Economic modelling of diagnostic innovations:

Early detection/prevention of neutropenic sepsis in cancer patients: a cost-utility evaluation

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Overview

- Decision problem
- Background
- Methods
- Results
- Conclusion
- Acknowledgements:

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- Chris Price – Visiting Professor in Clinical Biochemistry, Department of Primary Care Health Sciences, University of Oxford.
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- X-lab NETIMIS team.

Decision problem

- When conducting an economic evaluation the first step is to define the decision problem:
- Is home monitoring for early detection/prevention of side effects (myelosuppression, neutropenia) resulting from chemotherapy cost-effective in the UK?
  - Intervention: Home monitoring of patients undergoing chemotherapy
  - Comparator: No home monitoring (current practice)
- Breast cancer patients treated with adjuvant EC90
- Perspective: English National Health Service
- Outcome: Quality adjusted life years (QALYs) saved

Why an economic evaluation framework?

- Healthcare decision making is complex
  - Wide range of diseases, interventions, consequences, and considerable uncertainty
- Coherent framework that evaluates available evidence while considering all uncertainties
- Economic evaluation:
  - Premise: scarce (health care) resources
  - Aim: maximise health gain with available resources
  - Method: compare cost and effectiveness of interventions
  - Explicit, objective way of making choices

Comparative framework

- Interested in **incremental costs and outcomes**
- Can be expressed as an incremental cost-effectiveness ratio (ICER):

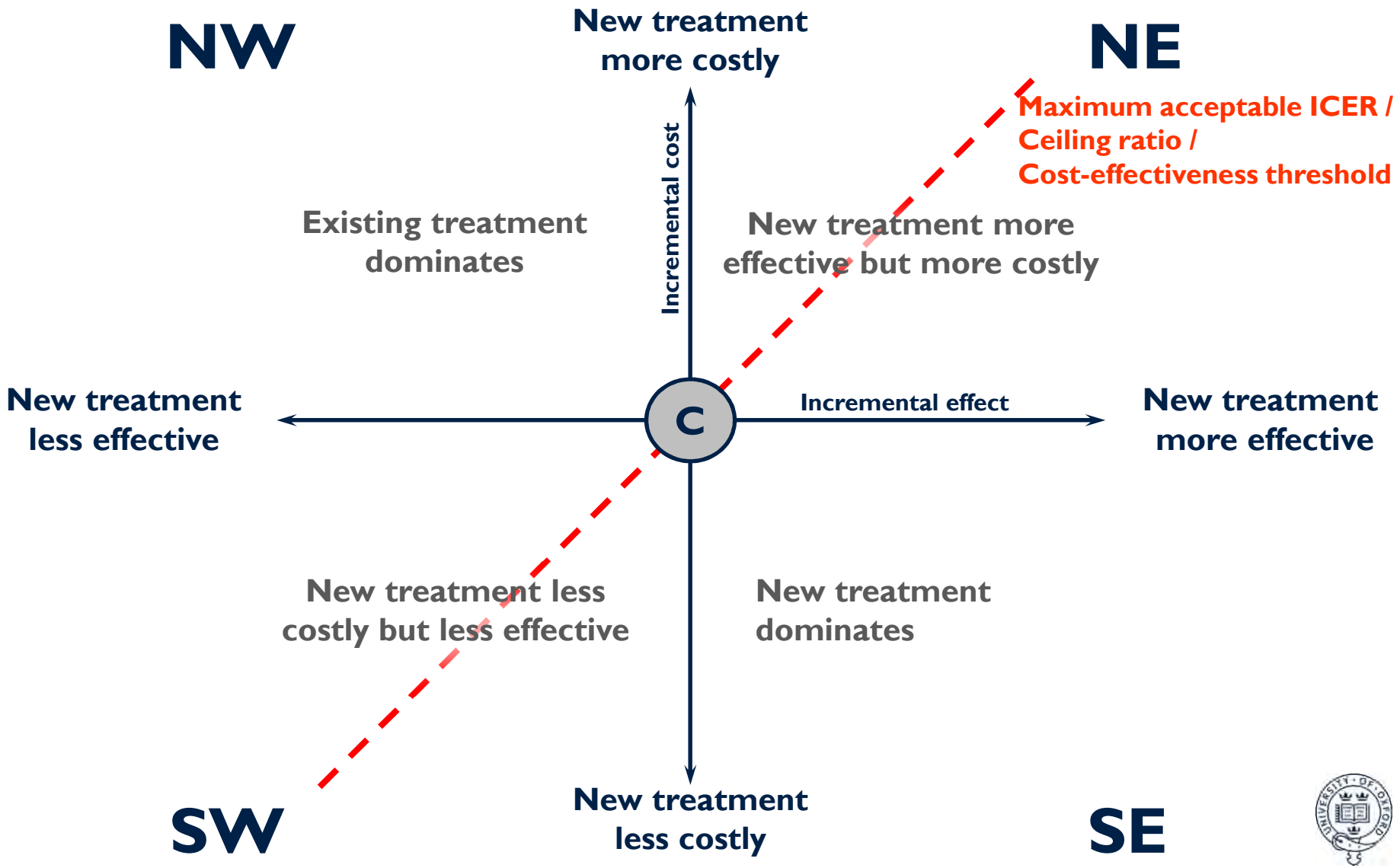
$$ICER = \frac{Cost_A - Cost_B}{Effect_A - Effect_B}$$

