
Decision Analysis – Markov Modeling

Parts 7 and 8

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Markov Modeling and Disease Simulation

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Outline

- Markov modeling
- Monte Carlo simulation
- Discrete event simulation
- Disease transmission models

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Disease models

- Why do we need to model long term disease progression?
 - many interventions (particularly pharmaceuticals) target chronic diseases that progress over decades
 - long-term costs and outcomes are important for CEA and HTA
 - long-term follow-up data on cost and outcomes often are lacking

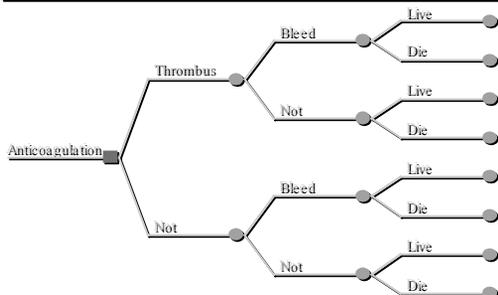
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How might we do this?

- Use decision analysis
 - include branches for relevant health outcomes over, say, 1 year
 - Add branches for outcomes at each subsequent year
 - Use probabilities that reflect 1-year timeframe

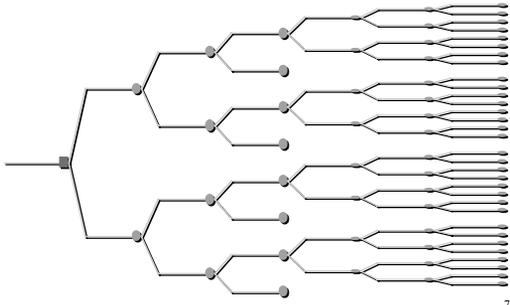
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Tree year 1

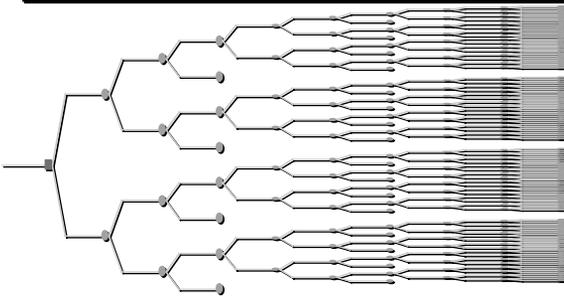


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Tree years 1-2



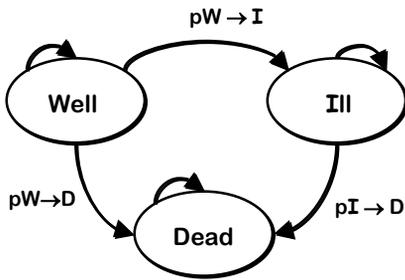
uh oh...



A solution: Markov modeling

- Define health states
- Determine allowed (logical) transitions between health states
- Determine transition probabilities between health states over a given period of time (cycle)
- "Run" model over multiple cycles

A Markov Model



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Who is Markov?

- Chekov's brother from Star Trek

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Origins

- Motivation for developing method
- Areas where Markov models are used
 - Information theory
 - Speech recognition software
 - DNA sequence matching (Hidden Markov Models, HMM)

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When?

- Use Markov Model when
 - transitions into and out of health states are possible, e.g. recurrence of events
 - modeling a complex disease
 - probabilities vary over time
 - the timeframe of the analysis is lengthy
 - a decision tree would become too complex

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Types of Markov Models

- Markov chain
 - Defined by **non-time varying** probabilities
 - Solution can be derived analytically using matrix algebra
- Markov Process
 - Uses **time-varying** probabilities
 - Solution requires calculation at each cycle

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How?

- 1) Define mutually exclusive health states
- 2) Determine “allowed” transitions (must sum to 1.0 for each health state)
- 3) Derive transition probabilities
- 4) Calculate outcomes for each cycle

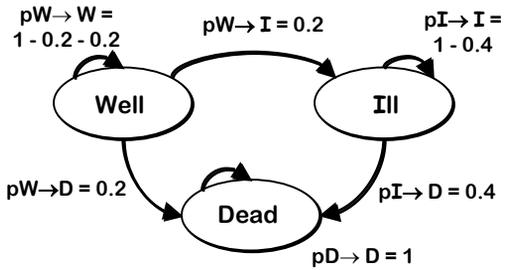
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Markov Chain: Example

- Three mutually exclusive health states:
 - Alive, Ill, Dead
- There are n^2 transitions where $n = \#$ of health states

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Transitions



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P Matrix

		To		
		Well	Ill	Dead
From	Well	0.6	0.2	0.2
	Ill	0	0.6	0.4
	Dead	0	0	1

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Matrix solution

- Fundamental matrix solution provides exact values for the time spent in each health state
 - see Beck and Pauker, Med Dec Making 1983;4:419 for matrix calculations
- Because of requirement for constant probabilities, Markov Chains are very rarely used in medical applications

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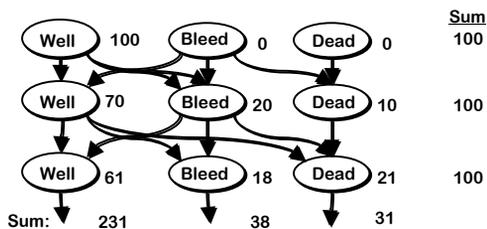
Markov Process

