MONTE CARLO SIMULATION

Increasing Flexibility of the Simple Cohort Model

Three extensions

- The combination of decision tree and cohort model
- Adding time dependency
- Loosening the memoryless restriction of the simple cohort model

Combining Decision Trees and Markov Models

- Markov models are just a form of recursive decision tree
- These can be joined by using Markov cycle trees

Time dependency in Markov Chains

There are ways of letting transition probabilities change over time

Example: Probability depends on the age of the cohort

The cohort is homogeneous (i.e. They are all at the same age)

State the starting age of the cohort

Use the keyword *_stage* in Tree Age pro to define probability as a function of the cohort age

Age dependent probabilities might be taken from national life tables

Monte Carlo Simulations

There are two types of Monte Carlo simulations

- First order MC Simulation (referred to as Trials or Microsimulations)
- Second order MC Simulation

- Both represent uncertainty that is not addressed in deterministic analysis (deterministic analysis uses point estimates for the parameters, e.g. Prevalence=0.5, sensitivity=0.75)

- However first and second order MC Simulations represent different types of uncertainties

For example

FOMCS

- If probability=50% then there is a 50% chance of event occurring

SOMCS

- Uncertainty about the true probability (is it 48% or 50 % or 52%?)
- In some trials it is 48% in some 50% and in some 52%

First Order MC Simulation

- Also referred to as Trials (Microsimulation)
- Addresses stochastic uncertainty (individual variability)
- Movement of multiple individuals through tree using results of random number generation and probabilities
- Probability that individuals go one way or another in a chance node is based on probability of that node
- (e.g. If probability of a disease is 80% then on average 800 in 1000 individuals will end up in the diseased “bin”)

First order Monte Carlo simulation

- Adds uncertainty to the model
- Uncertainty does not come from the parameter estimates themselves (point estimates are assumed to be known with certainty. e.g. p=0.5)
- Reported variance results from random walks
- These variance values are not sufficient for confidence interval estimation

Tracker Variables

Markov Property: No memory

The stochastic process is fully described by
- The current state
- The transition probabilities

•This strict property can be relaxed. Information can be maintained by tracking events as values in variables (tracker variables).

•Therefore, discrete events can be used to calculate state transition probabilities or rewards.

•This can be done using first order MC Simulation

First Order MC Simulation

- First order MC enables us overcome the Markovian property
- One can increase the number of states to save information (i.e. keeping history of the patient)
- However this might results in a “state explosion”, which eventually makes the model prone to errors
- Tracker variables offer an attractive way to incorporate discrete events to Markov models

(more on this later if time allows)

- First order MC can also be used to reflect heterogeneity in patient populations

Tracker Variables

- Used as the "memory" of the individuals, tracking their characteristics and individual disease stories
- Different types of tracker variables
  - Event counters
  - Trackers that only memorize current states
  - Trackers that memorize patient history and determine subsequent transition

Running MC Simulation

- If you want your results to be reproducible use seed
- \seeding\seed random number generator

Second order MC Simulation

- Addresses parameter uncertainty
- An example is probabilistic sensitivity analysis of cost-effectiveness models
- Probabilistic Sensitivity Analysis explores the joint effect of parameter uncertainty on the result, when randomly drawing from all distributions simultaneously

Sensitivity Analysis

There are several ways of undertaking a sensitivity analysis

- One-way sensitivity Analysis
  - The simplest form: Change one variable at a time and examine the impact of such a change
- Multi-way Sensitivity Analysis:
  - Change multiple parameters simultaneously, examine the results for each potential combination
  - Presentation and interpretation becomes difficult as the number of parameters increases
  - Extreme cases can be considered: the optimistic case, the pessimistic case etc.
- These are deterministic sensitivity analysis techniques
- So far we have only considered deterministic sensitivity analysis

- Deterministic Sensitivity Analysis
  - Each parameter is assigned a point estimate value
  - Requires variables
  - Calculate the expected value based on range/intervals of uncertain outputs
  - Repeating gives the same results

