Dealing with uncertainty in decision models

Susan Griffin

Centre for Health Economics, University of York

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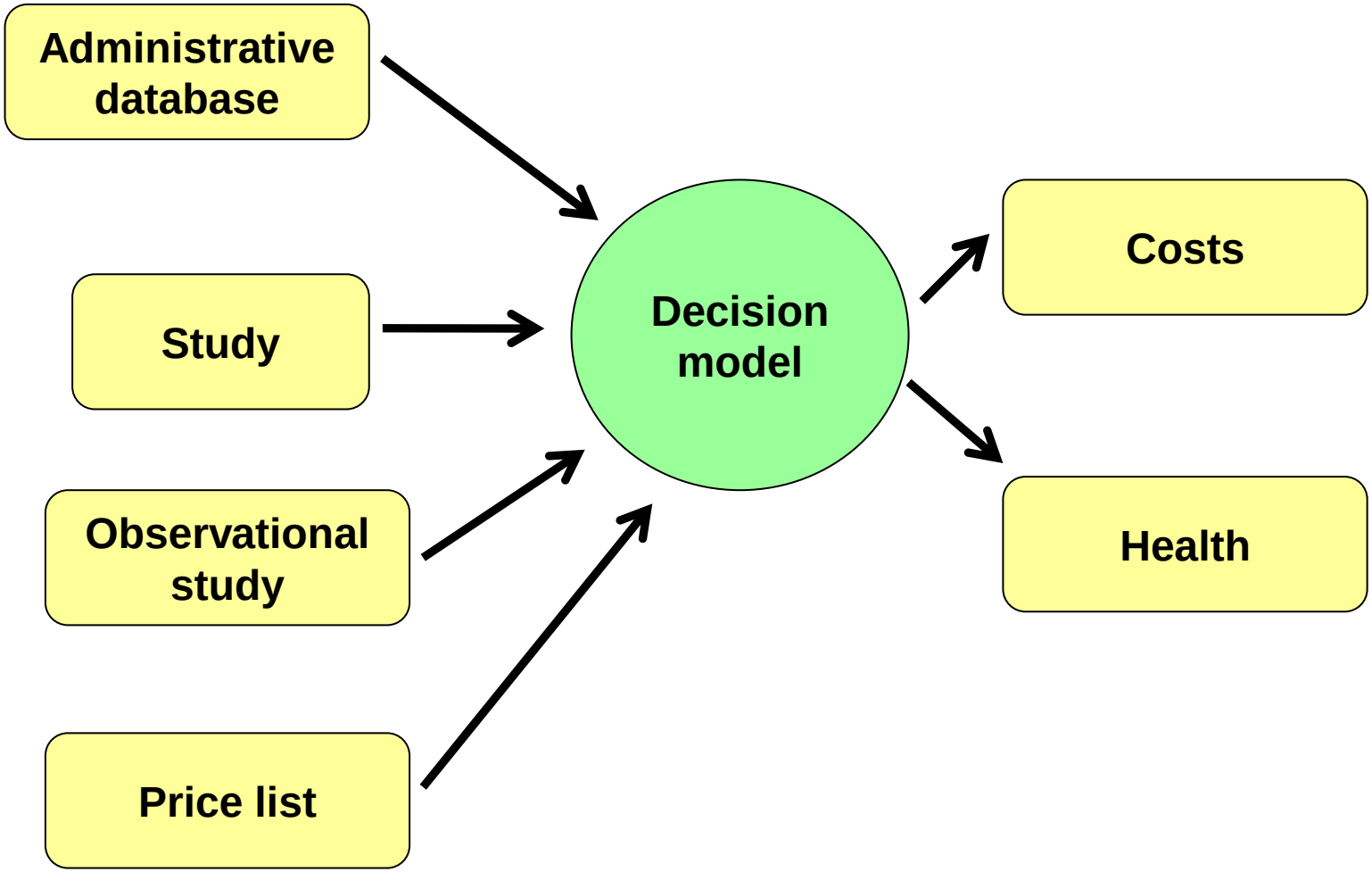
Economic evaluation in health care

