# Use of discrete event simulation in health service planning: a luxury or necessity?


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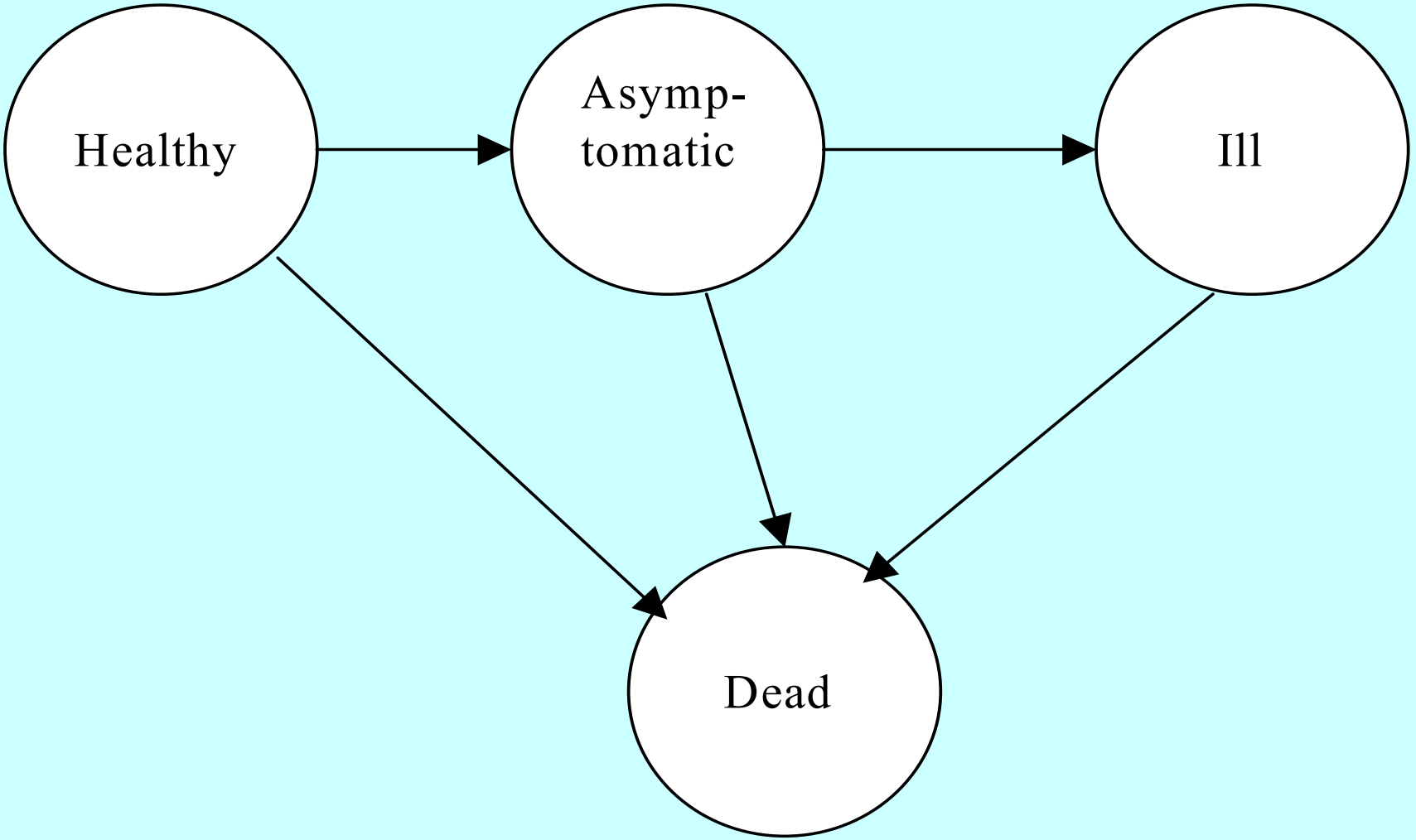
# Health service planning problems

- What services should be plan for patients with end-stage renal failure?
- Is it cost-effective to give CHD patients statins?
- Should we screen for diabetic retinopathy or breast cancer?

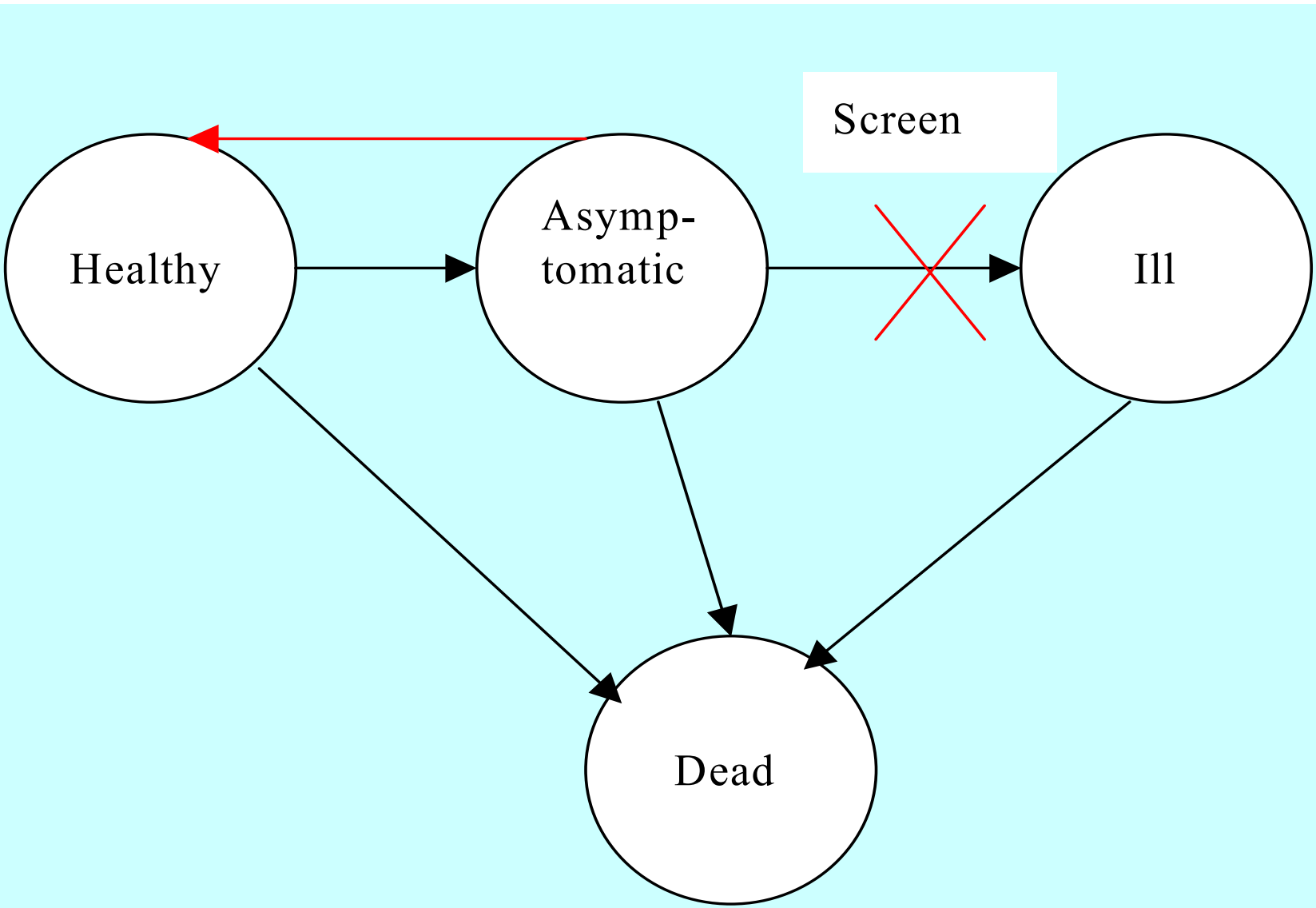
# General characteristics

- Individuals, often patients, move from state to state;
- The states may be different states of health or opportunities for treatment;
- Patient characteristics e.g. age are important;
- The populations are large and the difference in outcome may be small and occur over a long period of time.