$$Cost_A = £15{,}030 \qquad Cost_B = £7{,}199$$

$$Effect_A = 7.15 QALYs \qquad Effect_B = 6.11 QALYs$$

- ICER= £7,485 per QALY

The Cost-Effectiveness Plane: two uncertainties



Maximum ICER: threshold

- National Institute for Health and Care Excellence (NICE)
  - £20,000 to £30,000 QALY gained
  - Intervention is cost-effective if below the threshold
  - No empirical basis for threshold
- Revealed preference approach (Claxton 2013)
  - English Programme Budgeting expenditure data by disease with modelling of outcomes
  - £12,936 per QALY gained
  - Health Technology Assessment Volume: 19 Issue: 14 (February 2015)
  - CHE Research Paper 81, University of York

Decision models

- Decision models used to undertake economic evaluation
- Structure the economic question and compare all relevant alternatives
- Combine available evidence from different sources
- Mean cost-effectiveness and quantify uncertainty in the decision

The problem

- Myelosuppression: a common and significant adverse effects associated with chemotherapy.
- Significant myelosuppression: may delay treatment, and in more extreme cases lead to hospitalisation with febrile neutropenia, neutropenic sepsis and ultimately death.
- Recurrent neutropenia may lead to dose reductions in subsequent cycles which may adversely affect the efficacy of the treatment.
- A modest degree of myelosuppression may be used as a marker of adequate chemotherapy dosing

The problem

- No practical way to regularly monitor changes in white blood cell (WBC) or neutrophil count over the course of the chemotherapy cycle (unless the patient is in hospital).
  - Immediately before chemotherapy, and mid-cycle as a consequence of symptom-led emergency admissions, e.g. suspected febrile neutropenia or neutropenic sepsis.
- No cost-effective method to accurately predict which patients are likely to experience severe potentially life-threatening neutropenia until they become unwell, at which point hospital admission is required and costs to both the patient and the NHS may be significant.
- Not possible to identify patients in whom suboptimal doses of chemotherapy have been used and in whom clinical outcome may be compromised.

Home monitoring

- Patient self-monitoring system, with the patient collecting blood samples from a finger prick.
  - Measure WBC count, temperature, and record signs and symptoms (e.g. mucositis, nausea, fatigue, etc.)
- Real-time analysis of the patient-generated data by the oncology team.
- Being developed with grant from the SBRI
  - (i) a small self-test blood-cell count reader
  - (ii) a Bluetooth connected thermometer
  - (iii) a tele-hub including a touch screen with the facility for recording self-reported symptoms, and
  - (iv) secure communication technology with a server

Home monitoring – potential benefits

- Reduce frequency & severity of adverse events
- Reduce hospital admissions and/or outpatient assessment
  - no evidence of neutropenia - patient remains at home
- Reduce cancelled treatment events
  - Home measurement prior to chemotherapy treatment may identify significant myelosuppression > advise the patient not to travel (wasted journey)> chemotherapy prep and dose will not be wasted.
- Personalisation of treatment
  - Increase dose and shortening interval between doses