- Decision problem
  - Which interventions to provide given resource constraints?
- Assess health gains and costs associated with alternative interventions
  - Utilise available evidence
  - Attribute differences to use of particular interventions
  - Reimburse set of interventions that maximises net health benefit

Evidence base



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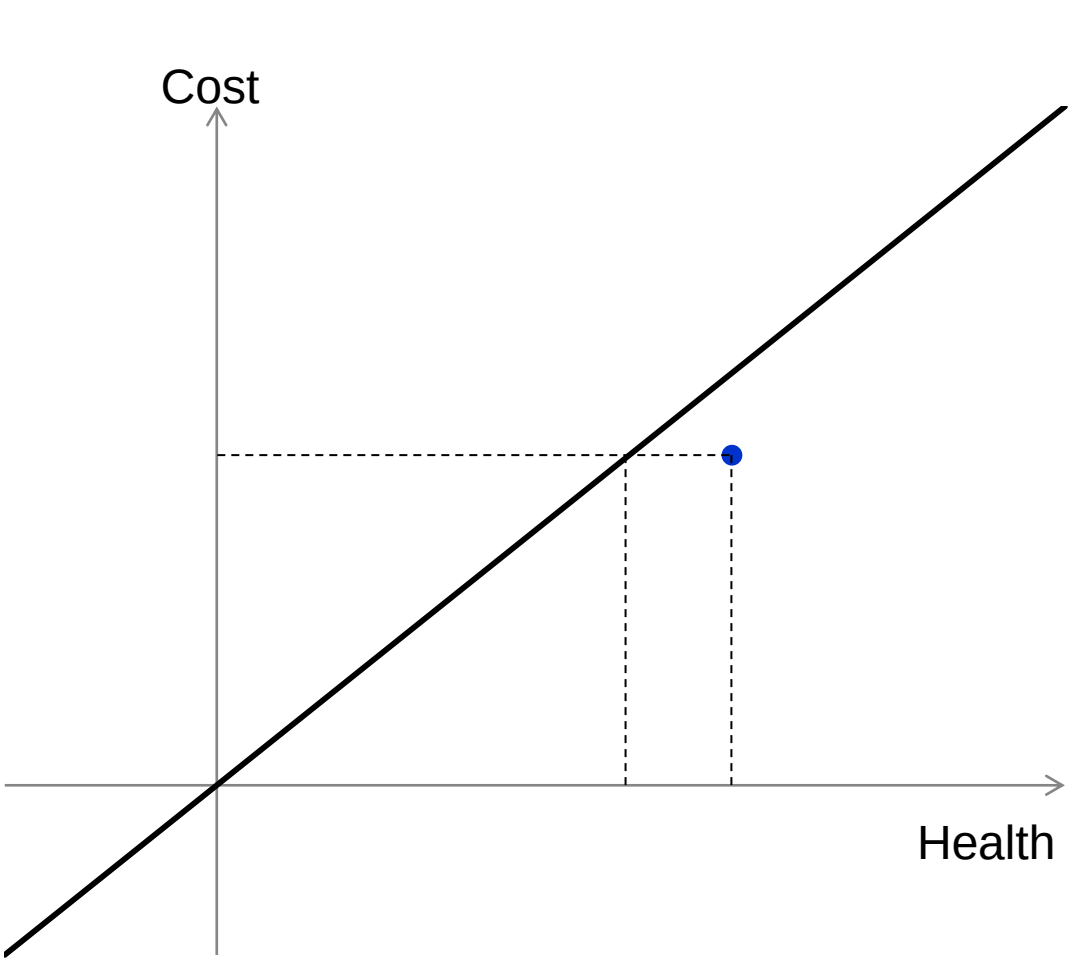
Cost-effectiveness plane



