from:	State A	State B	State C	State D
State A	0.858 (1-sum)	0.103 (0.202 x RR)	0.034 (0.067 x RR)	0.005 (0.01 x RR)
State B	0	0.787 (1-sum)	0.207 (0.407 x RR)	0.006 (0.012 x RR)
State C	0	0	0.873 (1-sum)	0.127 (0.25 x RR)
State D	0	0	0	1

Source: Chancellor *et al. PharmacoEconomics* 1997; 12: 54-66

Markov models for extrapolation



Part 1: Baseline event rates

- Observational data from PRAIS-UK (n=1046) and Leeds (n=112)
- Costs of drugs, hospitalisation and procedures

Part 2: GPA effects

- Data from meta-analysis of RCTs

Part 3: lifetime extrapolation

- Observational data from Nottingham Heart Attack Register (n=1279)
- Costs of hospitalisation and procedures

Source: Palmer *et al. Technology Assessment Report for NICE*, 2002

Summary

- Decision trees simplest but least flexible approach
  - Useful in specific circumstances e.g. acute one-off treatments
  - Can be combined with other model types
- Markov models most common approach
  - Increased flexibility
  - Basic Markov chain can be limiting in some circumstances
  - Some forms of time dependency can be incorporated
- Markov models can be used in different ways
  - Direct comparisons
  - Extrapolation