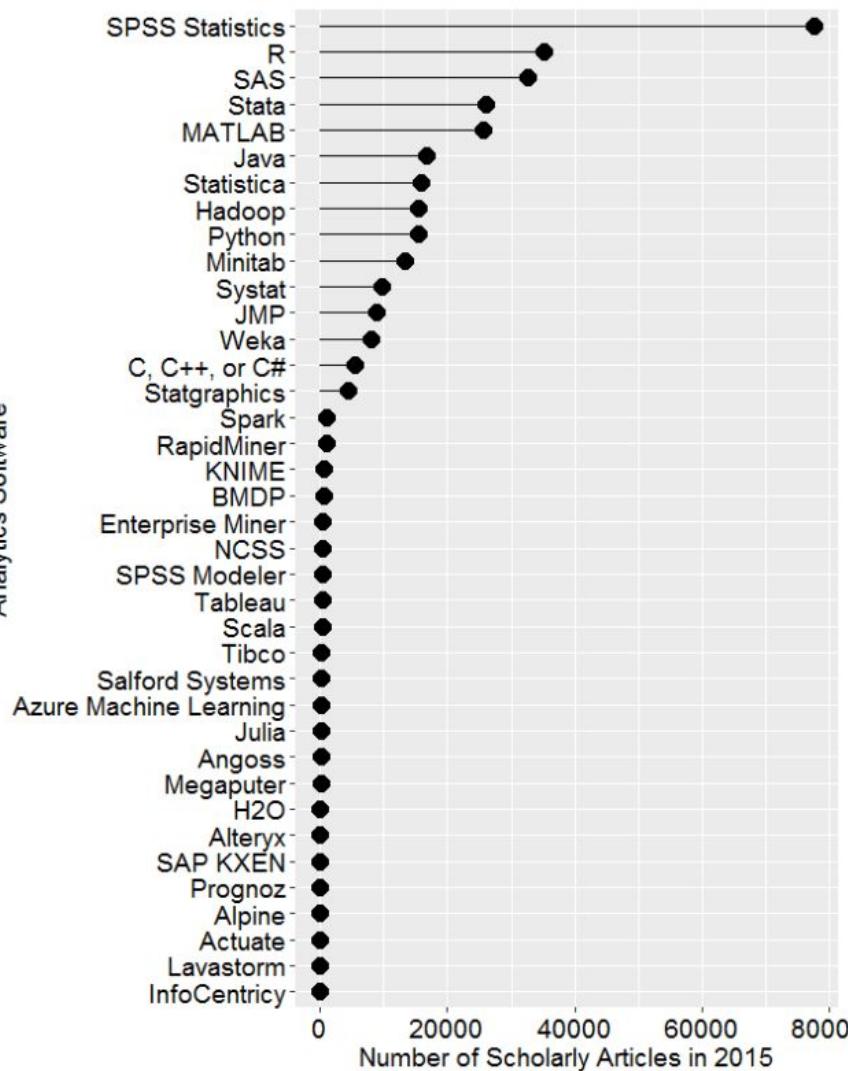


# Decision modeling in

...

Petros Pechlivanoglou, PhD

Canadian Centre for Health Economics,  
University Toronto ON  
October 13, 2017



# R Passes SAS ... in scholarly use

©<http://r4stats.com/2016/06/08/r-passes-sas-in-scholarly-use-finally/>



# Decision modeling software

## Three main approaches

- Specialized decision modeling software
  - TreeAge , Data, Crystal8, Arena etc
- Spreadsheet software
  - Microsoft Excel, Open/Libre Office
- Statistical/ Computer programing software
  - Matlab, R, C++, Python, WinBUGS, etc



# **REVIEW OF SOFTWARE FOR DECISION MODELLING.**

## DECISION SUPPORT UNIT

Jon Tosh and Allan Wailoo

Health Economics and Decision Science, School of Health and Related Research,  
University of Sheffield

**Table 1 - Software used for NICE Technology Appraisals**

Software	Respondents that used this software		Number of TAGs	Number of Manufacturers	Number of Consultancies
	n	%			
MS Excel	28	100%	6	14	8
TreeAge Pro	16	57%	6	7	3
WinBUGS	6	21%	1	2	3
R	5	18%	1	2	2
Arena	3	11%	0	2	1
SAS	3	11%	0	1	2
Crystal Ball	2	7%	1	0	1
Simu8	2	7%	1	0	1
STATA	1	4%	1	0	0
RevMAN	1	4%	1	0	0
Borland Delphi	1	4%	1	0	0
S-PLUS	1	4%	1	0	0
@risk	1	4%	0	0	1



# The Beginning : Medical Decision Making 2005

CLINICAL APPLICATIONS

## **Assessing the Cost-Effectiveness of New Pharmaceuticals in Epilepsy in Adults: The Results of a Probabilistic Decision Model**

*Neil Hawkins, PhD, David Epstein, MSc, Michael Drummond, DPhil, Jennifer Wilby, MPH, Anita Kainth, MSc, David Chadwick, DM, FRCP, FMed Sci, Mark Sculpher, PhD*

S IN PHARMACEUTICAL DECISION MAKING

## **Cost-Effectiveness Analysis of Treatments for Chronic Disease: Using *R* to Incorporate Time Dependency of Treatment Response**

*Neil Hawkins, PhD, Mark Sculpher, PhD, David Epstein, MSc*



# Hawkins et al 2005 MDM

---

*HAWKINS, SCULPHER, EPSTEIN*

---

and specific decision-analytic software. As seen in the appendix, decision models can be conveniently and transparently published as scripts. Models presented in this way can be easily inspected and assessed by a 3rd party. The availability of function calls allows the model structure to be separated from the model

parameterization; this simplifies development and maintenance, as the model structure only has to be defined once rather than being repeated for each treatment pathway being considered.

## APPENDIX

### *R* Code Used in the Epilepsy Case Study

---

```
txModel ← function (  
  trt1.fail=50,  
  trt1.n=50,  
  trt2.fail=60,  
  trt2.n=20,  
  trt3.fail=60,  
  trt3.n=20,
```



## When simple becomes complicated: why Excel should lose its place at the top table

Gianluca Baio, Anna Heath

Department of Statistical Science, University College, London - UK

### ABSTRACT

Traditionally, the majority of health economic modelling has been performed in spreadsheet calculators such as Microsoft Excel as it is perceived to be more transparent and easy to use. However, as the modelling requirements become more realistic and therefore complex, spreadsheets become increasingly cumbersome and difficult to manage. We argue that specialist statistical packages such as R should be used when the models become suitably complex. We acknowledge the difficulties associated with script-based statistical software, but argue that user-written packages designed for health-technology assessments simplify the analysis when compared to spreadsheet calculators. Additionally, we argue that the production of web-applications based on R will allow the statistical capabilities of specialist software to be available for all. All that is needed is a dialogue between the modellers and the academic to make the software available for all.

**Keywords:** Cost-effectiveness analysis, Decision-analytic models, R, Statistical packages



# Health Decision Sciences in the Era of Open-source Software

by **Fernando Alarid-Escudero** on behalf of the Decision Analysis in R for Technologies in Health (DARTH) workgroup



There's no doubt we are in the era of Open-Source Software (OSS), but how much has OSS infiltrated into health decision sciences? A quick search in Wikipedia for "[open-source programming language licensing](#)" yielded a list of 80 programs, such as R, Python and Haskell, among others. But what exactly does open-source software mean? According to the Open Source Initiative, "An open-source software can be freely accessed, used, changed, and shared (in modified or unmodified form) by anyone."

OSS has gained significant popularity across many academic disciplines such as statistics and engineering. There have been significant developments and exhibitions of the use of OSS in

Health Decision Sciences, but certainly not enough. Some of the most popular models used in Health Decision Sciences are being implemented in either domain-specific or proprietary software. There are many advantages to this approach, but there are also significant drawbacks. For example, if there is interest in replicating an analysis conducted using a licensed software package, individuals are constrained by not having access to the software. This could be problematic in financially constrained environments, such as academic fields where financial resources devoted to software are limited. The higher the entry costs, particularly financial costs, the less likely decision-analytic tools will become available and understood by a broader audience – an outcome that could threaten reproducibility and





TUTORIAL

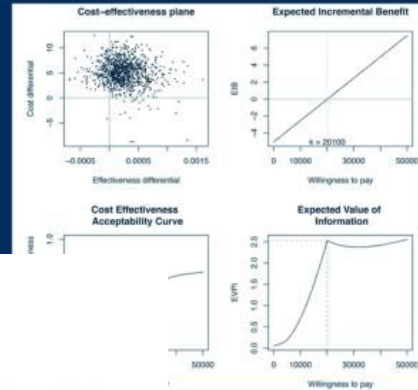
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# **Cost-effectiveness Analysis in R Using a Multi-state Modeling Survival Analysis Framework: A Tutorial**

*Claire Williams, MSc, James D. Lewsey, PhD, Andrew H. Briggs, DPhil,  
Daniel F. Mackay, PhD*

Chapman & Hall/CRC Biostatistics Series

## Bayesian Methods in Health Economics



Gianluca Baio

 **CRC Press**  
Taylor & Francis Group  
A CHAPMAN & HALL BOOK



## Markov Models for Health Economic Evaluations: The R Package heemod

Antoine Filipović-Pierucci  
URC-Eco

Kevin Zarca  
URC-Eco

Isabelle Durand-Zaleski  
URC-Eco


Use R!

Gianluca Baio  
Andrea Berardi  
Anna Heath

## Bayesian Cost- Effectiveness Analysis with the R package BCEA

 Springer



 This is an archived post. You won't be able to vote or comment.

↑  
1  
↓



### Cost effectiveness analysis with R? (self.rstats)

submitted 11 months ago by OttawaMD

Anyone know of any techniques or packages for performing basic cost-effectiveness (or cost-benefit, or cost-minimization, or decision analysis...) with R? TreeAge pro has a monopoly in this analytics technique, and the price tag is exorbitant!

7 comments share report

### all 7 comments

sorted by: best ▾

↑ [-] [lenwood](#) 2 points 11 months ago

↓ A quick search turned up these two options. I'm not familiar with either of them.

- [ArvoRe](#)
- [ICEinfer](#)

[permalink](#) [embed](#)

↑ [-] [\[deleted\]](#) 2 points 11 months ago

↓ Not a package specifically but you can use a markov chain with an attached cost function. The matrix package along with gRain can help you with setting up the matrices and and graph out the chains.