Rate at which existing activities generate health

- True value of health gains and costs of new alternative

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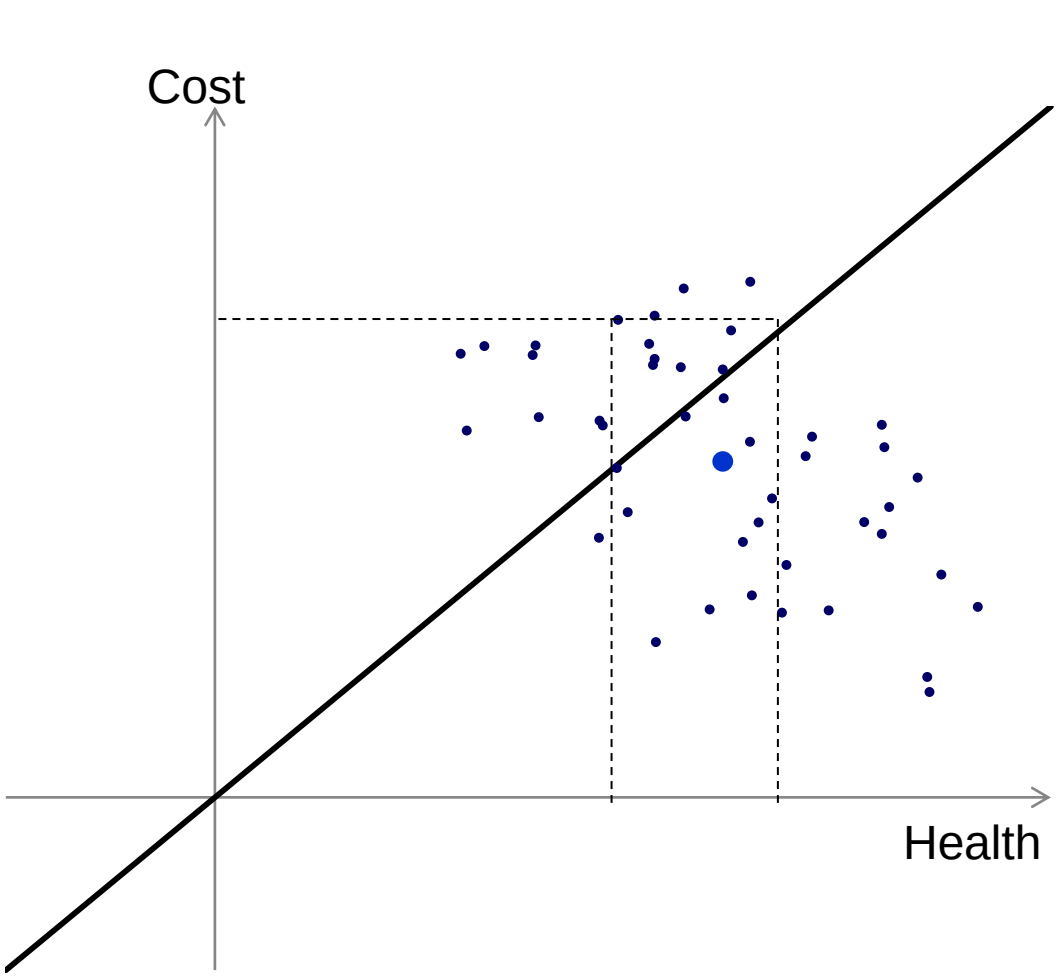
Uncertainty

- Stemming from incomplete knowledge
  - Which sources of evidence are relevant
  - Relationship between inputs
  - True/population values
- Reducible through further research
- Resolvable over time

Cost-effectiveness plane



- Possible values for health gains and costs for new alternative

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Sources of uncertainty

- Which sources of evidence
  - Internal validity, external validity, bias
  - Missing observations and outcomes
  - Sample size
- Relationship between inputs
- Value judgements