How many remain alive in each state in each year?



# Screening – what benefits are there? More people? More quality of life? More cost?



# Output measures

- Cost
- Deaths prevented
- Life years saved
- QALYS (quality adjusted life years) gained
- Cost per life year saved
- Cost per QALY gained

# Markov models

- Classifies system into states
- Need to know transition probabilities from state to state
- Assumes population is homogeneous
- Assumes probability of moving from one state to the next is independent of time spent in that state – Markov assumption.

Probabilities of moving on in a fixed time period
Death is an absorbing state

| States | Healthy | Asympto-matic | Ill | Dead |
|---|---|---|---|---|
| Healthy | $p_{11}$ | $p_{12}$ | 0 | $p_{14}$ |
| Asymptomatic | 0 | $p_{22}$ | $p_{23}$ | $p_{24}$ |
| Ill | 0 | 0 | $p_{33}$ | $p_{34}$ |
| Dead | 0 | 0 | 0 | 1 |

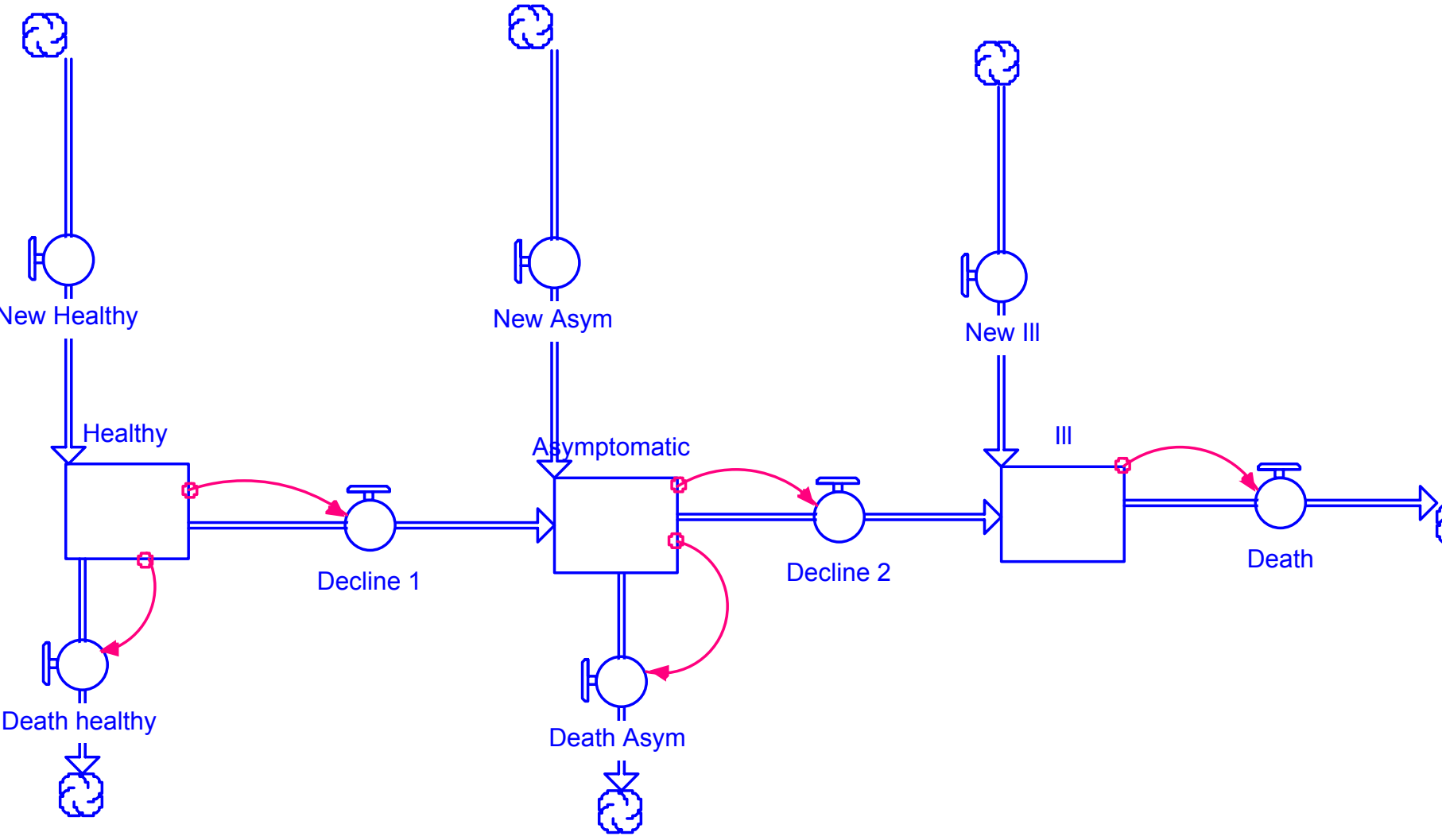
$$N(t) = N(t\text{-}1)\, P + M(t)\, I$$

Where N is the vector of the number in each state at time t,

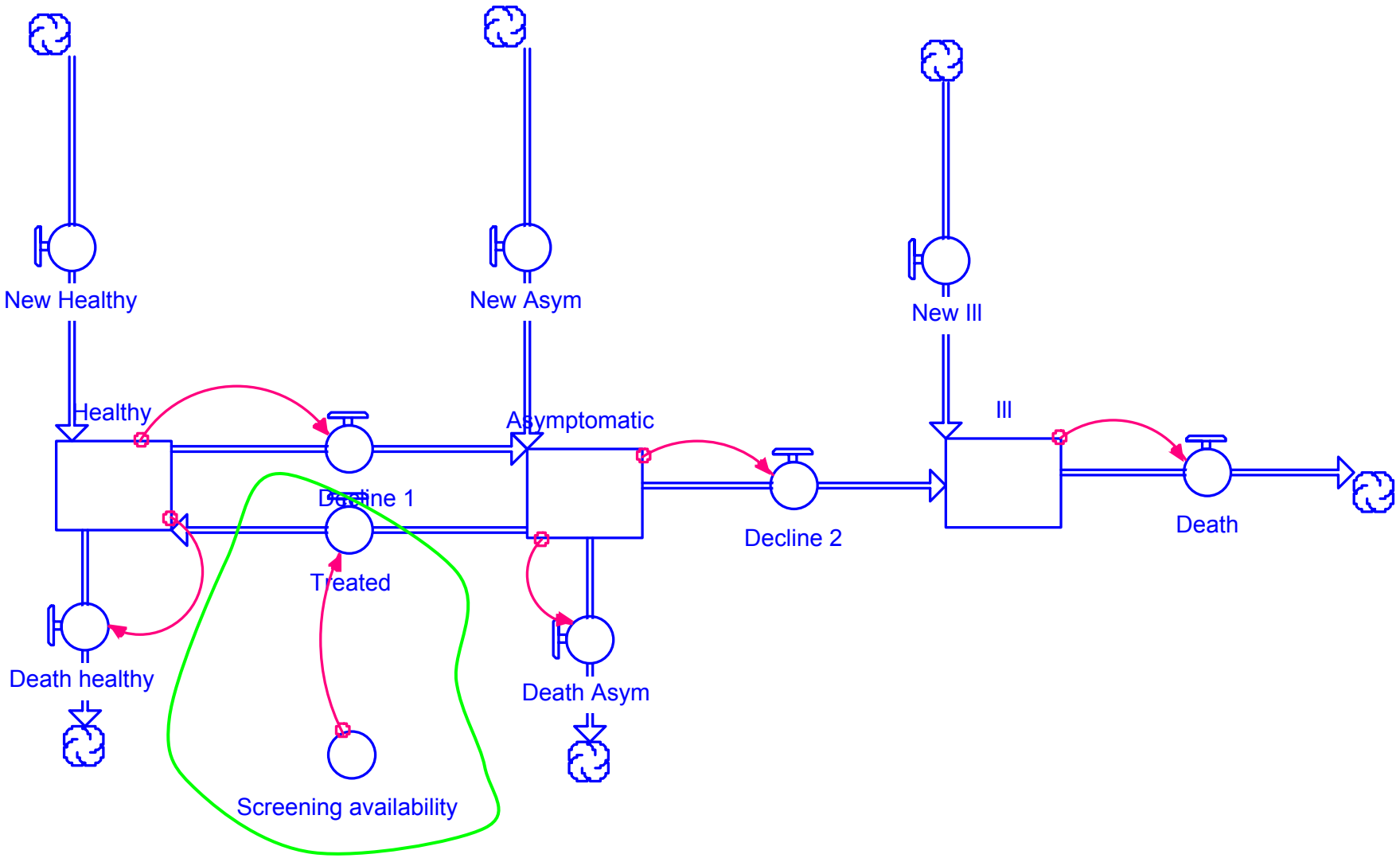
P is the matrix of probabilities,

M(t) are the new people entering each state in each time period and I is the identity matrix.

# Deterministic system dynamics model of the same system



# It is possible to include constraints – but limited



# Other software for aggregate transition models

- Spreadsheets may describe the transitions of proportions of patients in fixed time periods.
  - Deal with *average* numbers and are deterministic.
  - May incorporate exogenous influences e.g. screening at exact time periods.
- Another possibility is to use commercial software like Treeage.

# Sensitivity Analysis

It is possible to do sensitivity analysis on input parameters quite quickly with SD, commercial or spreadsheet software.

# Limitations

- Time intervals are discrete and equal
- Markovian assumption implies negative exponential decay from each state