[permalink](#) [embed](#)



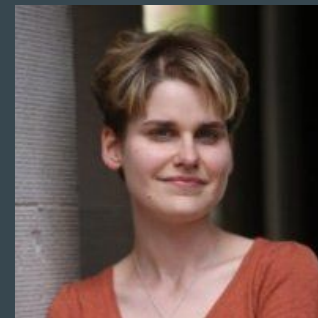
# Decision Analysis in R for Technologies in Health (DARTH)



F. Alarid-Escudero PhD



H. Jalal MD PhD



E. Enns PhD



E. Krijkamp PhDc



M. Hunink MD



P. Pechlivanoglou PhD



## 37th Annual Meeting of the Society for Medical Decision Making October 18 - 21, 2015

### AM07 DECISION MODELLING USING R

Sunday, October 18, 2015: 9:00 AM - 12:30 PM  
Mills Studio 5 (Hyatt Regency St. Louis at the Arch)

Course Director:

*Petros Pechlivanoglou, MSc, PhD*

Course Faculty:

*Nicholas Mitsakakis, MSc PhD, Lusine Abrahamyan, MD MPH PI*

## CONTENTS

- [General Information about the Course](#)
- [Program Overview](#)
- [Faculty](#)
- [Registration & Fees](#)

## DECISION MODELLING USING R

### General information about the course



Decision models are becoming more and more common in many conditions and to provide more and better around decision modelling are being developed. However, the techniques (e.g. model calibration, value of information, etc.) and the available software can be limiting as it sometimes provides limited statistical techniques within a decision model framework.

R is software that provides a flexible environment where advanced statistical models of varying complexity within the same framework and the results can be presented in graphical forms. R is freely available software, a fact that improves model transparency.

THETA in collaboration will Dr. Gianluca Baio from University College London, UK, will be giving a decision modelling using R between the 16th and the 18th of February 2016 at the University of Toronto, Canada.

### Participant experience

Participants will be expected to have some experience with decision modelling.

## 38th Annual North American Meeting of the Society for Medical Decision Making October 23 - 26, 2016

### AM4 DECISION MODELLING USING R

Sunday, October 23, 2016: 9:00 AM - 12:30 PM  
Cypress 1, Second Floor (Westin Bayshore Vancouver)

Course Type: Half Day

Course Level: Intermediate

Course Limit: 40



**39TH ANNUAL  
NORTH AMERICAN MEETING**  
October 22 - 25, 2017 | Pittsburgh, PA



## SHORT COURSE



### AM3: Introduction to Decision Modeling Using R

Sunday, October 22, 2017 09:00 AM - 12:30 PM

Wyndham



**39TH ANNUAL  
NORTH AMERICAN MEETING**  
October 22 - 25, 2017 | Pittsburgh, PA



## SHORT COURSE



### PM4: Microsimulation Modeling in R

Sunday, October 22, 2017 02:00 PM - 05:30 PM

Wyndham Grand Pittsburgh Downtown - Benedum



# 7-9 FEB 2017 Decision Modeling Using R

## Speakers



Petros Pechlivanoglou, PhD  
The Hospital for Sick Children  
Research Institute



Hawre Jalal MD, PhD  
University of Pittsburgh  
Health Policy and Management

## Topics

Introduction to Decision  
Modeling Using R  
Decision tree modeling  
State-transition modeling

Advanced Topics in Decision  
Modeling Using R  
Microsimulation modeling  
Model validation/calibration  
Evidence synthesis and decision

# Decision Modeling Using R 18 - 20 OCTOBER 2017

## Speakers



Petros Pechlivanoglou PhD  
The Hospital for Sick Children RI  
Child Health Evaluative Sciences

## Topics

Introduction to Decision  
Modeling Using R  
Decision trees  
State-transition models  
(Markov models)

## Location

The Hospital for Sick Children  
Peter Gilgan Centre for Research  
and Learning



## An Overview of R in Health Decision Sciences

*Hawre Jalal, MD, PhD, Petros Pechlivanoglou, MSc, PhD, Eline Krijkamp, MSc, Fernando Alarid-Escudero, MSc, Eva Enns, MS, PhD, M. G. Myriam Hunink, MD, PhD*

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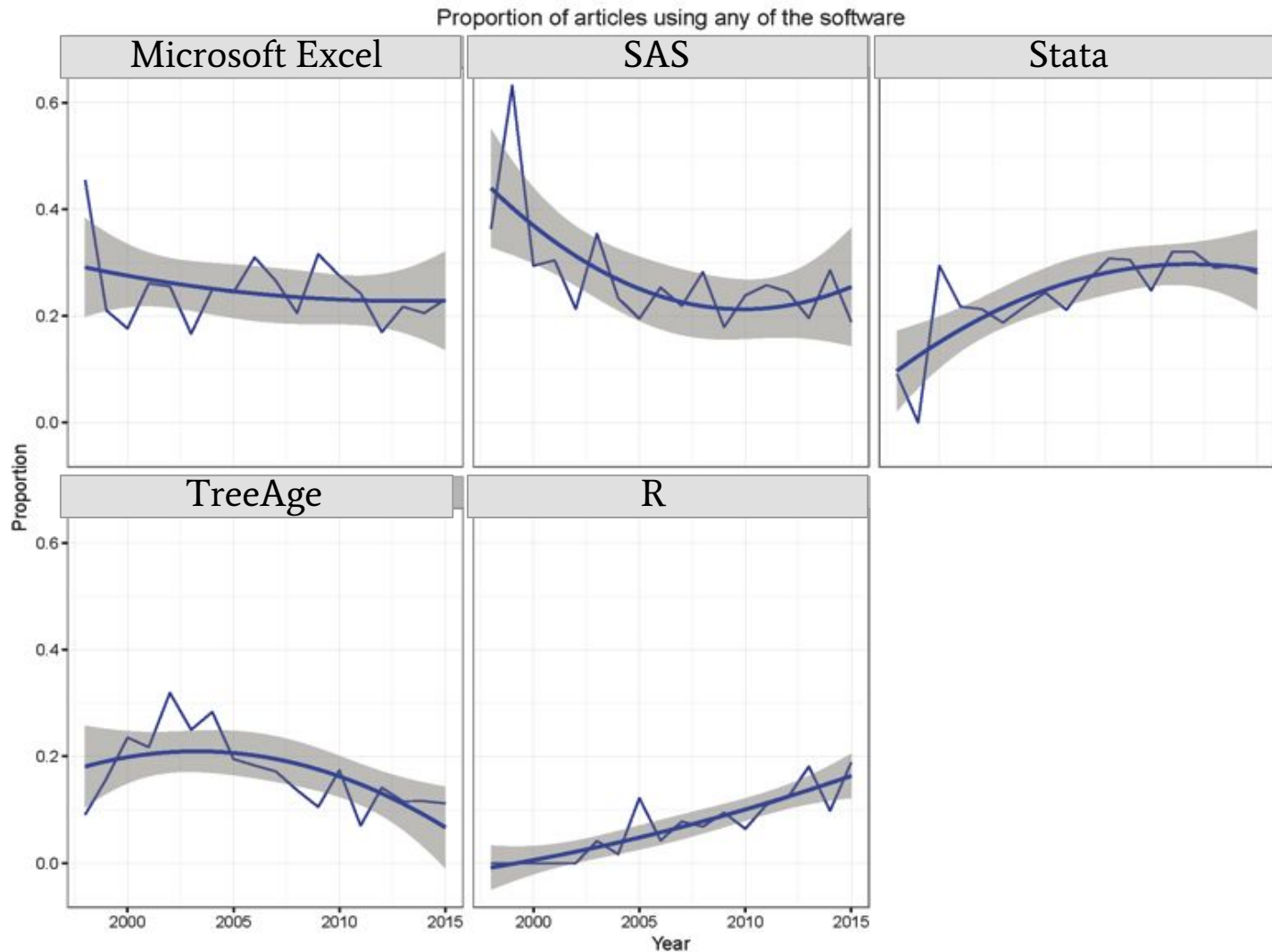
*As the complexity of health decision science applications increases, high-level programming languages are increasingly adopted for statistical analyses and numerical computations. These programming languages facilitate sophisticated modeling, model documentation, and analysis reproducibility. Among the high-level programming languages, the statistical programming framework R is gaining increased recognition. R is freely available, cross-platform compatible, and open source. A large community of users who have generated an extensive collection of well-documented packages and functions supports it. These functions facilitate applications of*

*health decision science methodology as well as the visualization and communication of results. Although R's popularity is increasing among health decision scientists, methodological extensions of R in the field of decision analysis remain isolated. The purpose of this article is to provide an overview of existing R functionality that is applicable to the various stages of decision analysis, including model design, input parameter estimation, and analysis of model outputs. **Key words:** R project; economic evaluation; cost-effectiveness analysis; literature review. (**Med Decis Making XXXX; XX:xx-xx**)*

---

# Software used in Decision analysis

Jalal et al. Overview of R in Health  
Decision Sciences, MDM, 2017



1 REVIEW ARTICLE

2 **A Comparison of Four Software Programs for Implementing**  
3 **Decision Analytic Cost-Effectiveness Models**

4 Chase Hollman<sup>1</sup> · Mike Paulden<sup>1,2</sup> · Petros Pechlivanoglou<sup>3,4,5</sup> · Christopher McCabe<sup>1</sup>

**Table 7** Time required for 10,000 simulations

	MATLAB	R	Excel		TreeAge		
	Seconds	Seconds	Seconds	Minutes	Seconds	Minutes	Hours
Average	11.22	31.83	872.65	14.54	15,798.72	263.31	4.39
Standard deviation	0.06	0.68	0.89	0.01	144.10	2.40	0.04
Minimum	11.10	31.03	871.55	14.53	15,560.81	259.35	4.32
Maximum	11.31	33.20	874.38	14.57	16,018.08	266.97	4.45
Median	11.23	31.75	872.53	14.54	15,808.27	263.47	4.39

**Table 8** Estimated time required for an expected value of partial perfect information analysis consisting of 1000 runs of 10,000 simulations each (via extrapolation)

	MATLAB	R	Excel	TreeAge
Hours	3.12	8.84	242.40	4388.53
Days	0.13	0.37	10.10	182.86

expertise of the analyst, the sophistication of analysis required, the time available for the completion of the analysis, and the financial resources available to support the work.