Relevant evidence for treatment effects

- Causal effects of interventions
- Internal validity
  - Impossible to directly observe health gains with intervention and health gains without
  - Ability to approximate counterfactual
    - E.g. RCT versus observational study
- External validity
  - Extent to which results in studied population hold true for target population
    - E.g. trial setting versus general practice

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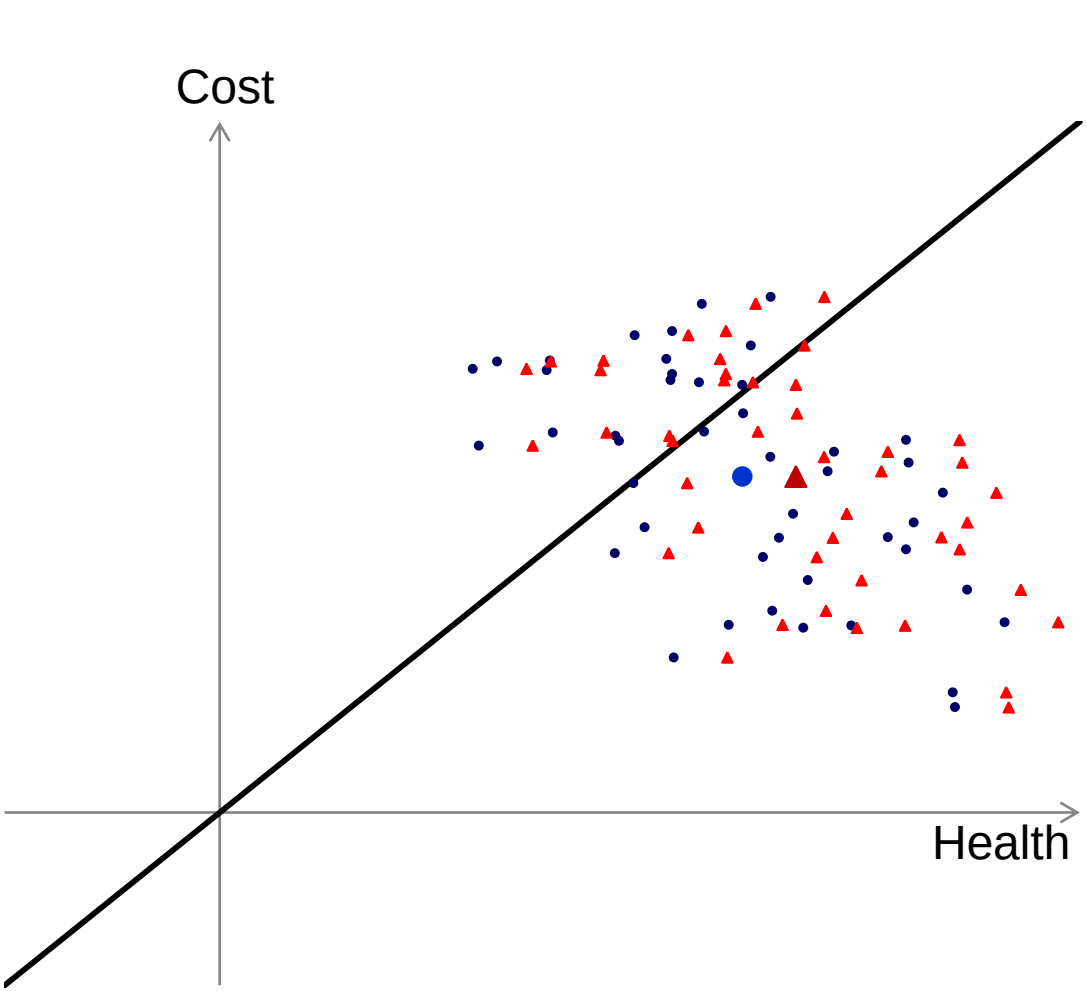
Relevant evidence for treatment effects