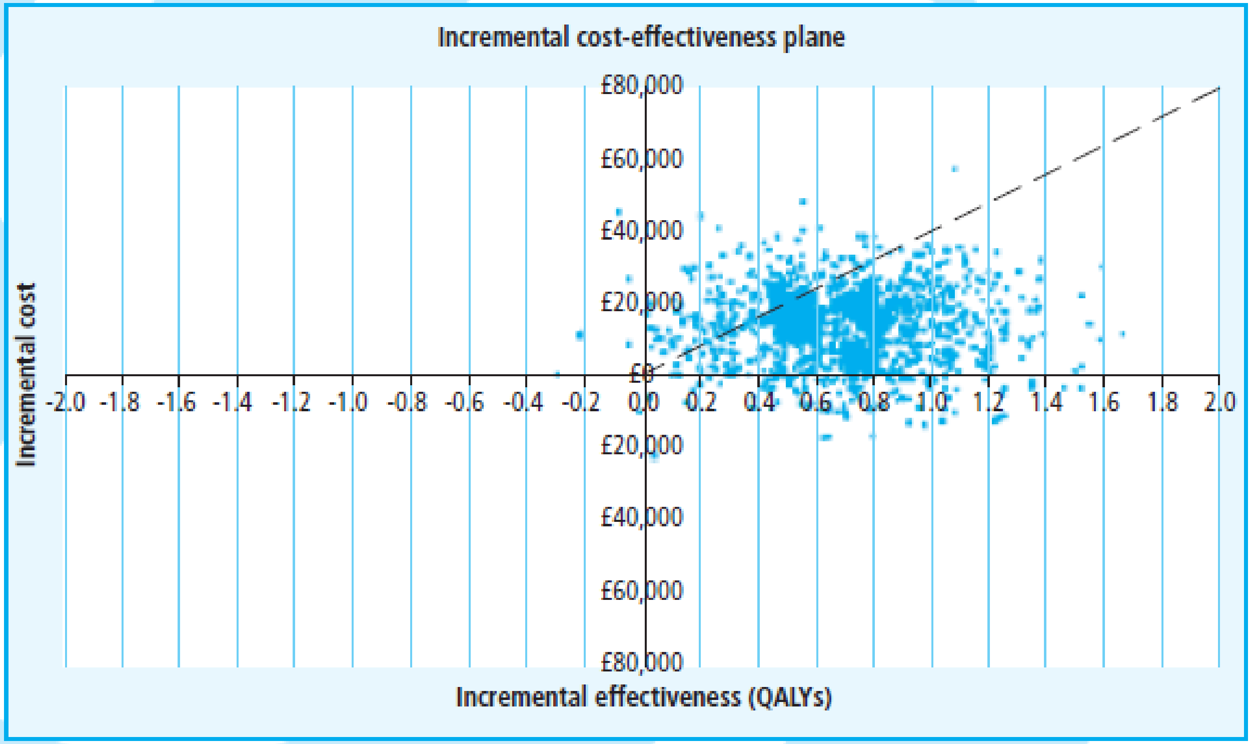
- Probabilistic Sensitivity Analysis
  - Assigns a distribution to the parameters in the model
  - Requires distributions
  - Calculates the expected value based on random samples for uncertain inputs
  - Repeating yields different results from different sampled input values

Probabilistic Sensitivity Analysis

- Each time the model is run the software randomly selects one value for each parameter and record the model's results
- The model is run a great number of times, the results are recorded each time
- At the end the variation in results is presented
- The results are typically depicted using
  - A cost effectiveness scatter plane: The incremental cost and effectiveness values for each iteration are plotted
  - A cost effectiveness acceptability curve