For educational users, the following observations may prove useful. TreeAge provides an environment in which it is possible to quickly and easily implement concepts discussed in a classroom. It does not require complex math-

**Table 9** Ranking of software on four domains of performance and purchase cost

Transparency and validation		Simulation time		Learning curve		Capability		Cost		
Rank	Software	Rank	Software	Rank	Software	Rank	Software	Rank	Software	
									Academic	Commercial
1	MATLAB	1	MATLAB	1	TreeAge	1	MATLAB	1	R	R
1	R	2	R	2	Excel <i>without</i> complex VBA	1	R	2	Excel	Excel
3	Excel	3	Excel	3	MATLAB	3	Excel	3	MATLAB	TreeAge
4	TreeAge	4	TreeAge	3	R	4	TreeAge	4	TreeAge	MATLAB
				3	Excel with complex VBA					

VBA Visual Basic for Applications



# Microsimulation modeling for health decision sciences using R: a tutorial



**Authors:** Eline M. Krijkamp, MSc  
Erasmus MC, Rotterdam, The Netherlands

Fernando Alarid-Escudero, MSc, PhD Candidate  
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Hawre J. Jalal, MD, PhD  
University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA

M.G. Myriam Hunink, MD, PhD  
Erasmus MC, Rotterdam, The Netherlands and Harvard T.H. Chan School of Public Health, Boston, USA

Petros Pechlivanoglou, MSc, PhD  
The Hospital for Sick Children, Toronto and University of Toronto, Toronto ON, Canada



# Working Papers

1. **Decision Tree Modeling for Health Decision Sciences Using R: A Tutorial**
2. **Introduction to cohort-based decision analytic modelling using R: a Tutorial**
3. **Improving performance in decision modeling in health using R**





# Choosing decision modeling software

## Criteria of decision on software use

- The end user
- The type of question answered
- The capacity of the decision modeler
- The need for transparency/ accountability
- Accessibility/ User-Friendliness
- Incorporating new methods
- Computational complexity / capacity



# When to build a decision model in R

You are building a:

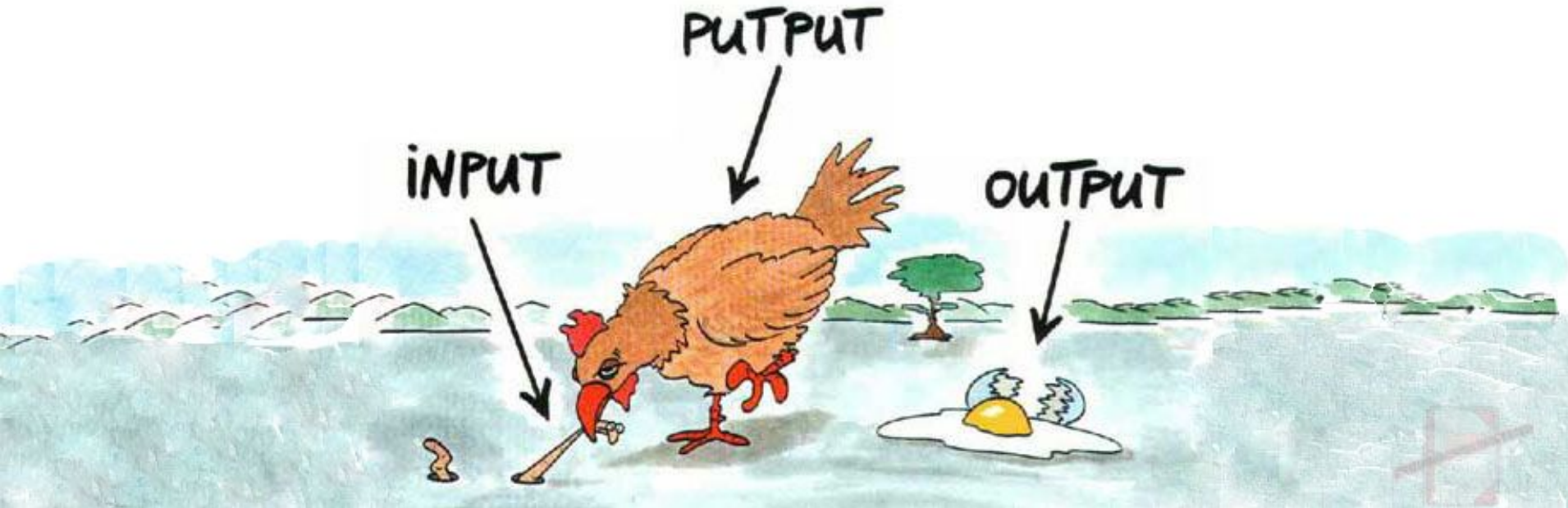
- Decision model based on survival data and you want to fit different parametric distributions and properly take into account uncertainty
- Microsimulation model and/or you want to embed risk predicting regression equations in the decision model
- State transition model based on Bayesian methods and you want to integrate BUGS functionality

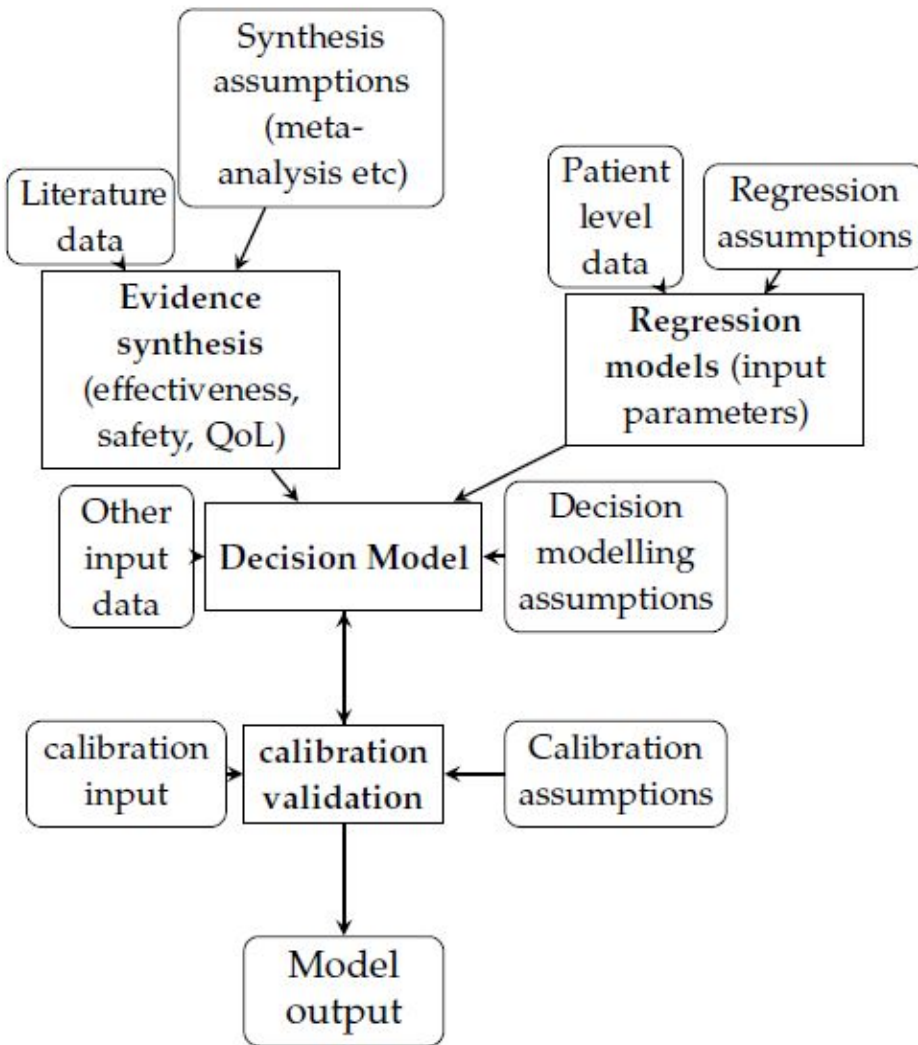


# When to build a decision model in R

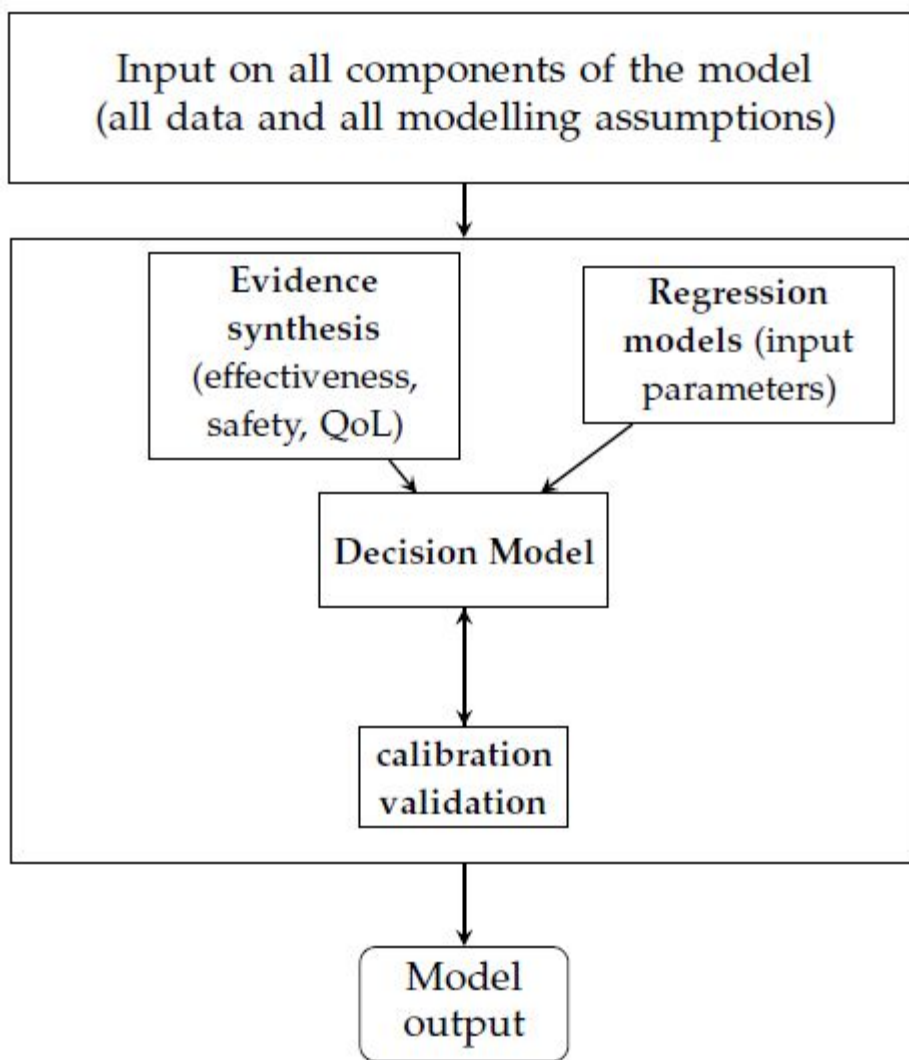
- A decision model that requires calibration of model parameters
- A model that is too complex to be designed easily in TreeAge or Excel
- You care about execution time and computational efficiency
- You want to embed statistical models and the associated uncertainty
- You want to have a transparent decision model with open access to any user

# Conceptualizing a decision model in R





**Conceptualizing a  
decision model in  
conventional software**



# Conceptualizing a decision model in R

---



# Conceptualizing a decision model in R

**INPUT:** Load input data relevant to the decision model

**INITIALIZATION:** Declare and initialize all variables that will be used to store information in the decision model. The dimensions of the variables are defined.