- Lack of validity indicates bias
  - Systematic difference between estimate and true value
  - Bias is source of uncertainty
- Missing observations
  - If not missing completely at random, complete case analysis will be biased

Cost-effectiveness plane



- Biased estimates of health gains and costs for new alternative

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Dealing with bias

- Eliminate or minimise
  - E.g. rely on RCTs for treatment effect if suitable
  - Adjust for selection bias in analysis
    - E.g. regression model, propensity score, IV, selection model
  - Utilise imputation for missing observations
    - E.g. multiple imputation
- Characterise as additional parameter
  - E.g. elicitation, informative prior

Relationships between inputs

- Several studies reporting same information
  - Meta-analysis
  - Generalised evidence synthesis
- Missing outcomes
  - Required for CEA, not measured directly
  - Expected survival: extrapolation
  - HRQL: cross-walks/mapping
- Decision model
  - Explicit framework
  - Assumptions, logical relationship between inputs

Structural uncertainty

- Modelling or structural uncertainty
  - Alternative model structures or assumptions could generate different results
- Model validity
  - Assess how accurately available info characterised
  - Typically no source for external validation
    - Value judgements
    - Can identify some models as invalid, but may not identify single best structure

Sampling uncertainty

- Inputs informed by sample data
  - Underlying population values estimated with uncertainty
  - Evidence supports a range of plausible values with varying degrees of likelihood
- Direct data unavailable
  - Cannot omit important variable from analysis
  - Elicitation

Dealing with uncertainty

- Describe range of
  - True values of inputs
  - Possible relationships between inputs
  - Value judgements
    - Describe outputs from alternative values deterministic sensitivity analysis
- Also describe likelihood of particular values
  - Probabilistic sensitivity analysis for parameters
  - Bayesian model averaging

Probabilistic sensitivity analysis

- Produces distribution of model outputs
  - Best estimates of mean costs and health outcomes non-linear model
- Estimate decision uncertainty
  - How likely is the decision to be in error?
  - What are the consequences of that error?
  - Attributable to uncertainty characterised for parameters