- Similar idea to Markov Chain, but probabilities vary over time, and time spent in each health state must be calculated at each cycle

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Markov Process: Example

$p_{W \rightarrow B} = 0.2$, $p_{W \rightarrow D} = 0.1$, $p_{B \rightarrow W} = 0.6$, $p_{B \rightarrow D} = 0.2$
 $(p_{W \rightarrow W} = 0.7, p_{B \rightarrow B} = 0.2, p_{D \rightarrow D} = 1.0)$



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Terminal states

- Also referred to as an “absorbing state”
- The Markov Motel: Patients check in but they don’t check out
- In health care, usually the “Dead” state
- Allows models to be run until all patients have died - can then calculate life expectancies (sum time spent in alive states)

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Markovian Assumption

- The past does not matter
- I.e., this year’s transition probability does not depend on *last* year’s health state
- I.e., do not keep track of health states that have been visited

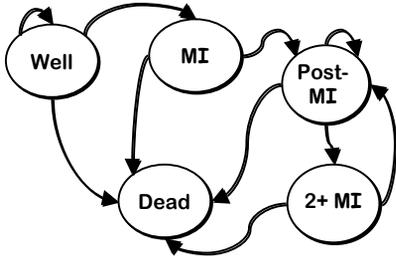
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Shortcomings due to Markovian Assumption

- A patient’s past history (which health states they were in during previous cycles) does not affect their future health
- Not realistic for many diseases

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But *can* account for disease history: add health states



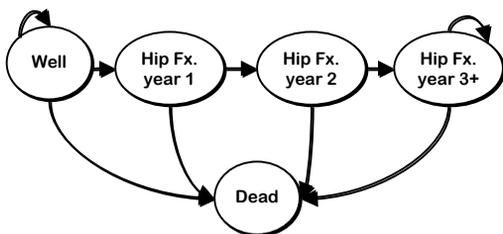
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Tunnel states

- Definition: patient cannot stay in a tunnel stay more than 1 cycle
- Useful for time-dependent probabilities
- Useful when time-dependent costs

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Tunnel states



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Deriving Transition Probabilities

- Usually obtained from the literature
- Often have data over, say 5 years, when you want to use 1 year cycles
- How do you derive a 1-year transition probability?

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Divide by 5?

- After 5 years, 50 out of 100 people are ill: $p(1 \text{ year}) = 0.10$?
 - end of year 1: 10 ill, 90 well
 - end of year 2: 19 ill, 81 well
 - end of year 3: 27 ill, 73 well
 - end of year 4: 34 ill, 66 well
 - end of year 5: 41 ill, 59 well

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Use formula

- $tp_1 = 1 - (1 - tp_t)^{1/t}$
- tp_1 is yearly transition probability
- tp_t is the overall probability over time t
- So,
 - $tp_1 = 1 - (1 - 0.50)^{1/5} = 0.129$

Can also incorporate discounting

- Apply formula to each year -> discounted costs, QALYS
- $V_0 = V_t / (1 + r)^t$
- V_0 is the net present value, V_t is the value at time t, and r is the discount rate

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Rates vs. Risk

- Many texts and articles give a formula for converting rates (over t years) into probabilities (over 1 year) [e.g. Pettiti, Sonnenberg and Beck, Beck and Pauker]
- $p = 1 - e^{-rt}$
- However, use of this formula is only appropriate when actual rates are given
- Serious errors can otherwise occur

Miller and Homan, Med Decis Making 1994;14:52

Rate vs. Risk

- A Rate is
 - events/(population time)
 - in a fixed cohort, a person's time after an event is *removed* from the denominator
- A Risk is
 - probability a person will experience an event over a given period of time
 - in a fixed cohort, a person's time is kept in the denominator
 - most clinical studies give us this

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Rate vs. Risk

- A Rate is
 - Hazard
 - Incidence density
 - Instantaneous risk
- A Risk is
 - probability
 - likelihood
 - cumulative incidence

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So

- Make sure you are using proper formula for converting risks or rates

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For complex situations, consider discrete event simulation

- Avoid Markov model with hundreds or more states
- Track history of every event that occurs to patient
- Probabilities, costs, utilities may depend on history
- Requires extensive programming

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Choosing an approach

Technique	Pros	Cons
Decision Analysis	Simple	Not inherently time dependent
Markov Models	Easier than DA for long timeframes	Difficult to obtain necessary data
Discrete event simulation	Accounts for previous history, detail	Time-consuming
Differential equations	Easier to model populations	Not detailed

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Diseases and models

Technique	Diseases
Decision Analysis	Acute: Infection
Markov Models	Chronic: HTN, hypercholesteremia
Discrete event simulation	Complex: AIDS
Differential equations	Population-based: Communicable diseases, e.g. TB, HIV

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In-class modelling

- Draw the structure of a Markov model that models Hepatitis C
- The following are the health states
 - Mild chronic hepatitis C (MCH)
 - Cirrhosis
 - Hepatocellular carcinoma
 - Ascites
 - Esophageal varices
 - Hepatic encephalopathy
 - Liver transplantation

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