**MODEL:** The main component of the decision model; here is where the model outcomes (expected costs, expected outcomes, incremental costs and effects and incremental cost-effectiveness/net-benefits etc) are estimated.

**OUTPUT:** Tabular and graphical representation of the findings



# Building Decision Models in R

TreeAge Pro 2011

File Edit Node Subtree Tree Analysis Window Help

Views Debug Markov Tree

Tree Expl Model Ov

Evaluate new treatment

- Standard treatment: Radiation
- New treatment: Surgery and radiat
- Surgery and radiation eradicate
- Surgery and radiation fail to era

Example02-Variables.trex Example01-Intro.trex

1 2 3 4 5 6

Evaluate new treatment

Standard treatment: Radiation

New treatment: Surgery and radiation

cFollowupAnnual = 2K  
 cRadiation = 30K  
 cSurgery = 50K  
 effEradicated = 10  
 effNotEradicated = 3  
 pEradicateRad = 0.6  
 pEradicateRadSurg = 0.8

Radiation eradicates tumor  
 pEradicateRad [cRadiation]

Radiation fails to eradicate tumor  
 # [cRadiation]

Surgery and radiation eradicate tumor  
 pEradicateRadSurg [cRadiation]

Surgery and radiation fail to eradicate tumor  
 # [cRadiation]

Chance  
 Terminal  
 Decision  
 Logic  
 Markov  
 Label

Notes and Arr...  
 Note  
 Arrow

Projects

Examples

- Tutorial Trees
- \_backup
- ActiveX
- Clemen Marshall Skinner et
- Excel
- Healthcare
- \_backup
- Healthcare Training Exa
- Example01-Intro.trex
- Example02-Variables
- Example03-Clones.tr
- Example04-Dominar
- Example05-ArthritisE
- Example06-PSA.trex

Tree Properties Node Properties Variable Properties Variable Definitions Probability Wheel

type filter text Clear

Name	Definition	Info/Comment
---Defined @ Evaluate r		
cFollowupAnnual	2K	
cRadiation	30K	
cSurgery		
effEradicated	10	
effNotEradicated	3	
pEradicateRad	0.6	
pEradicateRadSurg	0.8	

Right-click for copy and paste.

CALC: C/E=1\2

RStudio

File Edit Code View Plots Session Build Debug Profile Tools Help

Go to file/function Addins

Decision\_tree\_example2.R

Source on Save

Run Source

Environment History

Global Environment

Environment is empty

Files Plots Packages Help Viewer

Zoom Export

```
1 ##### Decision trees in R #####
2 ## Decision tree example for the Medical Decision Making article: ##
3 ## Introduction to decision trees in R ##
4 ## Child Health Evaluative Sciences, The Hospital for Sick Children, 2017 ##
5 ## Credits for the R Code: Petros Pechlivanoglou, Fernando Alarid- Escudero ##
6 ## Hawre Jalal, Eline Krijkamp ##
7 ## Credits for the example: Buxton and O' Brien 1992 ##
8 ## Economic evaluation of ondansetron: preliminary analysis using ##
9 ## clinical trial data prior to price setting. ##
10 ## Strategies: Ondansetron, Metoclopramide ##
11 #####
12
13
14 rm(list = ls()) # clear memory (removes all the variables from the workspace)
15
16 ##### Input Model Parameters #####
17
18 Strategies <- c("Ondansetron", "Metoclopramide") # Names of strategies to be studied
19 n.levels <- 4 # number of levels in the decision tree
20 n.leafs.ON <- n.leafs.MET <- 10 # number of terminal pathways, or leaves, in the decision tree
21
22
```

16:55 Input Model Parameters

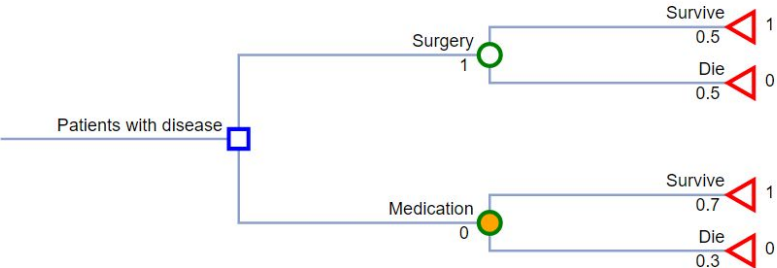
R Script

Console C:/Users/Petros/Dropbox/Greek Census/

> |

Open Tree

OpenTree



University of Pittsburgh

File

Node

Name:

Medication

Type

- ☐ Decision
- ☒ Chance
- ☐ Terminal
- ☐ Markov

Probability:

0

Variables:

# The Decision Tree

# The Decision Tree

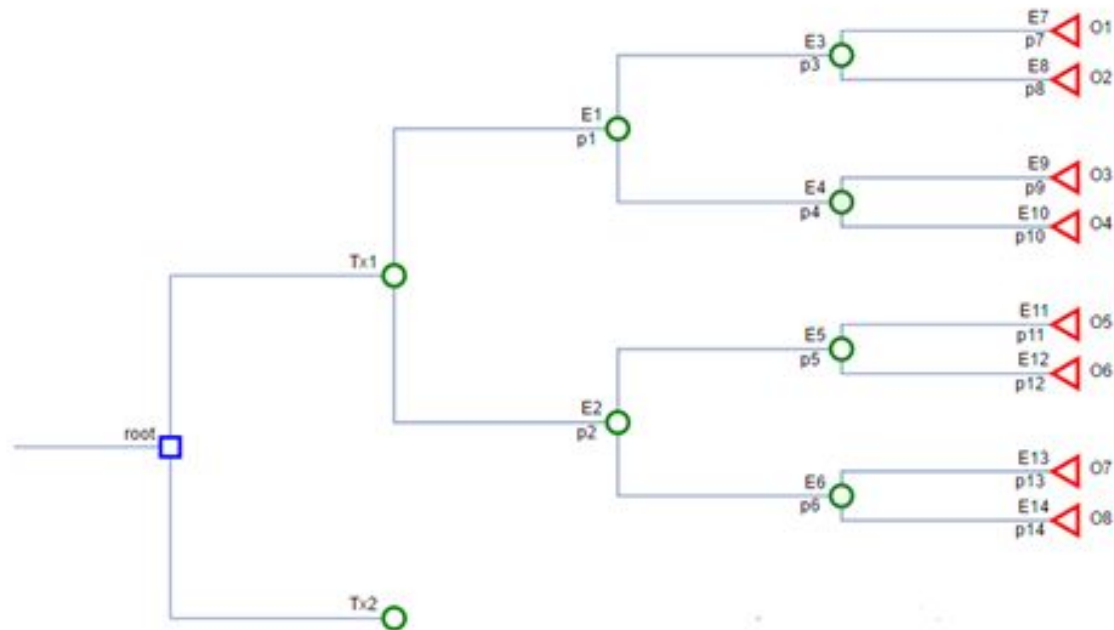
- The most common decision modeling tool to be used for CEA purposes.