- Homogeneous populations
- Rule of thumb – time interval should be at less than half the average activity time of the shortest activity
- States can be split to overcome this problem – to give Gamma distributions
- Replicate all states for each risk group

# What are the potential problems?

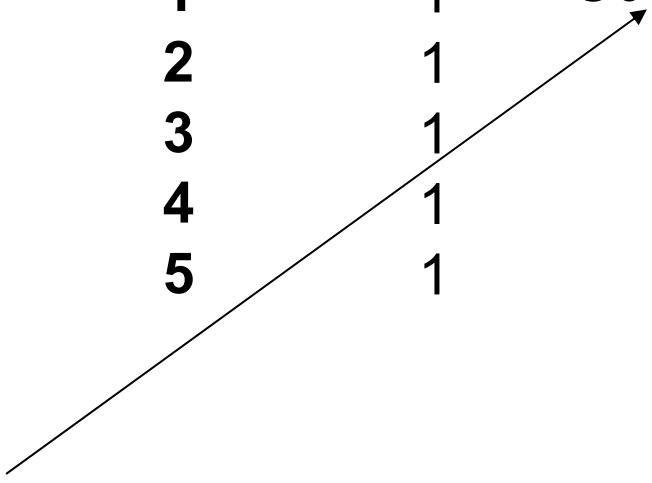
- Assumption system is deterministic
- Subdivide states to take account of risk groups
- Subdivide states to model distributions
- Explosion of states
- Over-simplification of model
- Limited view of output

**Suppose we are interested in the stochastic aspects of the system?**
**Use Monte Carlo simulation of a Markov process**.

- Sample to decide when each individual goes from one state to the next;
- Like tossing a coin, throwing a die;
- Have to do it many times to get reliable averages for each time period;
- Can measure uncertainty.

| | G |
|---|---|
| Probability of going from healthy to asymptomatic in one year | 0.3 |
| Probability of going from asymptomatic to ill in one year | 0.2 |

| | Year | | | | | |
|---|---|---|---|---|---|---|
| **Patients** | **1** | **2** | **3** | **4** | **5** | **6** |
| **1** | 1 | 2 | 3 | 3 | 3 | 3 |
| **2** | 1 | 1 | 1 | 2 | 2 | 2 |
| **3** | 1 | 1 | 1 | 2 | 2 | 2 |
| **4** | 1 | 1 | 1 | 1 | 1 | 2 |
| **5** | 1 | 1 | 2 | 2 | 2 | 2 |




=IF(B6=1,IF(RAND()>$G$2,1,2),IF(B6=2,IF(RAND()>$G$3,2,3),3)

Output

=COUNTIF($K$6:$K$25,3)

# Monte Carlo simulation 1

- With @Risk or Crystal Ball can simulate just one individual over and over again
- Eg. Run scenario with screening and without and compare output
- Possible to use Treeage

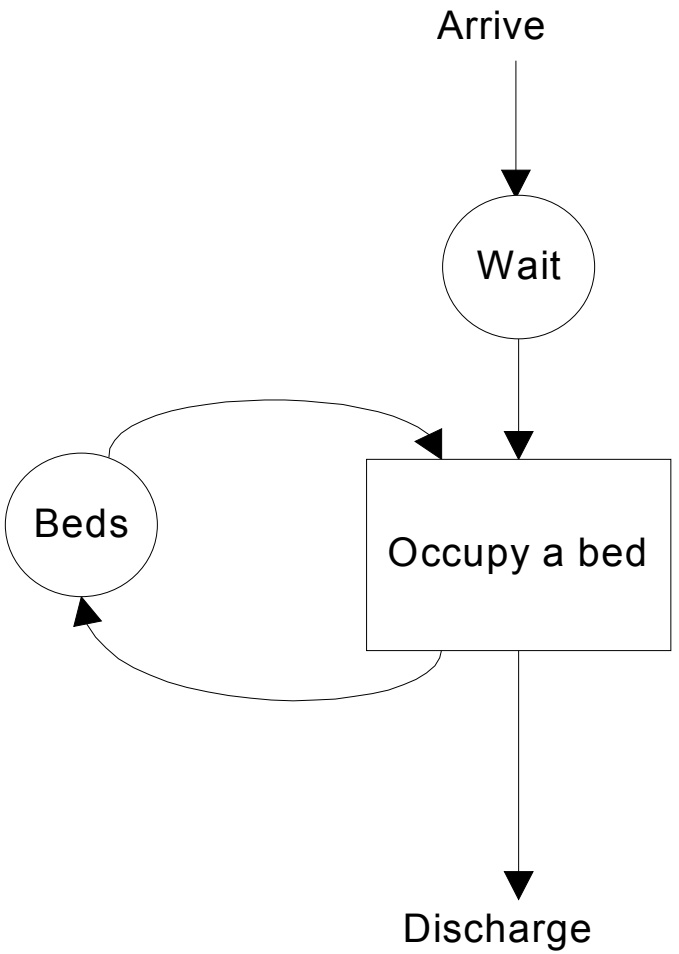
# Monte Carlo simulation 2

- Individuals can be given random *characteristics* which affect their progress
- Have to finish with one patient before starting with next.
- Can use @Risk – very fast and can process lots of people.