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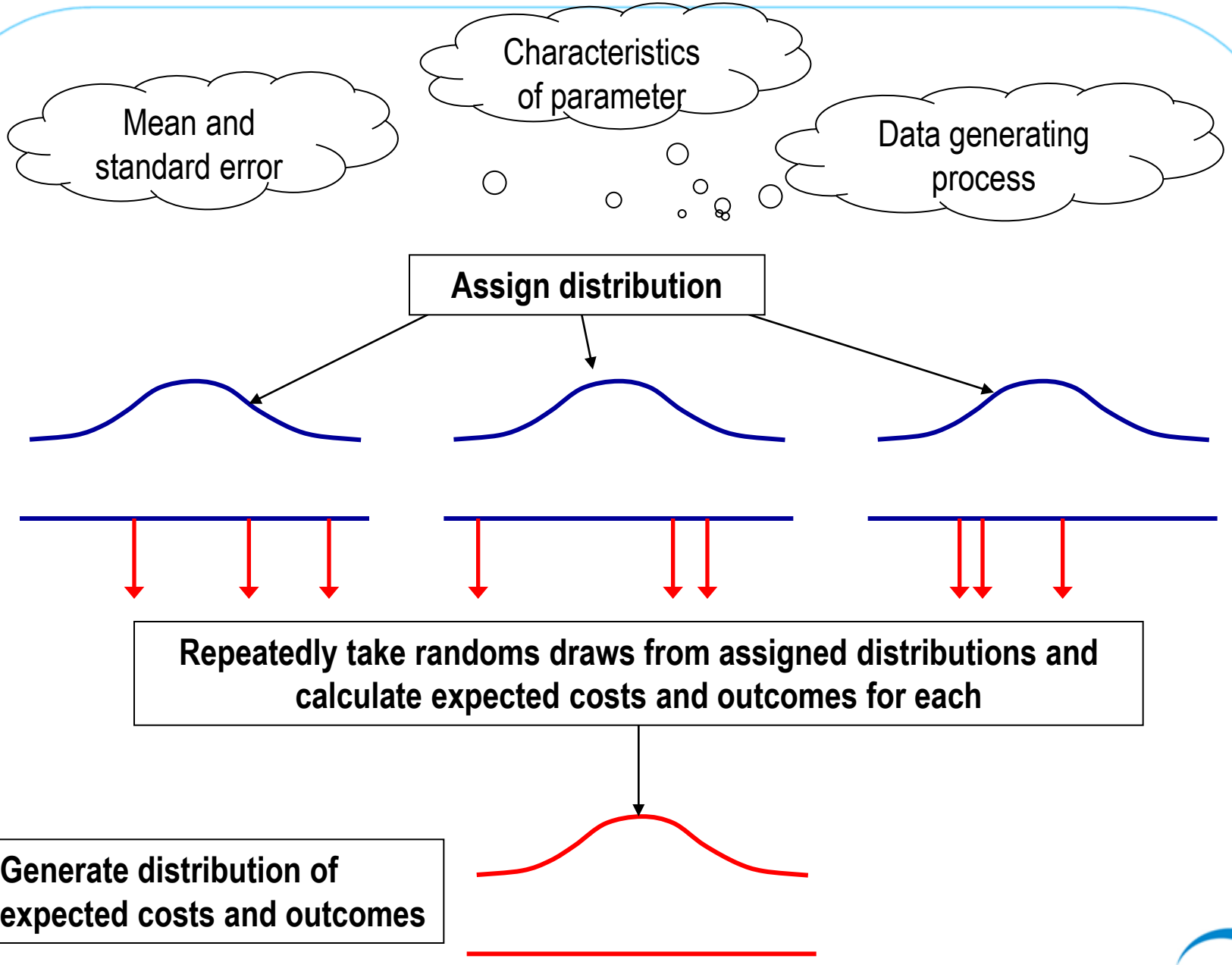
Mean and standard error
Characteristics of parameter
Data generating process
Assign distribution
Repeatedly take randoms draws from assigned distributions and calculate expected costs and outcomes for each
Generate distribution of expected costs and outcomes
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Why uncertainty?