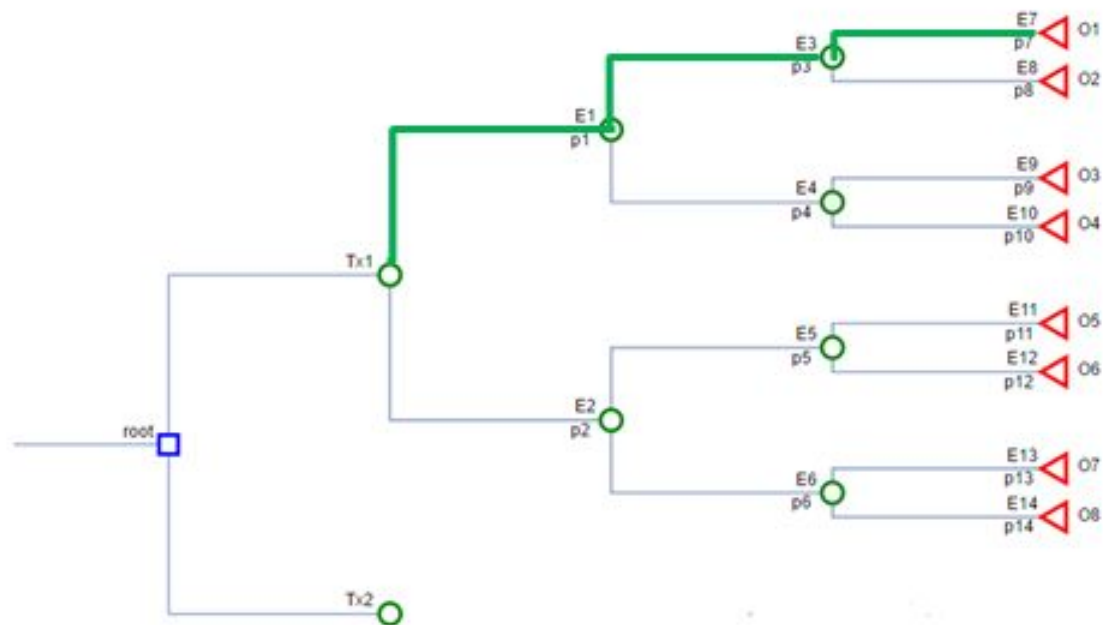
# Calculate Expected Value

$EV = ?$



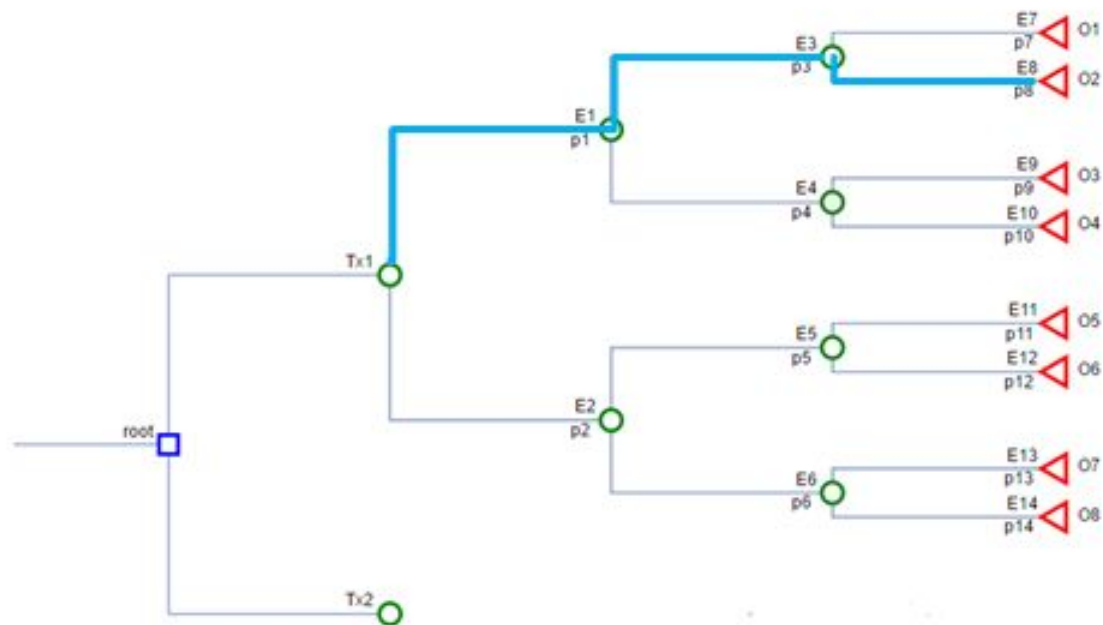
# Calculate Expected Value

$$EV = p_1 \cdot p_3 \cdot p_7 \cdot O_1$$



# Calculate Expected value

$$EV = p_1 \cdot p_3 \cdot p_7 \cdot O_1 + \\ p_1 \cdot p_3 \cdot p_8 \cdot O_2$$



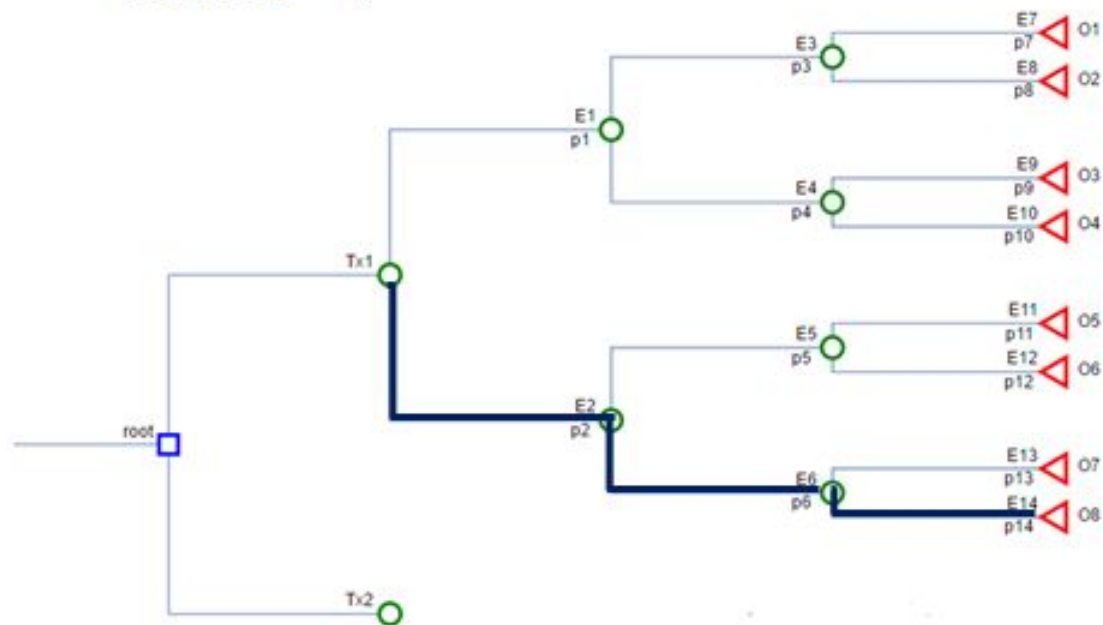
# Calculate Expected Value

$$EV = p_1 \cdot p_3 \cdot p_7 \cdot O_1 +$$

$$p_1 \cdot p_3 \cdot p_8 \cdot O_2 +$$

$$\dots +$$

$$p_2 \cdot p_6 \cdot p_{14} \cdot O_8$$



# Challenges with conventional EV

$$EV = p_1 \cdot p_3 \cdot p_7 \cdot O_1 +$$
$$p_1 \cdot p_3 \cdot p_8 \cdot O_2 +$$
$$\dots +$$
$$p_2 \cdot p_6 \cdot p_{14} \cdot O_8$$

← 31 Operations

- Computationally demanding = slow
- Not a formal, general solution
- Tedious to implement in computer programming
- Efficiency important for large trees with PSA
- Increased room for error

# Decision trees in R: Example



# Example Decision Tree no 2

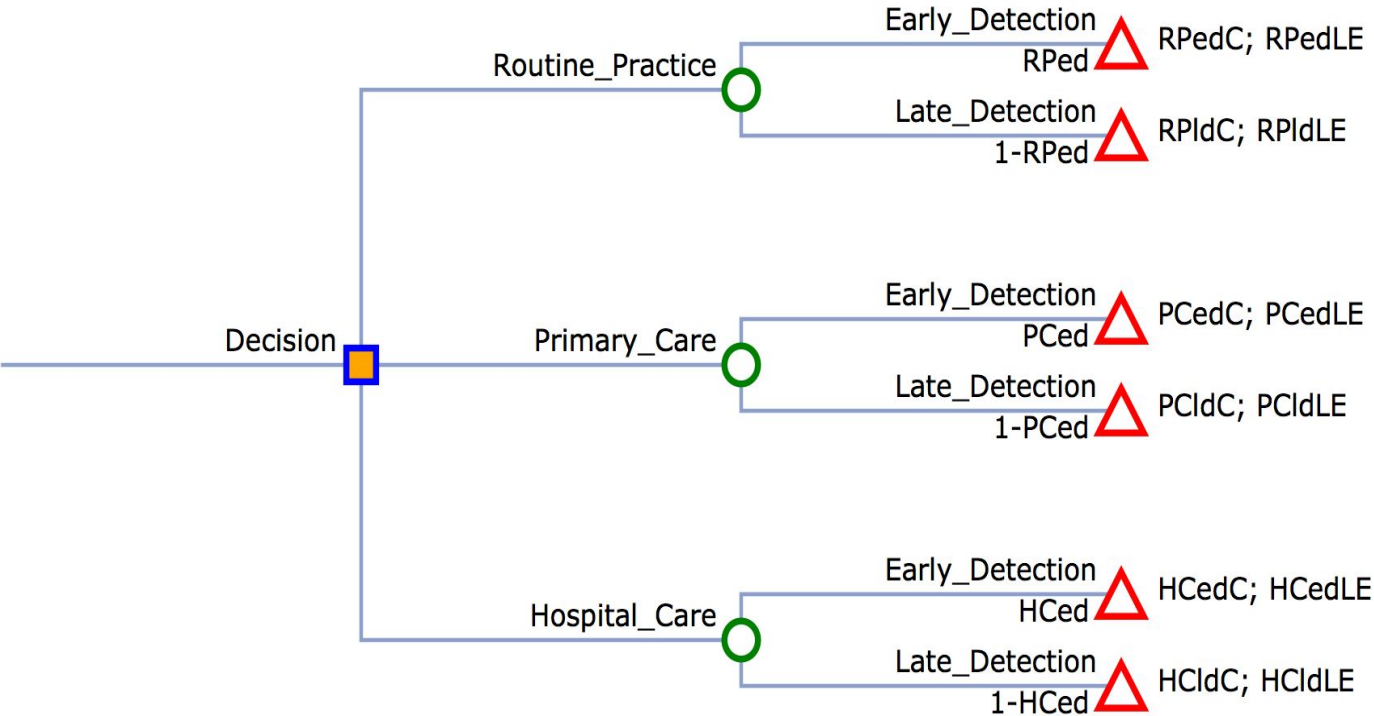
Estimating the cost-effectiveness of three follow-up practices for colorectal cancer after colorectal cancer treatment (Gray et al, 2011).

- Follow-up in primary care (PC),
- Follow-up in hospital care (HC) or
- Continue routine practice (RP).