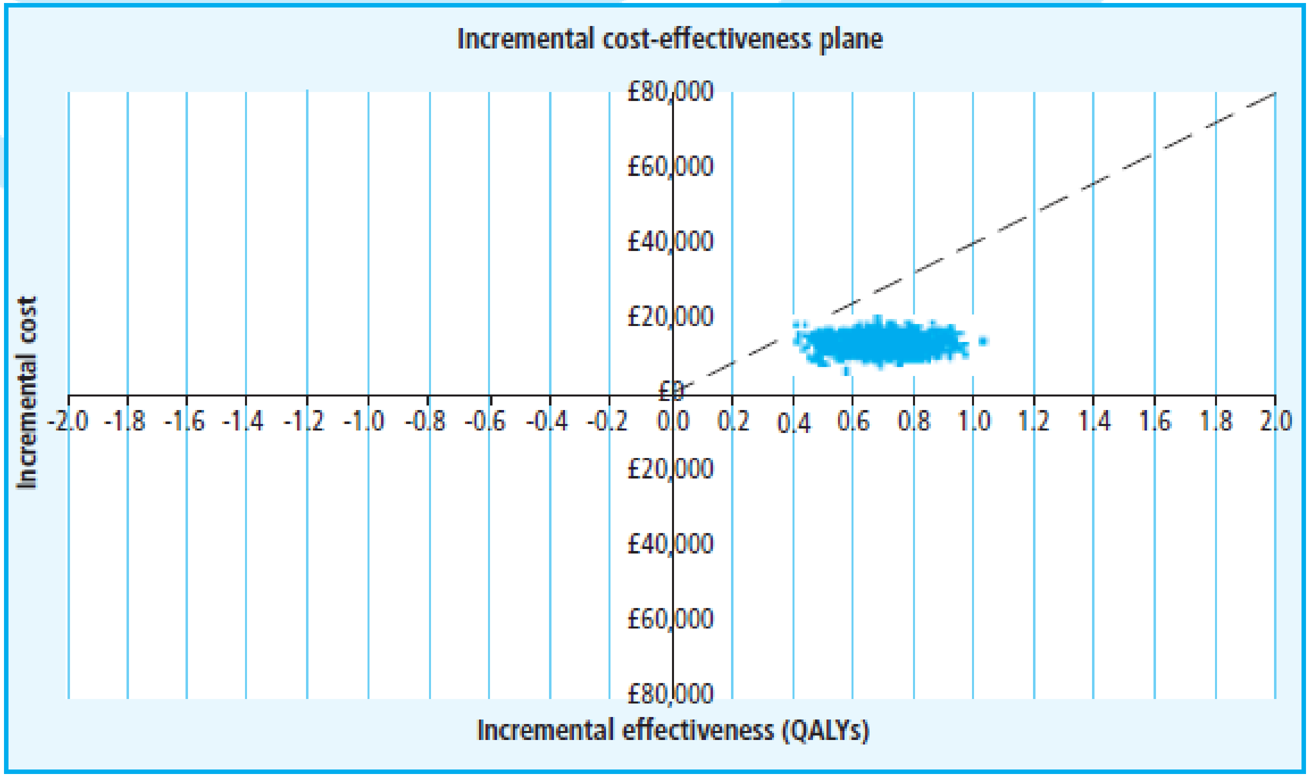
Cost effectiveness scatter plane

Figures 3a and 3b.
Cost-effectiveness scatter planes



http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/What_is_sens_analy.pdf