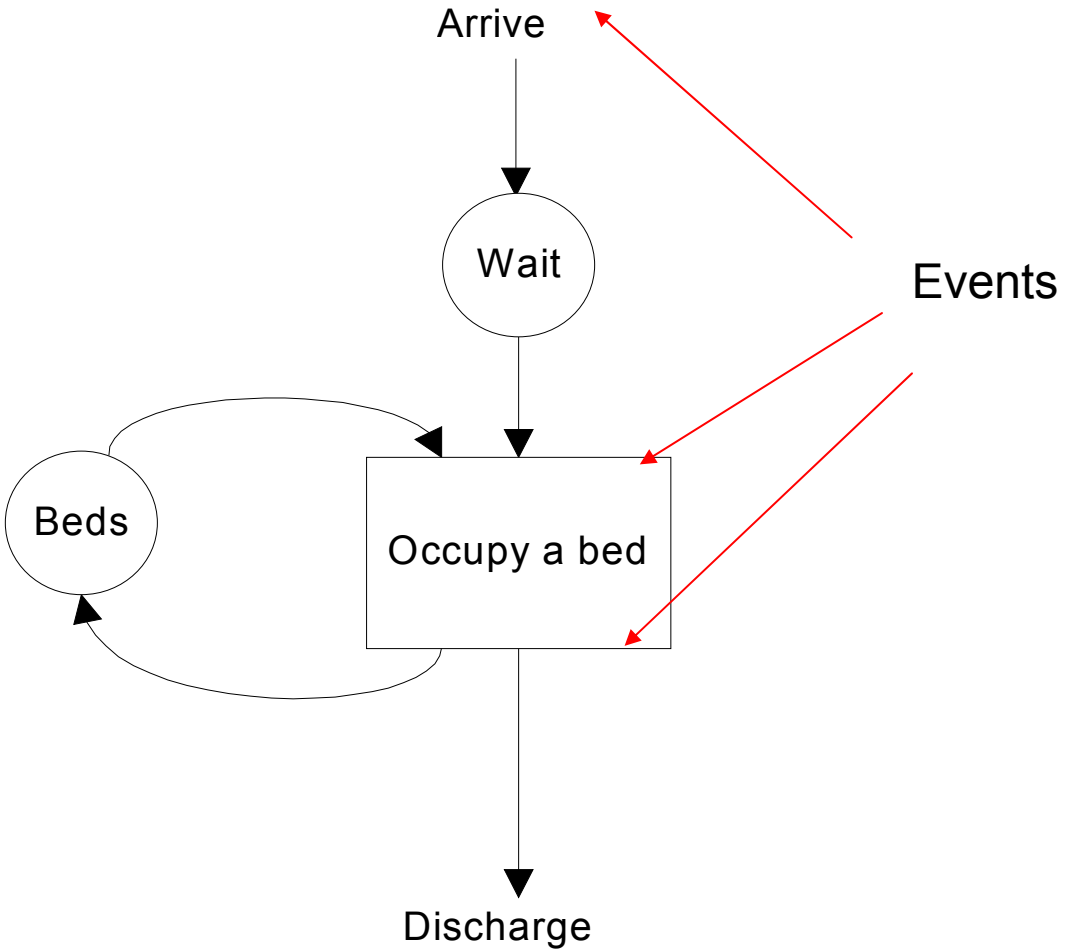
# What is Discrete Event Simulation?

- The system is represented by a series of events.
- Individual, called entities, take part in these events.
- Simulation moves from one event to the next in continuous time.
- Future events are kept in a list and performed in time order.