Strategies are different on:

- Probability of early detection (ed) vs late detection (ld) of recurrence of colorectal cancer
- Follow-up costs (C) in UK pounds.
- Differences in early detection rates are associated with life expectancy (LE)

# Example Decision Tree no 2





**R Session...**

# Building Markov Models in R



# State Transition Cohort Models

Models where proportions of a cohort occupy states at each moment in time (e.g. healthy, sick, stable, progressed, dead)

Transition between states with some probability

Transitions occur in cycles (months, years etc)

Each state associated with a cost and a health outcome (\$'s, LYs or QALYs)

Markov assumption: no “memory” within states



# Building a state transition cohort Model

Determine health states

Determine transitions

Choose cycle length

Estimate transition probabilities

Estimate state utilities and costs per cycle

Calculate

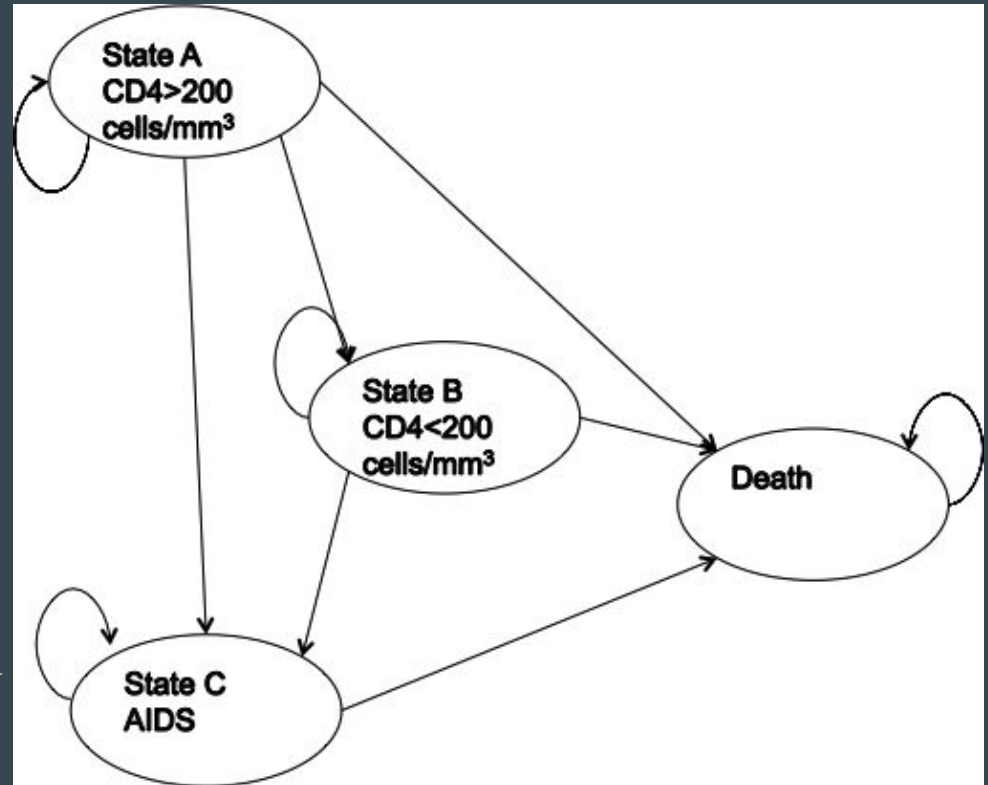
(Sensitivity analysis)

# Markov model of HIV progression

Transition matrix:

Monotherapy				
Transition from	Transition to			
	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

State-transition diagram



# Markov Trace

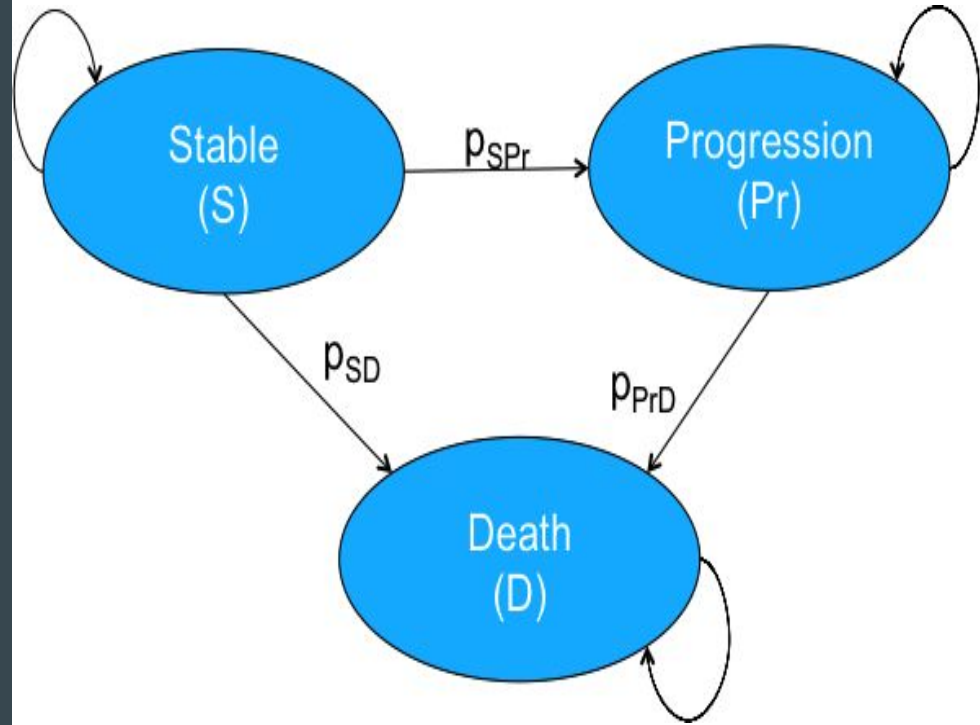
Number or distribution of individuals at each cycle

Cycle	State A	State B	State C	State D	Total
0	1000	0	0	0	1000
	$1000 \times 0.721$	$1000 \times 0.202$	$1000 \times 0.067$	$1000 \times 0.01$	
	↓	↓	↓	↓	
1	721	202	67	10	1000
2	520	263	181	36	1000
3	375	258	277	90	1000
4	270	226	338	166	1000
5	195	186	363	256	1000
6	140	147	361	351	1000
7	101	114	340	445	1000
8	73	87	308	532	1000
9	53	65	271	611	1000
10	38	48	234	680	1000
11	27	36	197	739	1000
12	20	26	164	789	1000
13	14	19	135	831	1000
14	10	14	110	865	1000
15	7	10	89	893	1000
16	5	7	72	916	1000
17	4	5	57	934	1000
18	3	4	45	948	1000
19	2	3	36	959	1000
20	1	2	28	968	1000

# Conceptualizing the Markov model in R



# Simple state transition model





# Simple state transition model

Model input:

$p_{SPr}$ : transition probability from  $S$  to  $Pr$

$p_{PrD}$ : transition probability  $Pr$  to  $D$

$p_{SD}$ : transition probability  $S$  to  $D$

$c_S$ : cost of being in state  $S$

$c_{Pr}$ : cost of being state  $Pr$

$e_S$ : outcomes associated with state  $S$

$e_{Pr}$ : outcomes associated with state  $Pr$

No cost or disutility associated with death



# Implementing the state transition model in R

At least two different implementations to build and execute a Markov model:

1. Difference equations setup
2. Matrix setup



# Implementing the state transition model in R

Create the state vectors  $S$ ,  $Pr$  and  $D$  that will store the number of people in each state each cycle until the end of time horizon  $T$

At  $t=0$  the cohort starts at  $S$ :

$$S_0=1; \quad Pr_0=0; \quad D_0=0$$

For  $t \leq T$ , proportions of the cohort will transition in the following fashion:

$$S_t = S_{t-1} - p_{SPr} \square S_{t-1} - p_{SD} \square S_{t-1};$$

$$Pr_t = Pr_{t-1} - p_{PrD} \square Pr_{t-1} + p_{SPr} \square S_{t-1};$$

$$D_t = D_{t-1} + p_{PrD} \square Pr_{t-1} + p_{SD} \square S_{t-1}$$

# Calculating total costs & effects

Total effectiveness at time  $t$  ( $E_t$ )

$$E_t = S_t e_s + Pr_t e_{pr}$$

Total effects ( $TE$ ):

$$TE = \sum_t E_t$$

Total cost at time  $t$  ( $C_t$ )

$$C_t = S_t c_s + Pr_t c_{pr}$$

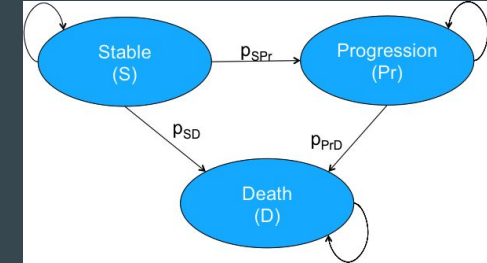
Total costs ( $TC$ ):

$$TC = \sum_t C_t$$

# Matrix Implementation of the Markov Model

Transition probability matrix

$$\mathbf{P} = \begin{array}{c} \begin{array}{ccc} & \mathbf{S} & \mathbf{Pr} & \mathbf{D} \end{array} \\ \begin{bmatrix} 1 - p_{SPr} - p_{SD} & p_{SPr} & p_{SD} \\ 0 & 1 - p_{PrD} & p_{PrD} \\ 0 & 0 & 1 \end{bmatrix} \begin{array}{l} \mathbf{S} \\ \mathbf{Pr} \\ \mathbf{D} \end{array} \end{array}$$



Vector of cycle's cost/outcomes

$$\begin{array}{c} \begin{array}{ccc} \mathbf{S} & \mathbf{Pr} & \mathbf{D} \end{array} \\ c = [c_S, c_{Pr}, 0] \\ e = [e_S, e_{Pr}, 0] \end{array}$$



# Matrix Implementation of the Markov Model

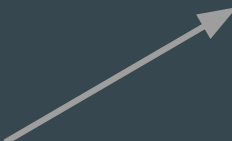
Create the  $t \times 3$  matrix  $\mathbf{M}$  that will store the proportion of the cohort at each state and cycle:

At  $t = 0$ :

$$M_0 = [1, 0, 0]$$

For  $t < T$ :

$$M_t = M_{t-1} P$$


$$P = \begin{bmatrix} 1 - p_{SPr} - p_{SD} & p_{SPr} & p_{SD} \\ 0 & 1 - p_{PrD} & p_{PrD} \\ 0 & 0 & 1 \end{bmatrix}$$



# Calculating total costs & effects

Total effects (TE):

$$E = M e$$

$$TE = \iota_T E$$

Total costs (TC):