Cost effectiveness scatter plane



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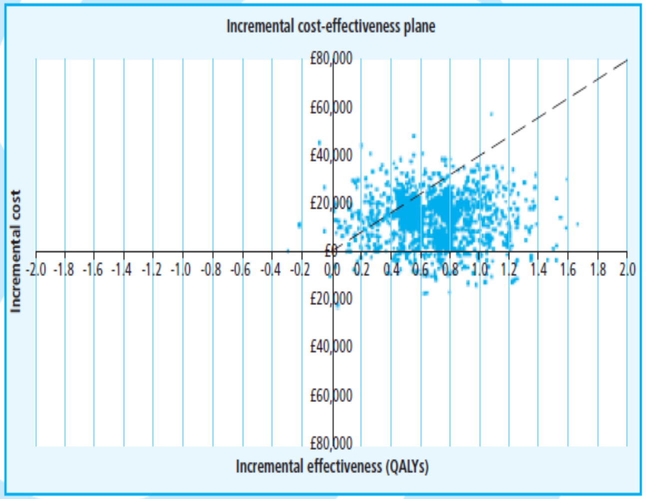
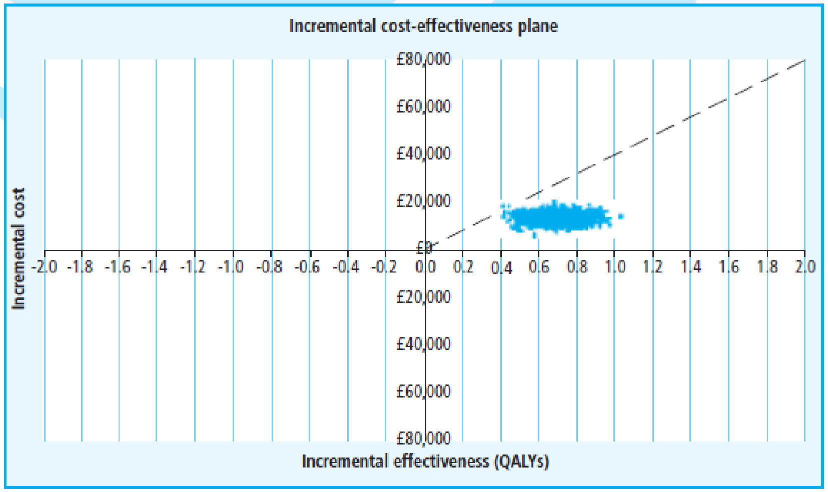
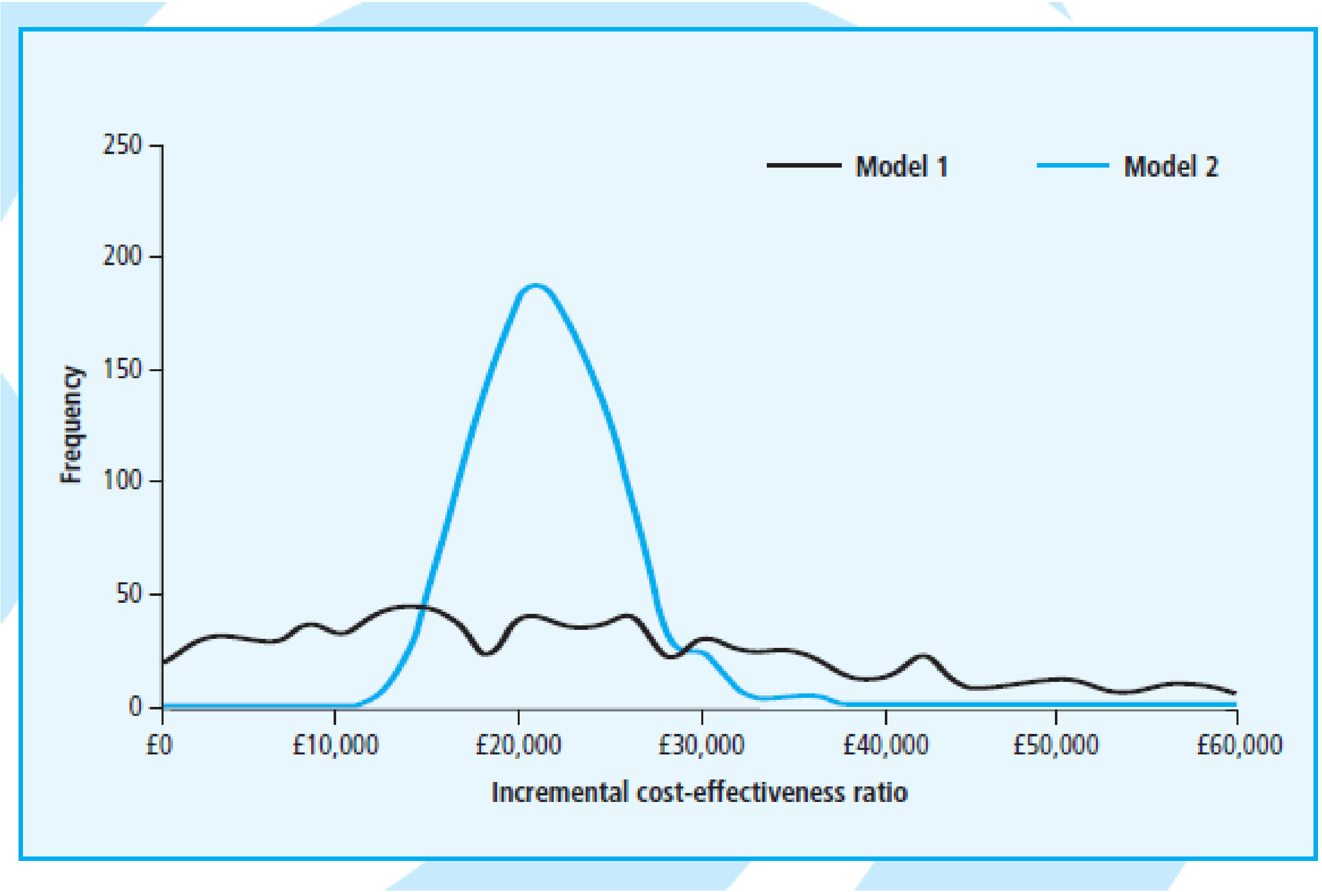