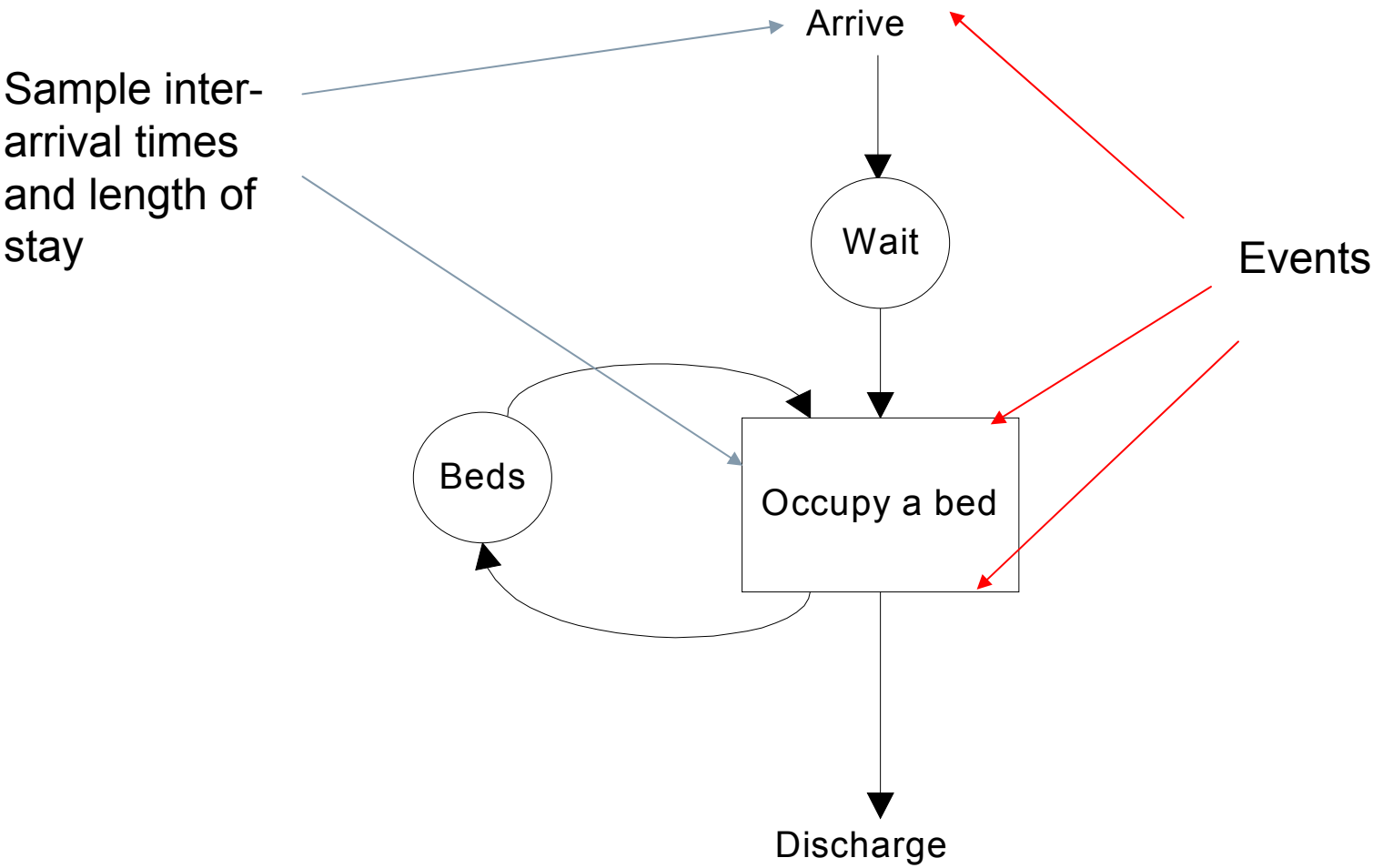
# Simple DES structure

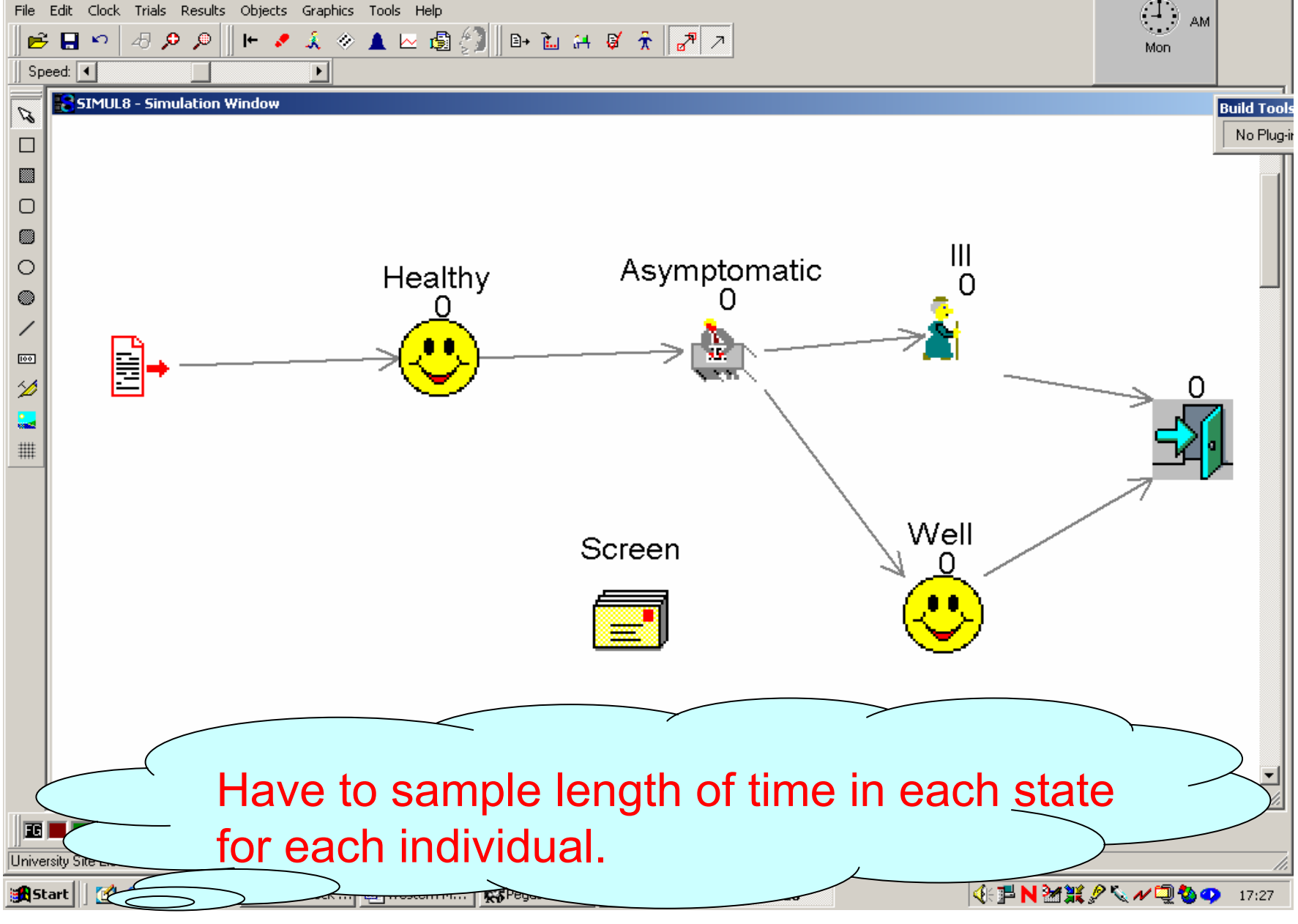


# Simple DES structure



# Simple DES structure




File Edit Clock Trials Results Objects Graphics Tools Help
Speed:
AM
Mon
SIMUL8 - Simulation Window
Build Tools
No Plug-in
Healthy
0
Asymptomatic
0
Ill
0
0
Screen
Well
0
Have to sample length of time in each state for each individual.
Start
17:27

# Advantages of Discrete Event Simulation

- Characteristics influence progression – No explosion of states
- Time advances in continuous time, as necessary
- Use of any activity time distribution
- Can incorporate more complex logic
- Can incorporate delays or interactions
- Can incorporate constraints

# Disadvantages of Discrete Event Simulation

- Lots of software available but most not specifically designed for patient modelling
  - Simul8 – generic DES software
  - Program in high level language eg POST
  - ModGen
- Temptation to make model complex
- Time consuming to get statistically significant results
- Even more time consuming to do sensitivity analyses.

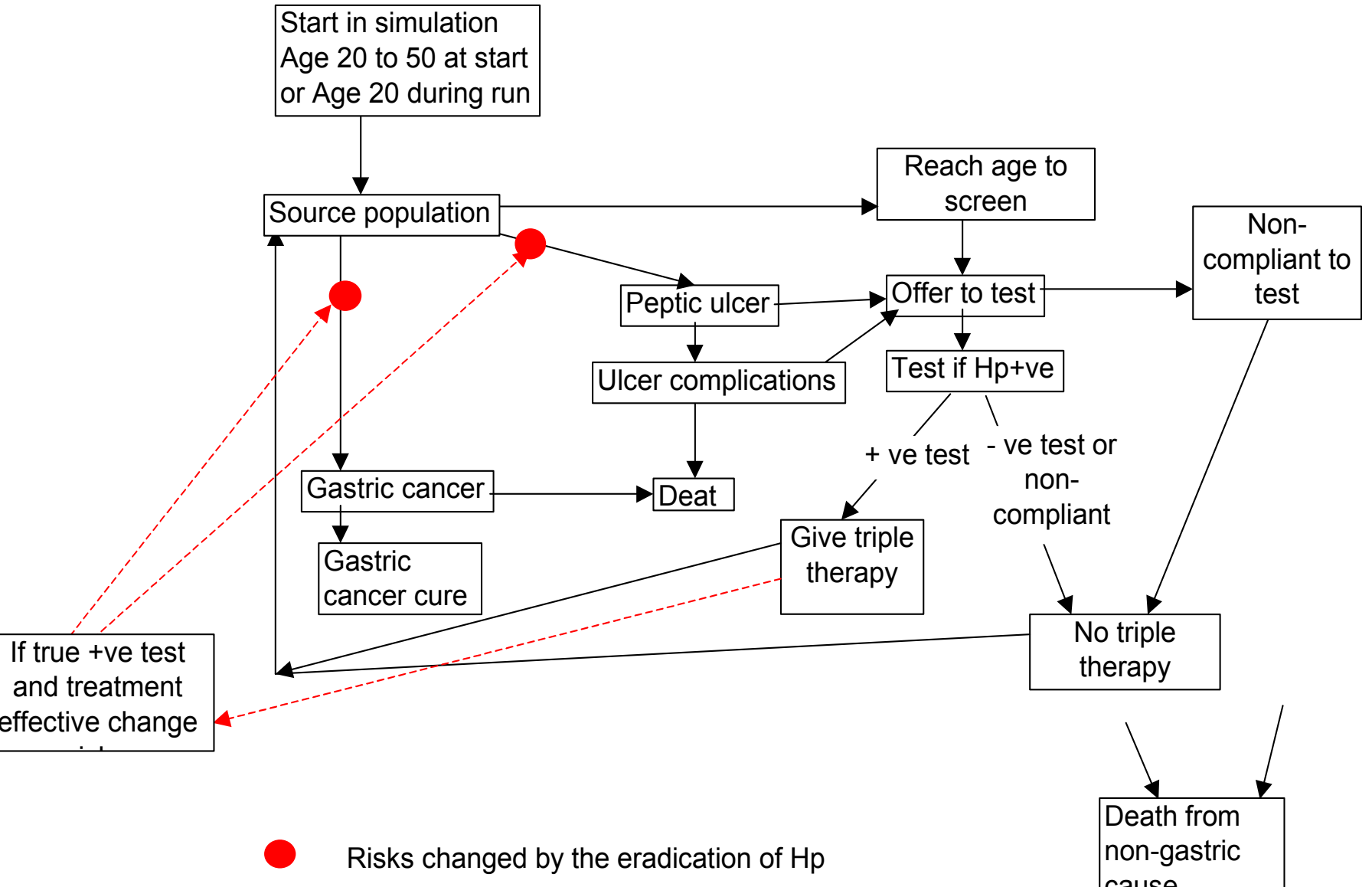
# CASE STUDY Helicobacter Pylori

- Bacteria which populate the stomach
- Affects approximately 50% of those now 60 years old but only 15% or fewer of 20 year olds
- Is implicated in gastric and duodenal ulcers
- Is thought to be responsible for much gastric cancer

# Should we screen and eliminate Hp?

- Screening for Hp fulfils some of the criteria for screening programs:
  - burden of disease (gastric cancer, peptic ulcer)
  - test available – blood test or saliva test
  - effective treatment – two antibiotics and proton pump inhibitor for two weeks.