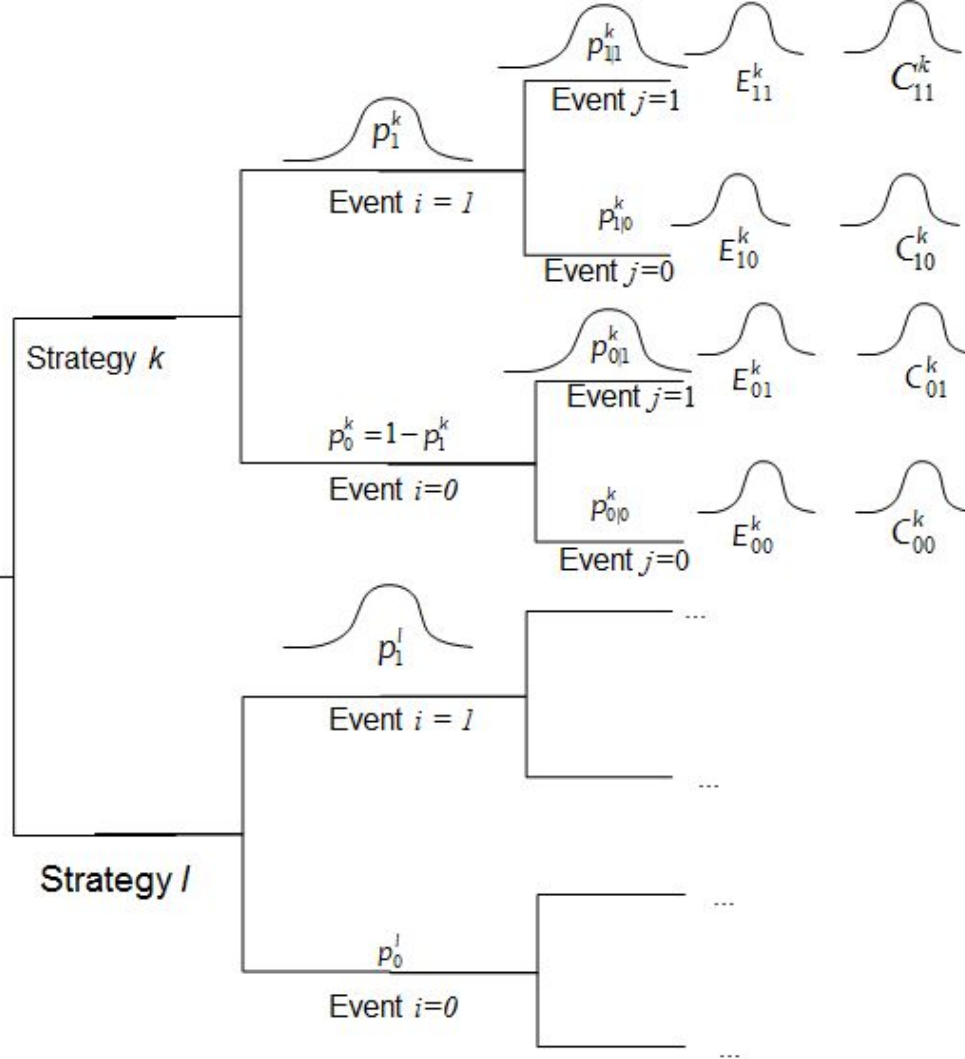
$$C = M c$$

$$TC = \iota_T C$$

$\iota_T$ :  $1 \times T$  vector of ones

R Session...

# Probabilistic Decision Models



# The Probabilistic Decision Tree

# Inputting data in R

## Input

$\mathbf{P}_i^k$  : Vector of N realizations from a distribution function of the probability of an event i in treatment group k for N simulations.

$\mathbf{P}_{j|i}^k$  : Vector of N probability realizations from a distribution function of an event j given an event i in treatment group k for N simulations.

$\mathbf{E}_{ij}^k$  : Vector of N effectiveness realizations associated with experiencing the combination of events i and j in treatment group k,

$\mathbf{C}_{ij}^k$  : Vector of N cost realizations associated with experiencing the combination of events i and j in treatment group k

# Conceptualizing a decision tree

Initialize the vectors  $TC^k$ ,  $TE^k$  of size  $N$  that will store the expected costs and effects for each of the  $N$  simulations

The expected cost and effectiveness for each of the interventions can be estimated using a “for” loop that will run the decision tree  $N$  times

for  $n \leq N$ :

$$TE^k_n = \sum_i \sum_j p^k_{i_n} p^k_{j|i_n} E^k_{ij_n}$$

$$TC^k_n = \sum_i \sum_j p^k_{i_n} p^k_{j|i_n} C^k_{ij_n}$$

# Conceptualizing a decision tree v.2.0

Initialize the vectors  $TC^k$ ,  $TE^k$  of size  $N$  that will store the expected costs and effects for each of the  $N$  simulations

The expected cost and effectiveness for each of the interventions can be described in the decision model with one single equation

◦: elementwise multiplication

$$TC^k = \sum_i \sum_j P_i^k \circ P_{j|i}^k \circ C_{ij}^k$$

$$TE^k = \sum_i \sum_j P_i^k \circ P_{j|i}^k \circ E_{ij}^k$$



# Real-world Applications of R in Decision models/ EE



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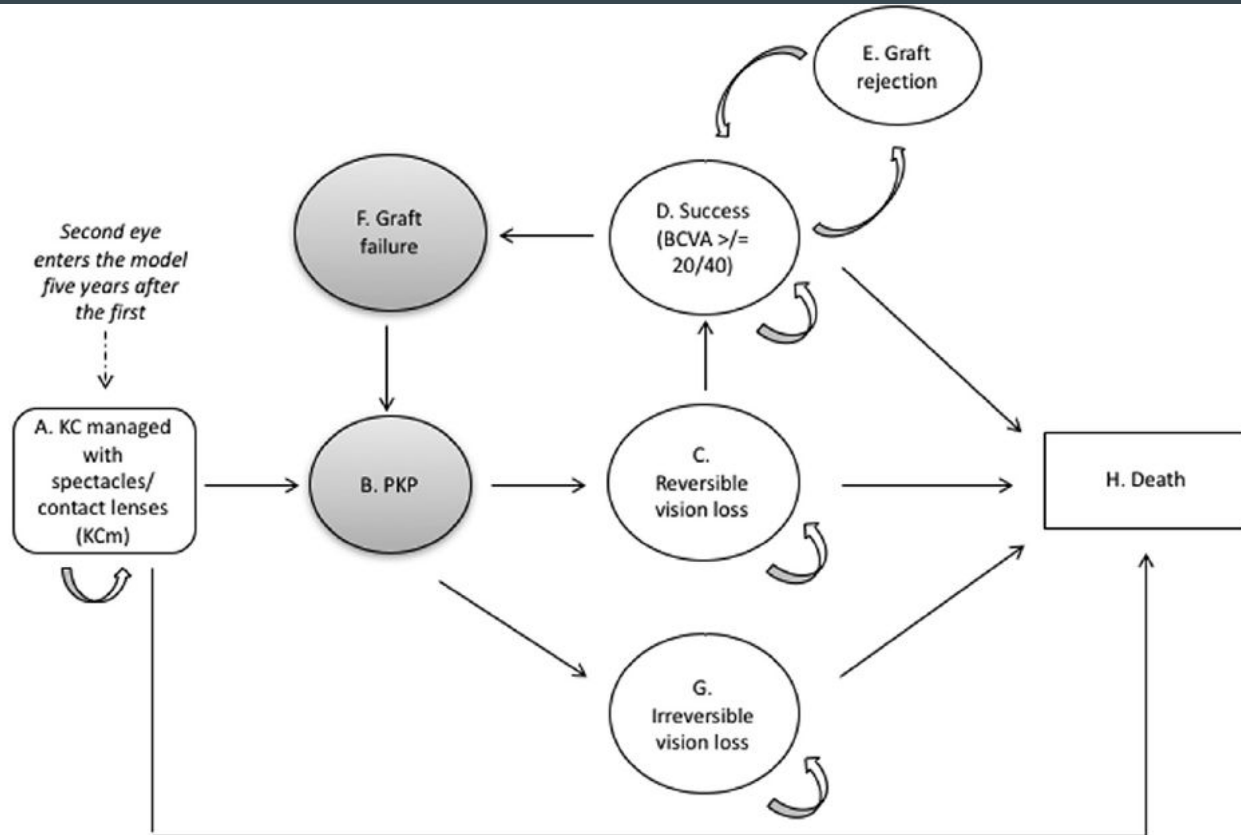
# Corneal Collagen Cross-Linking in the Management of Keratoconus in Canada

## *A Cost-Effectiveness Analysis*

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Victoria C. Leung, MD,<sup>1</sup> Petros Pechlivanoglou, MSc, PhD,<sup>2,3,4</sup> Hall F. Chew, MD, FRCSC,<sup>1,5</sup>  
Wendy Hatch, OD, MSc<sup>1,6</sup>

# Microsimulation example

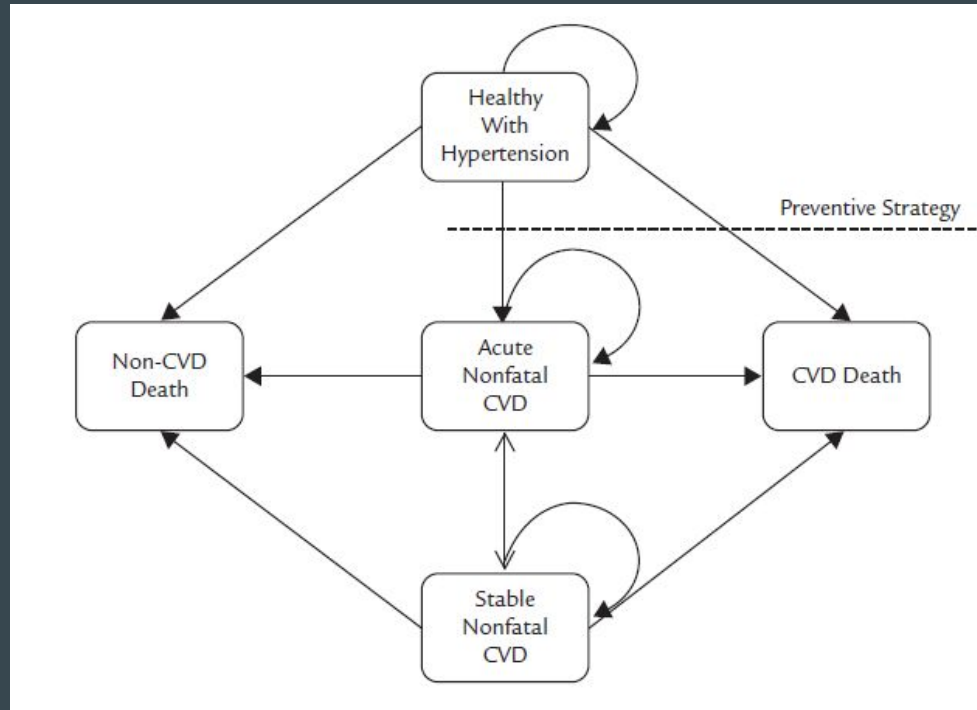


# Economic Evaluation of Primary Prevention of Cardiovascular Diseases in Mild Hypertension: A Scenario Analysis for the Netherlands

Jelena Stevanović, MSc<sup>1</sup>; Anouk C. O'Prinsen, MSc<sup>2</sup>; Bram G. Verheggen, MSc<sup>3</sup>; Nynke Schuiling-Veninga, PhD<sup>1</sup>; Maarten J. Postma, PhD<sup>1</sup>; and Petros Pechlivanoglou, PhD<sup>4,5</sup>