Note that the *average* results are identical

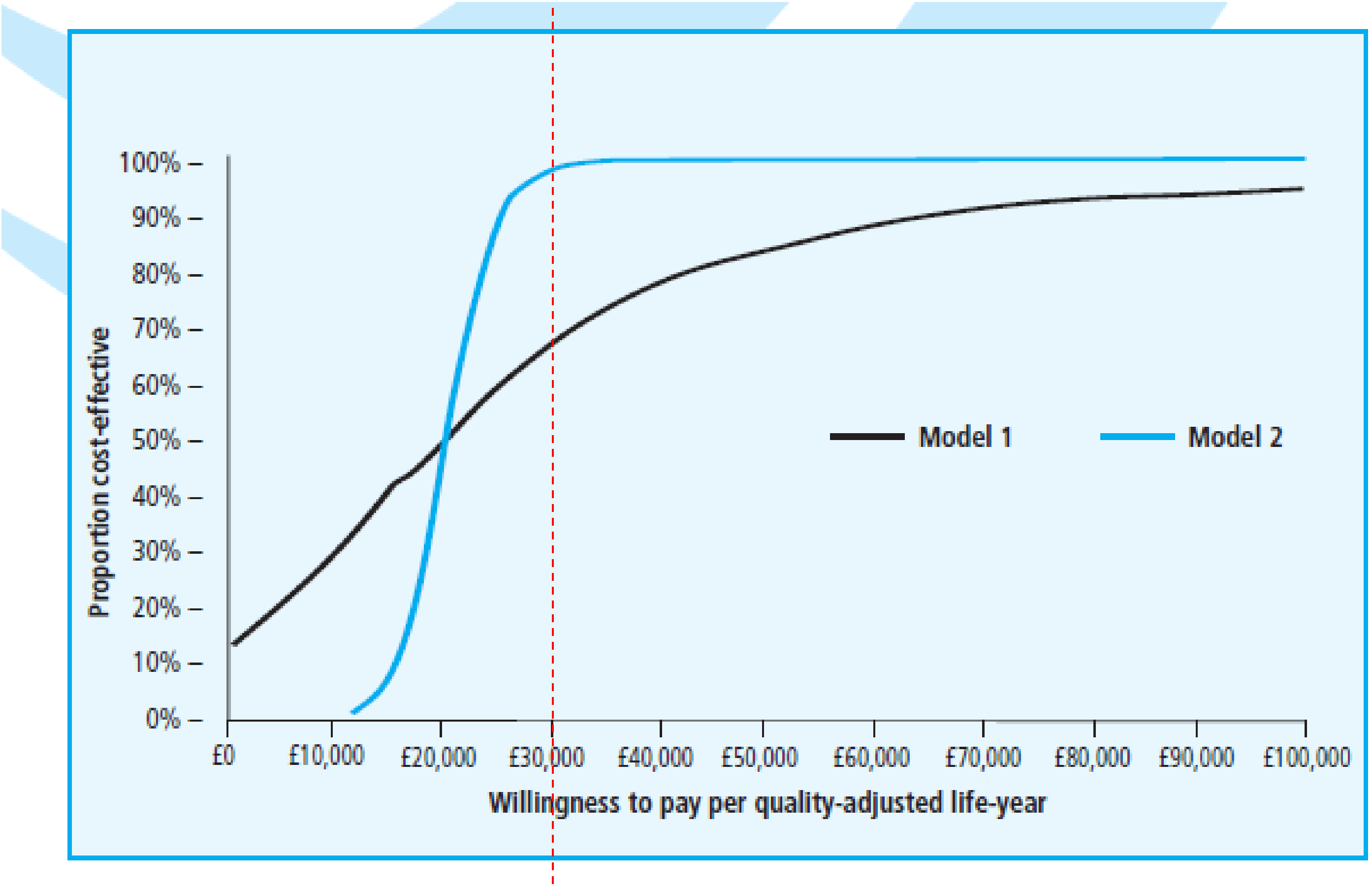
http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/What_is_sens_analy.pdf

Range of cost effectiveness ratios



Can be used to give an indication of the proportion of iterations in each model that provide results below a prespecified cost-effectiveness threshold

Cost Effectiveness Acceptability Curve



For each threshold value (on the X axis) we can see the percentage likelihood that the cost-effectiveness of the technology will fall below that threshold (On the Y axis)

- Even though the average cost-effectiveness in each model is the same, the decision maker can have more confidence on the results of model 2.

Probabilistic Sensitivity Analysis

- More robust
- More parameters
- More recalculations
- More interpretation

To sum up,

- Parameters are defined using probability distributions
- At each iteration
  - Sample parameter value from each distribution
  - Calculate expected values for tree using sampled values
- Repeat for a predefined number of iterations
- Examine results
  - Mean/Median of EVs
  - Distribution of EVs
  - High/ Low EVs (extremes)
  - Confidence intervals

Some Distributions available in TreeAge Pro

- Normal
- Uniform
- Beta
- Triangular
- Dirichlet

Avoid distributions that can yield probabilities <0 or >1