Flow chart showing the effects of a screening program



## Characteristics of the model

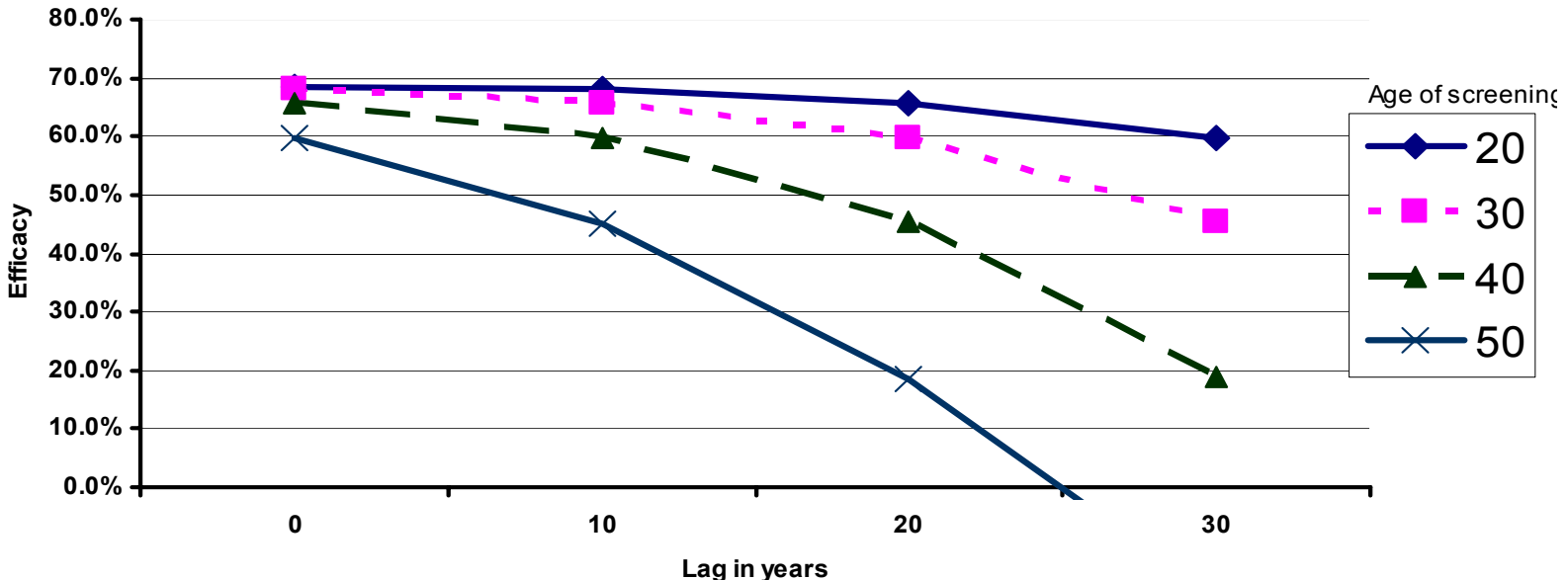
### Ulcers

- Ulcer – some to hospital – some of those to death;
- Test, if Hp+, treat, if eradicated, reduce relative risk of next ulcer and of cancer.

# Characteristics of the model

## Cancer

- If patient goes from Hp+ to Hp- then increase time to cancer, subject to a lag.
- Lag ensures that those about to get cancer do not benefit.