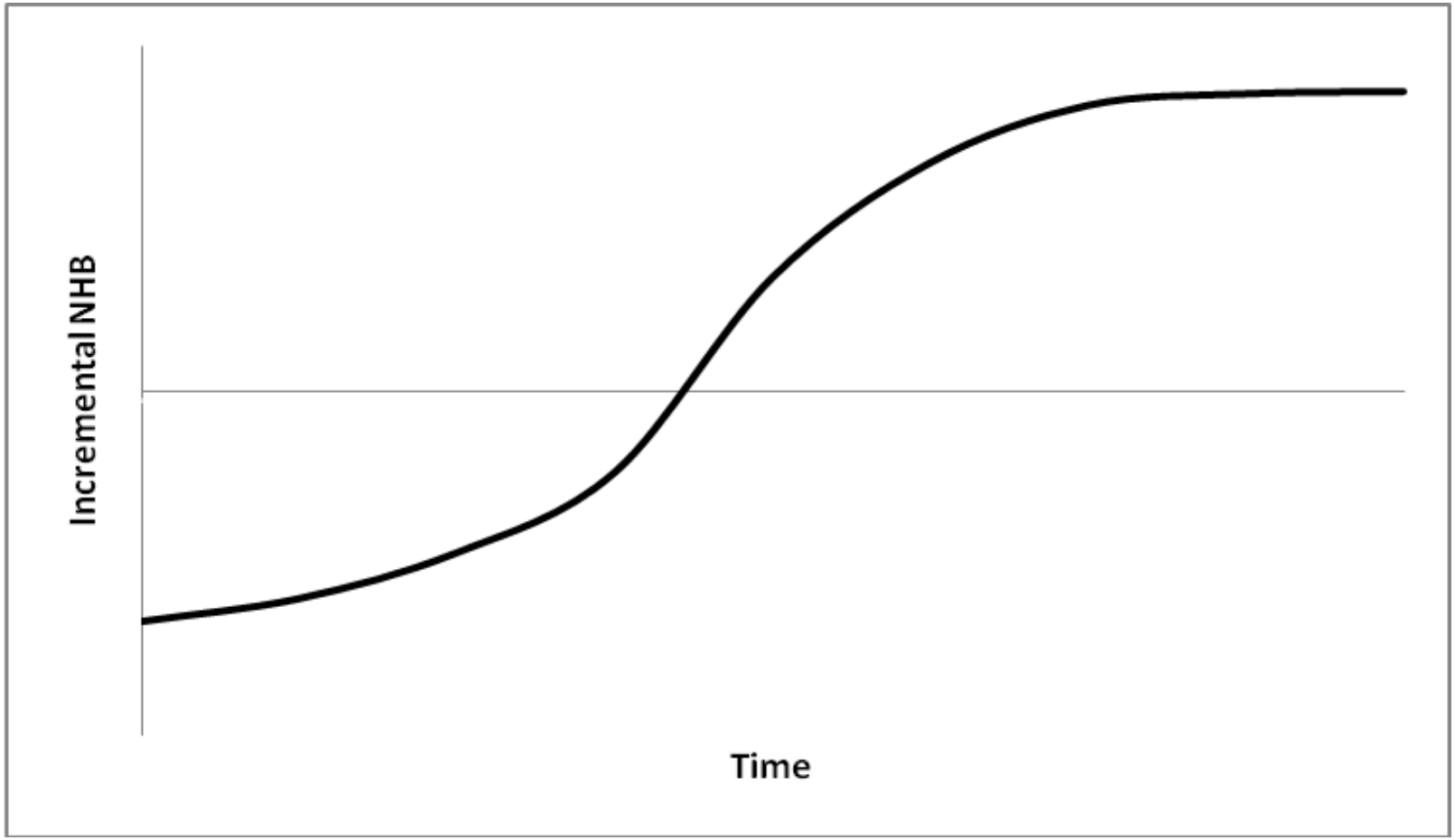
- Non-linear model
- Value of evidence
  - Is current evidence sufficient?
  - Is further research valuable?
- Consequences of uncertain decision
  - New evidence emerge suggesting change in decision
  - Resource implications: Investment/reversal
- Dependence between reimbursement and research
  - Value of information forgone
  - OIR, coverage with evidence development

Is evidence sufficient?

- Additional evidence expected to reduce decision uncertainty
  - Reduce probability of error
  - Reduce opportunity cost of uncertainty
- Compare expected improvement in health gains with reduced uncertainty to cost of research
  - Perfect information: EVPI, EVPPI
  - Imperfect information: EVSI, ENBS

Impact of uncertainty

- Investment cost
  - Sunk costs, irrecoverable if decision changed
  - Gains from new technology must be sufficient to outweigh investment cost
- Reversal cost
  - Incurred only when decision revised
- Characterising uncertainty helps estimate likelihood of change
  - Additional info on when new evidence could emerge



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Interaction between research and reimbursement

- Some research not possible once technology in widespread use
  - Approval removes option to collect further evidence
  - Value of information forgone
  - Compare to opportunity cost of delaying access (OIR)
- Some research easier after approval (AWR)
- Reimbursement decision conditional on uncertainty
  - E.g. Patient access schemes, risk sharing

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Summary

- Uncertainty inherent to resource allocation decisions
  - Regardless of whether based on formal or informal analysis
- Characterisation of uncertainty essential to inform reimbursement decisions
  - Appropriate response to uncertainty required to achieve best possible health outcomes
  - Even for decision maker with remit for reimbursement not research

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