TSB SBRI funded: workstreams of Phase I

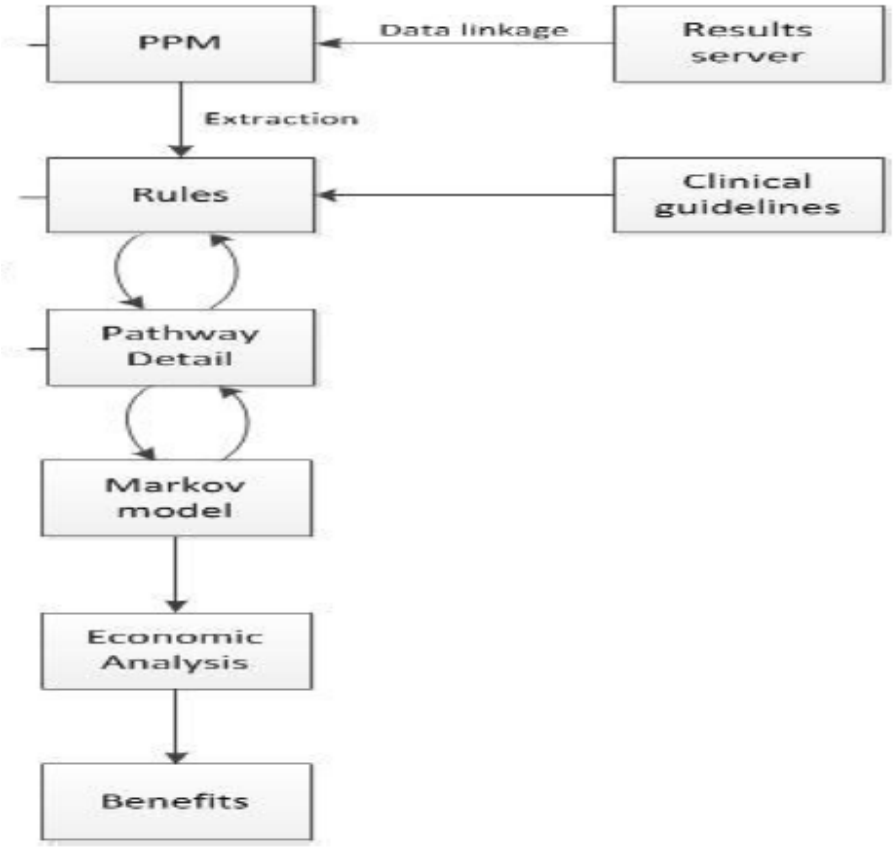
- (1) data mining PPM (Patient Pathway Manager), a coded database and electronic patient record containing comprehensive electronic records of treatment, results and outcomes.
- (2) Cost-effectiveness evaluation
- (3) to determine whether the self-testing technology could be used by nurses and patients to generate results, primarily focusing on WBC count measurements, comparable to those generated by the laboratory (i.e. current practice) and further that the practice of blood count measurement was acceptable to patients.

Decision model

- Markov model
  - Cycle length: 21 days
- Simulation period: expected/planned number of cycles within one course of chemotherapy (6 cycles for EC90),
  - Simulation starts with the first cycle of EC90 being delivered to the patient (S1) and the respective costs and utilities are attributed to the events arising from it.
- Data inputs
  - Leeds PPM, literature review and expert opinion
- Built in MS Excel

Model building process

- Iterative process
- Current practice for all BC patients with EC90
  - Guidelines and expert opinion
  - Data from patient specific linked HES and pathology data from Yorkshire Centre for Health Informatics and Department of Oncology at the University of Leeds PPM database
- Impact of home monitoring
  - Expert opinion