# Is it cost-effective to screen?

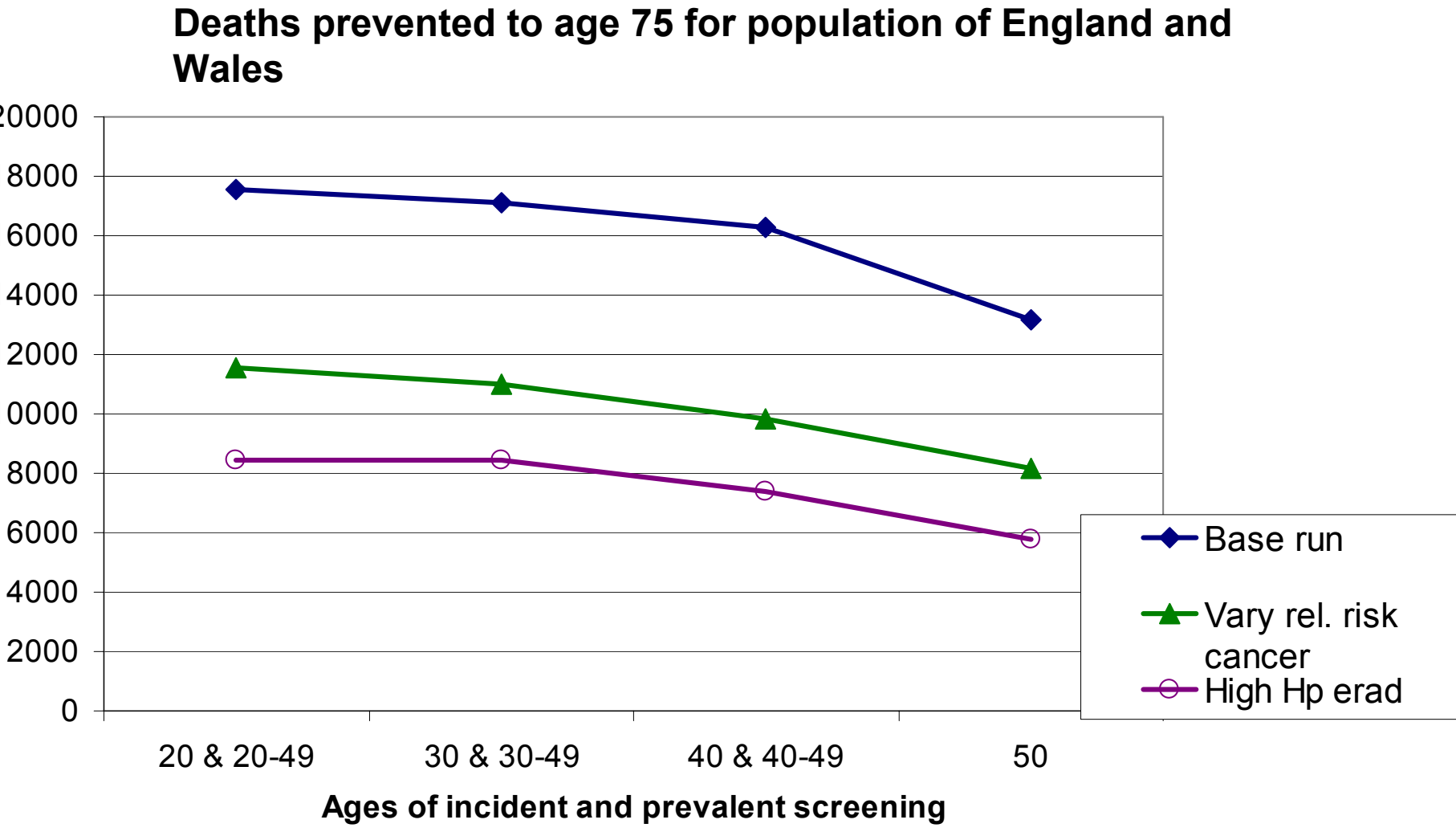
But……

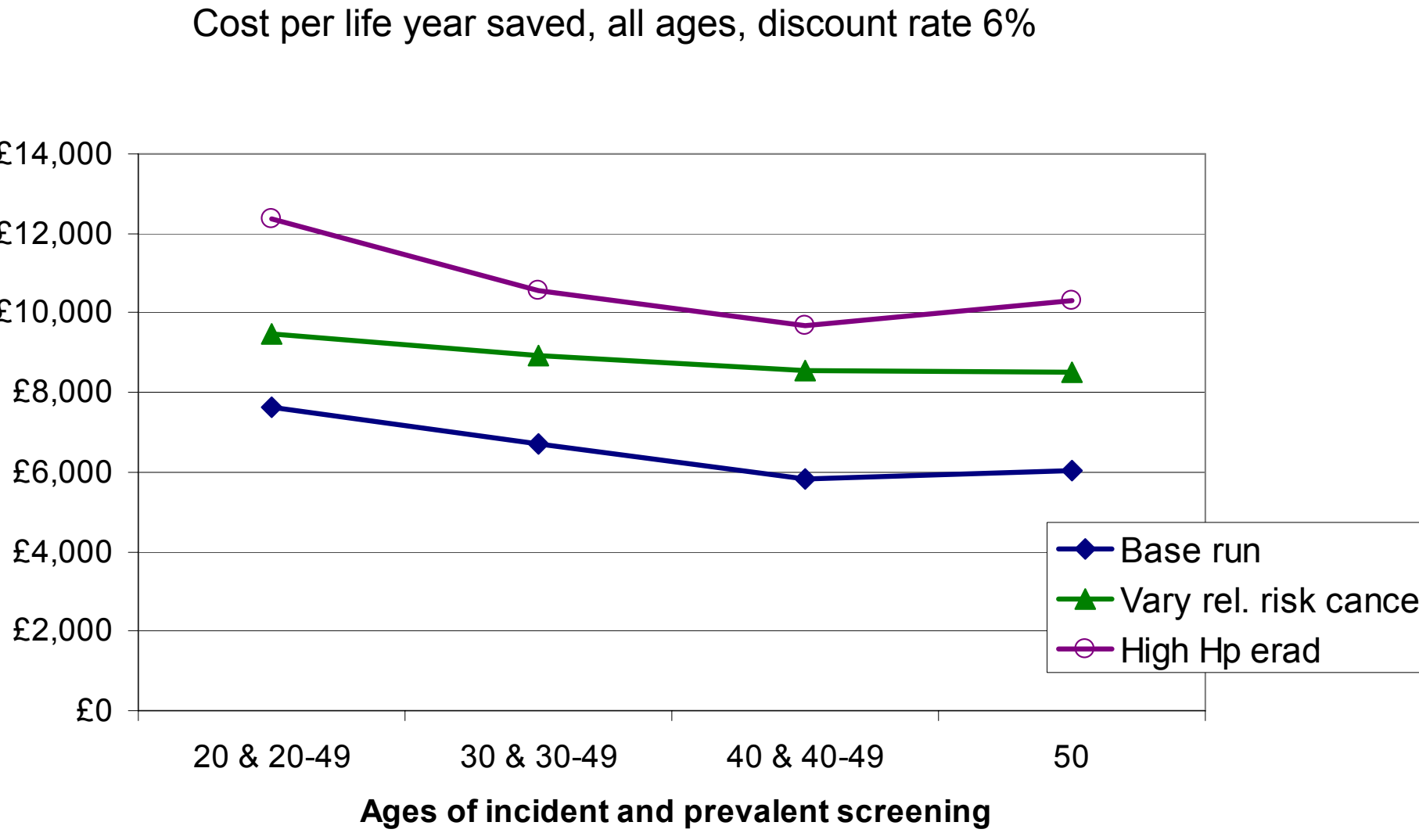
At what age?

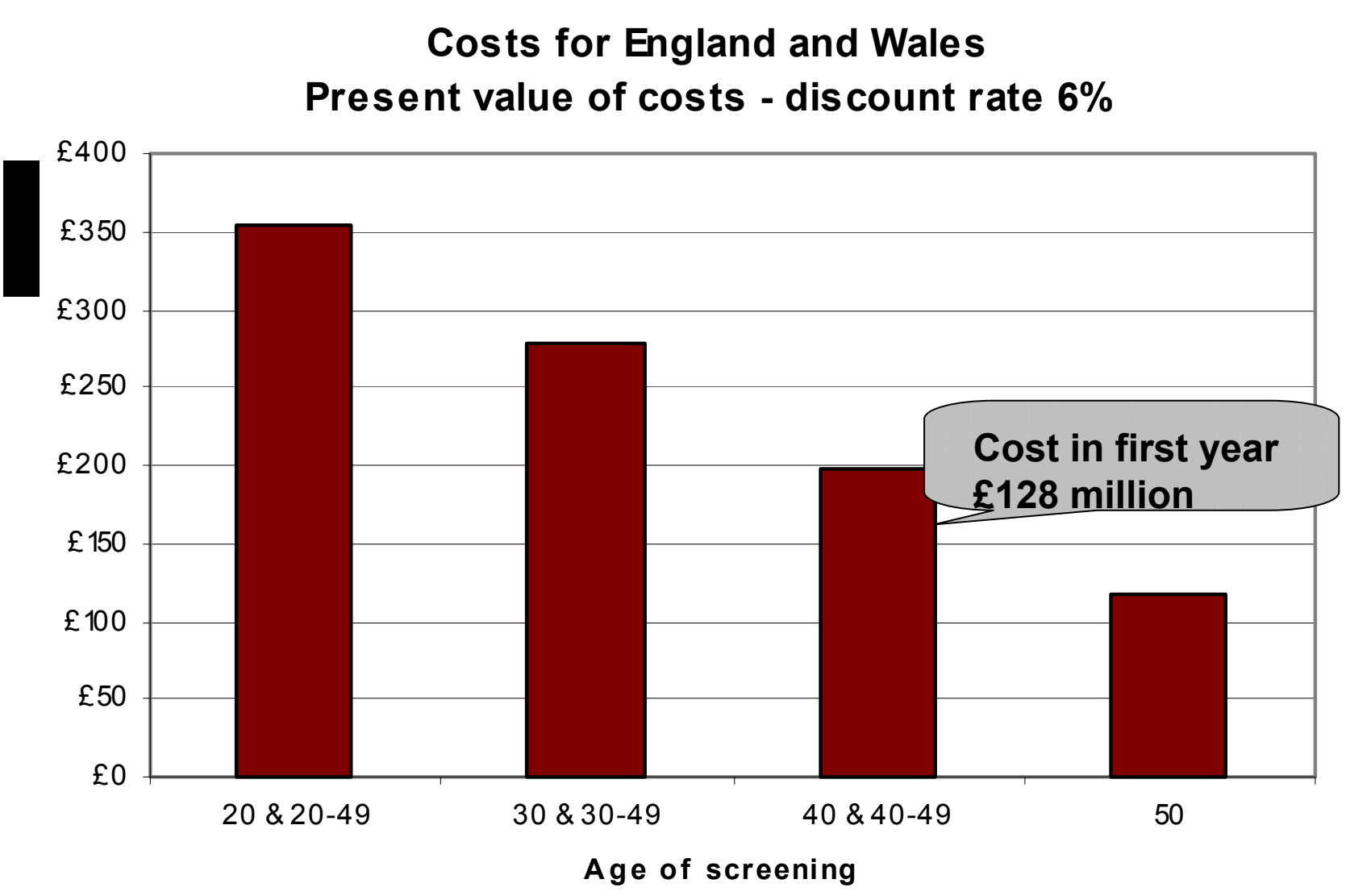
What do we do with the prevalent unscreened population?