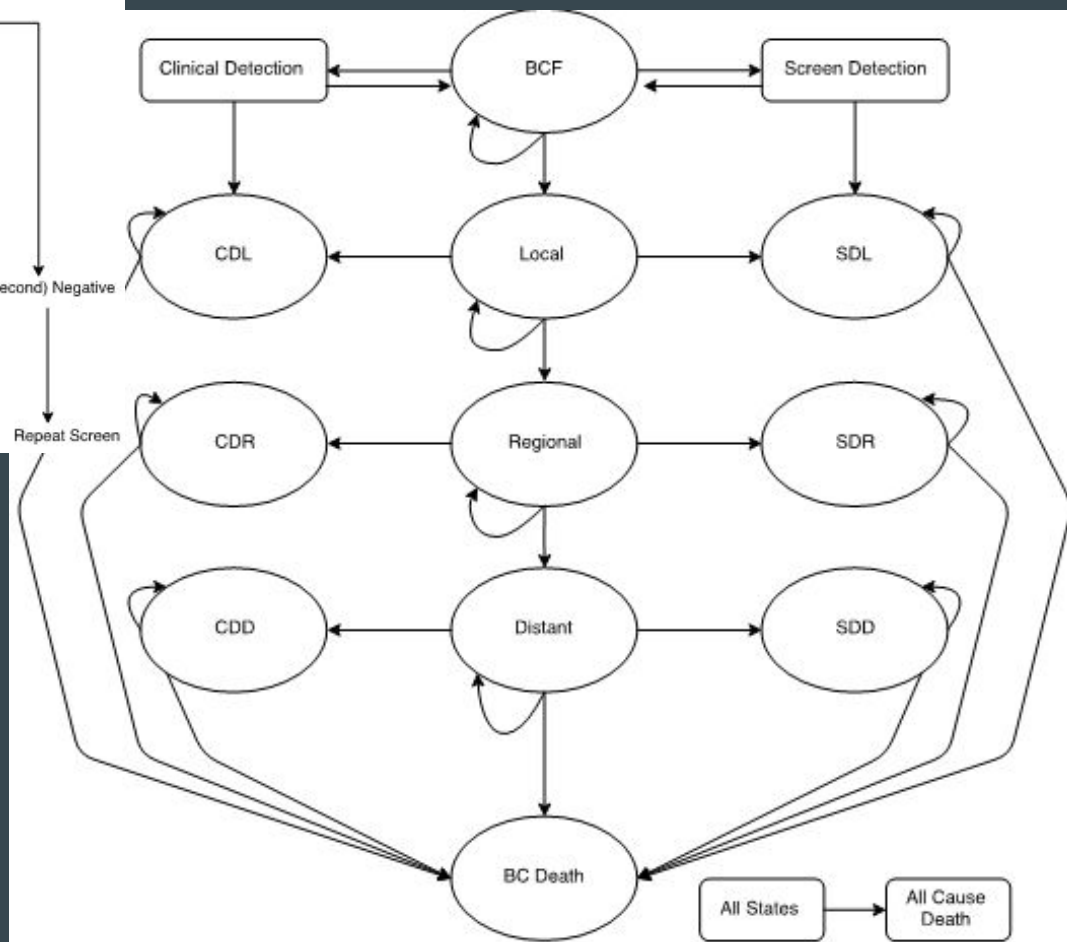
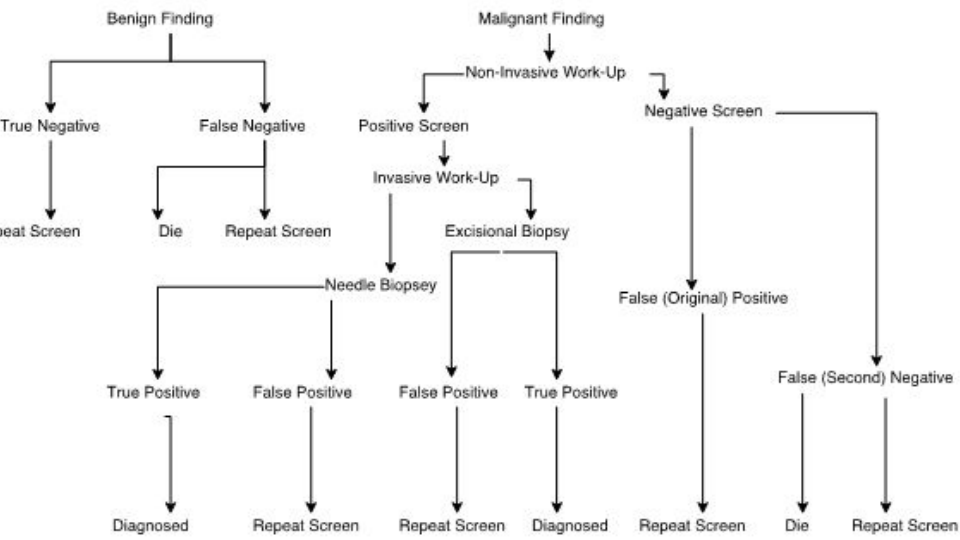
<sup>1</sup>Unit of Pharmacoepidemiology and Pharmacoeconomics, Department of Pharmacy, University of Groningen, Groningen, the Netherlands; <sup>2</sup>Sanofi, Gouda, the Netherlands; <sup>3</sup>Pharmerit, Rotterdam, the Netherlands; <sup>4</sup>Toronto Health Economics and Technology Assessment, Toronto, Ontario, Canada; and <sup>5</sup>Institute of Health Policy, Management, and Evaluation, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

# Markov Modeling example



# Assessing the cost-utility of early breast cancer screening for Survivors of Adolescent Hodgkin's lymphoma using a Discrete Event Simulation

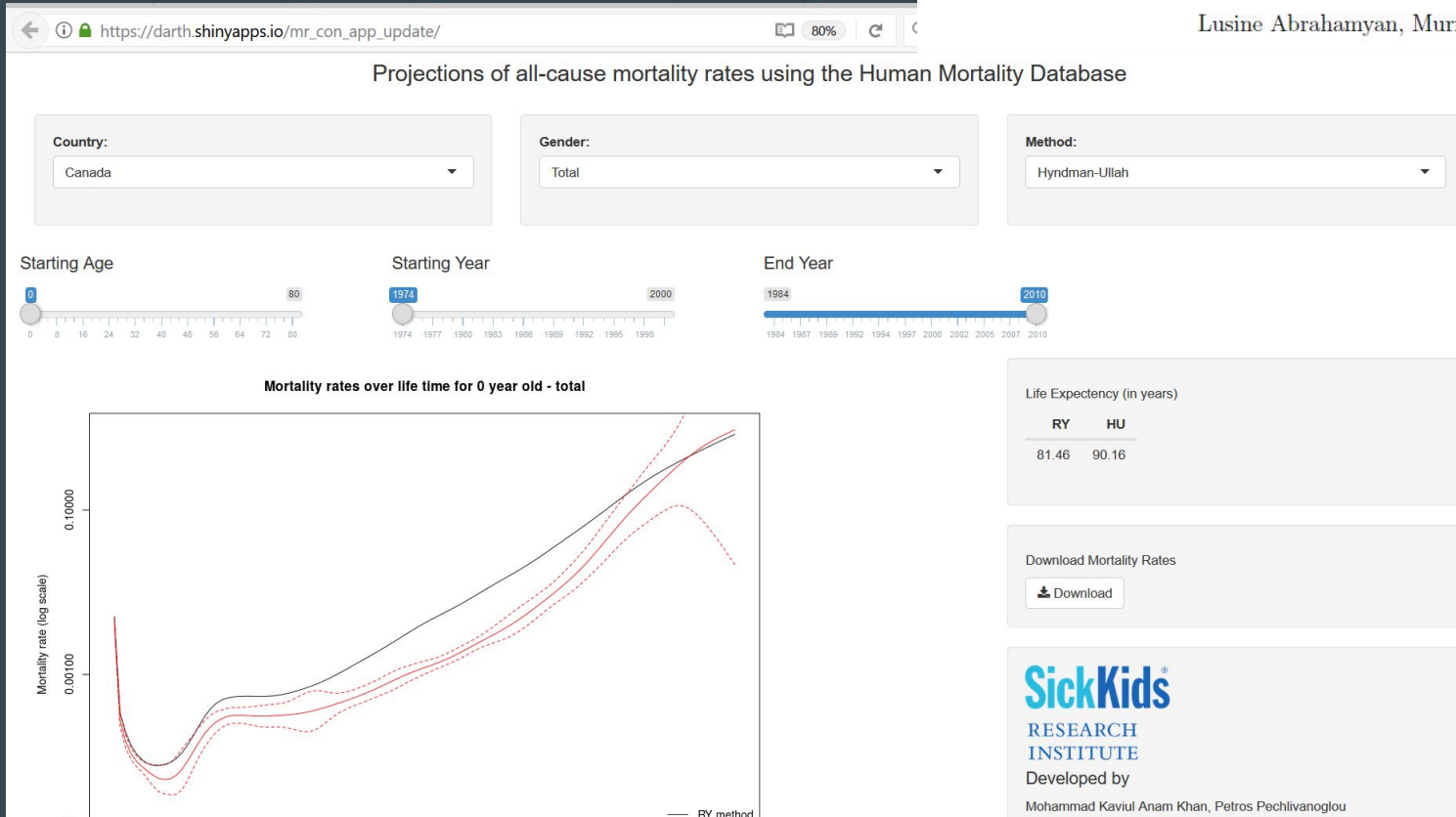
Jill Furzer, Laura Tessier, Sarah Kratina, Phat Chau, Cecilia Cotton, David Hodgson, Paul Nathan, Peter Coyte, Petros Pechlivanoglou



# Using mortality rate projections in health economic evaluation

Petros Pechlivanoglou, Mohammad Kaviul Anam Khan, Mike Paulden,  
Lusine Abrahamyan, Murray Krahn

[https://darth.shinyapps.io/mr\\_con\\_app\\_update/](https://darth.shinyapps.io/mr_con_app_update/)







# Conclusion

No software platform is perfect but:

R offers **potential** for  
transparency,  
reproducibility,  
incorporating model complexity,  
improved performance,  
a unified framework,  
a great educational platform  
GUI capabilities,  
which is FREE!

The **price to pay**:  
Steep learning curve,  
Programming skills,  
Poorer GUI compared to other software  
Poorer documentation

.....but Stay Tuned!!!!

Thank you!!!!