What assumptions have we made about the opportunistic treatment?

What will it cost and how soon will we have pay-back?


Deaths prevented to age 75 for population of England and Wales
20000
8000
6000
4000
2000
0000
8000
6000
4000
2000
0
20 & 20-49
30 & 30-49
40 & 40-49
50
Ages of incident and prevalent screening
Base run
Vary rel. risk cancer
High Hp erad


Cost per life year saved, all ages, discount rate 6%
£14,000
£12,000
£10,000
£8,000
£6,000
£4,000
£2,000
£0
20 & 20-49
30 & 30-49
40 & 40-49
50
Ages of incident and prevalent screening
Base run
Vary rel. risk cance
High Hp erad


Costs for England and Wales
Present value of costs - discount rate 6%
£400
£350
£300
£250
£200
£150
£100
£50
£0
Cost in first year
£128 million
20 & 20-49
30 & 30-49
40 & 40-49
50
Age of screening

# Variability

Needed 3 million individuals, aged 20 to 50 for statistical significance between no-screening and screening scenario

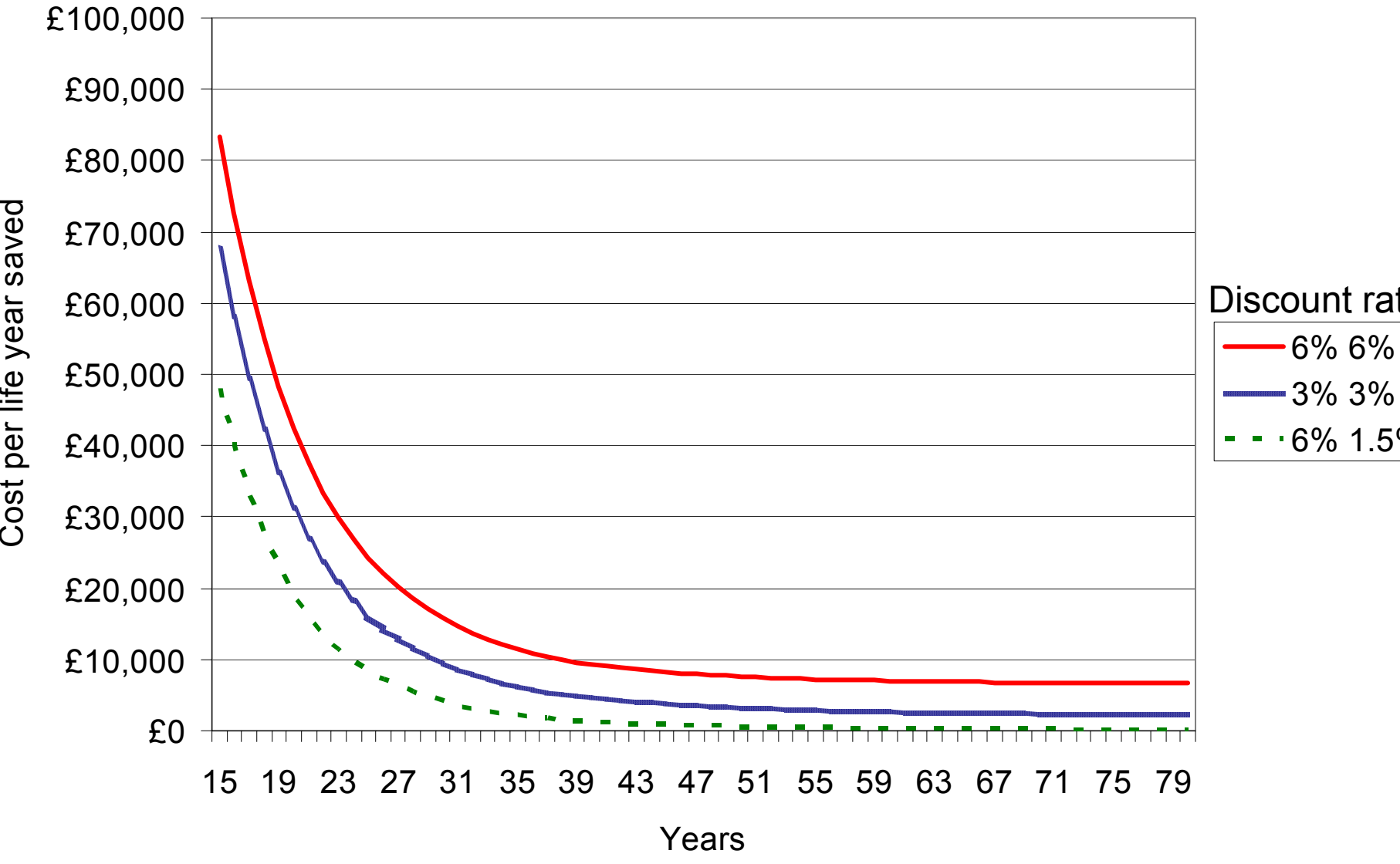
Screening at 40 years -170 deaths prevented in a population of 500,000 (population of Sheffield) over 80 years. Most after 20 years. Many years no deaths prevented.

# CPLYS – screening at 40 years

| Upper age limit | Deaths prevented | Life years saved | CLYS no averted costs, no disc | CLYS with averted costs, no disc | CLYS no averted costs, disc 6%. | CLYS with averted costs, disc 6%. |
|---|---|---|---|---|---|---|
| 75 | 16,263 | 130,315 | £4,402 | £1,593 | £15,553 | £10,924 |
| 85 | 27,684 | 270,949 | £2,117 | £700 | £10,155 | £6,834 |
| None | 34,456 | 368,045 | £1,559 | £334 | £8,799 | £5,866 |

**CPLY maximum 50,000 in sensitivity analysis of parameter input**

# Accumulated cost per life years saved over different numbers of years
## Screening at 40 years



# Why simulation?

- Prevent explosion of states → Age, Hp status
- Incorporates risk factors which change over time for individuals → Interaction between opportunistic interventions and screening giving incremental cost effectiveness
- Variability → Large random variation in benefits between populations and over time
- Interaction → Not present

# Why simulation? (cont)

- More complex modelling → Use of time delay in onset of cancer gives overall effect of screening and describes age dependent efficacy of treatment
- Time advance over many years → Models lifetime disease, treatment, costs and CE
- Time advance over many years → Shows changes in cumulative CE over time.
- Can explore a range of output → Proved to be valuable.

## Simulation run times

Simulation lengthy to run

- need to compare difference from base case scenario;
- used variance reduction (common random numbers);
- possible to model patient by patient if no interaction.

Need many runs to

- investigate sensitivity of model to uncertainty in input parameters (probabilistic sensitivity analysis)
- derive “best” scenario

## Analysis of output in various ways showed CLYS to be dependent on:

- age of screening,
- opportunistic activity,
- random effects – population by population,
- upper age for life years saved,
- discount rates,
- time horizon for calculations.

ARRIVES AT DIFFERENT CONCLUSIONS FROM OTHER STUDIES.

# Need for Research

- Appropriate model for particular problem
- Development of user friendly, efficient simulation software for this type of problem
- Range of output necessary/ desirable for evaluating screening and treatment for policy decisions
- Development of easy-to-use meta-models

# References


- Paper
- Davies R, Roderick P, Raftery J. The evaluation of disease prevention and treatment using simulation models. *European Journal of OR*. 2003, 150:1, 53-66.
- Book
- Robinson S. Simulation. The practice of model development and use.  2004, Wiley, Chichester