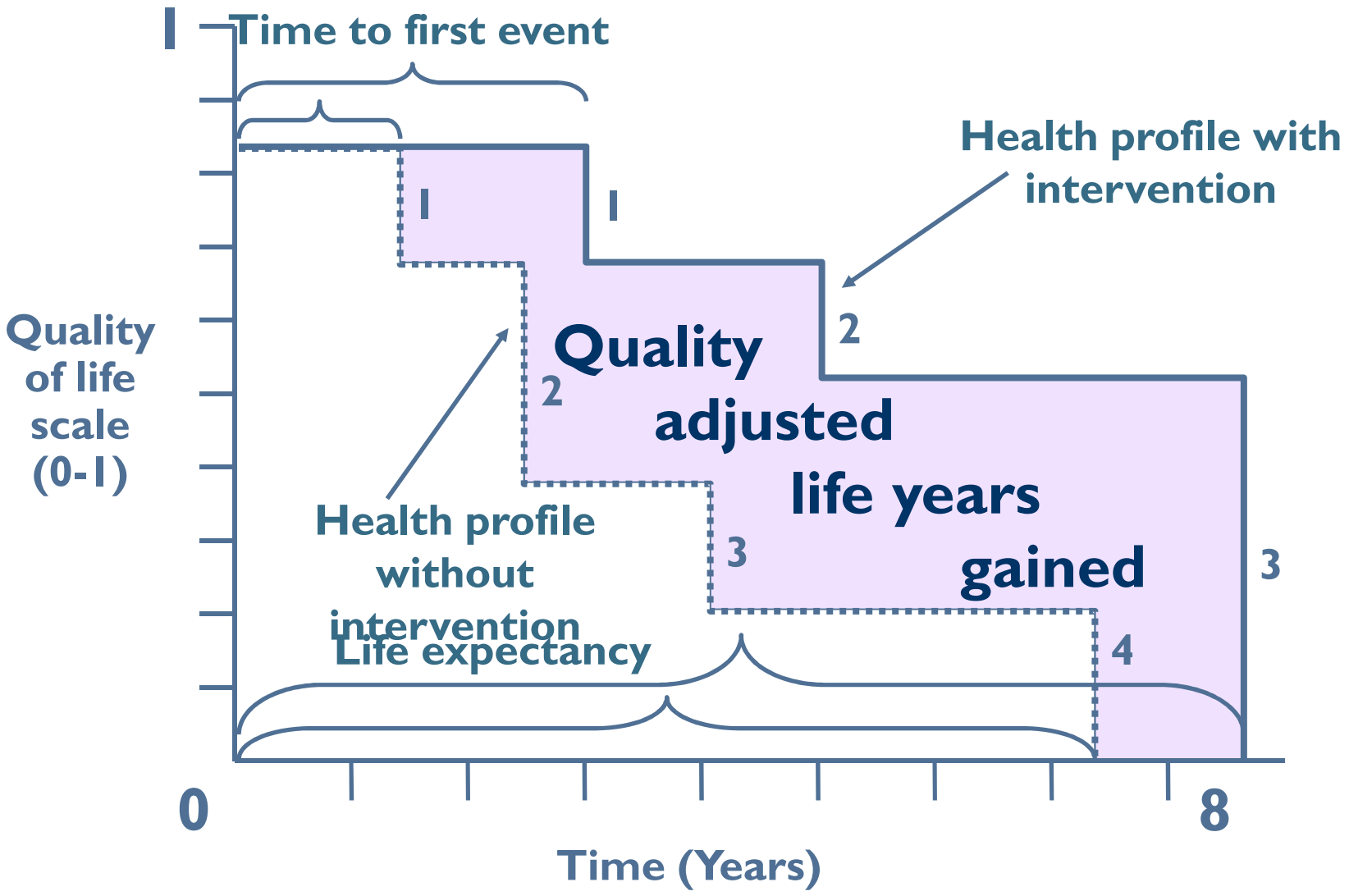
Model Parameter Inputs

- Transition probabilities (probability of cohort moving from one health state to another): 531 breast cancer patients receiving (PPM) database.
- Effectiveness (impact of introducing self-testing on transition probabilties): Expert opinion e.g. reduction in admissions or urgent OP visits, reduction/increase in phone contacts.
- Resource use: PPM data.
- Unit costs: England NHS reference costs 2011/12
- Utilities:

Utilities

- Utility weights were required to estimate quality adjusted life years (QALYs).
- The use of QALY's aims to capture the impact of disease progression and non-fatal events on quality of life in addition to any impact on survival.

Using QALYs to measure health gain



Utilities

- Literature review
- EuroQol EQ-5D instrument is the most widely utilized to obtain patients' preference-based health-related quality of life.
  - 5-dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety and depression)
  - Utility score on a 0 to 1 scale where 0 is equivalent to dead, and 1, to perfect health.
- Wherever possible, utility data was taken from studies conducted in the UK and using EQ-5D instrument.

Analysis

- Model simulates progression of a hypothetical cohort of patients through the model structure governed by the transition probabilities that accrue costs and outcomes as they move across states during the 6 cycles of EC90 treatment
- Costs and outcomes used to estimate ICER

$$ICER = \frac{Costs\ (I) - Costs\ (C)}{QALYs\ (I) - QALYs\ (C)}$$

- Cost effective if ICER<£20,000 QALY gained

Uncertainty

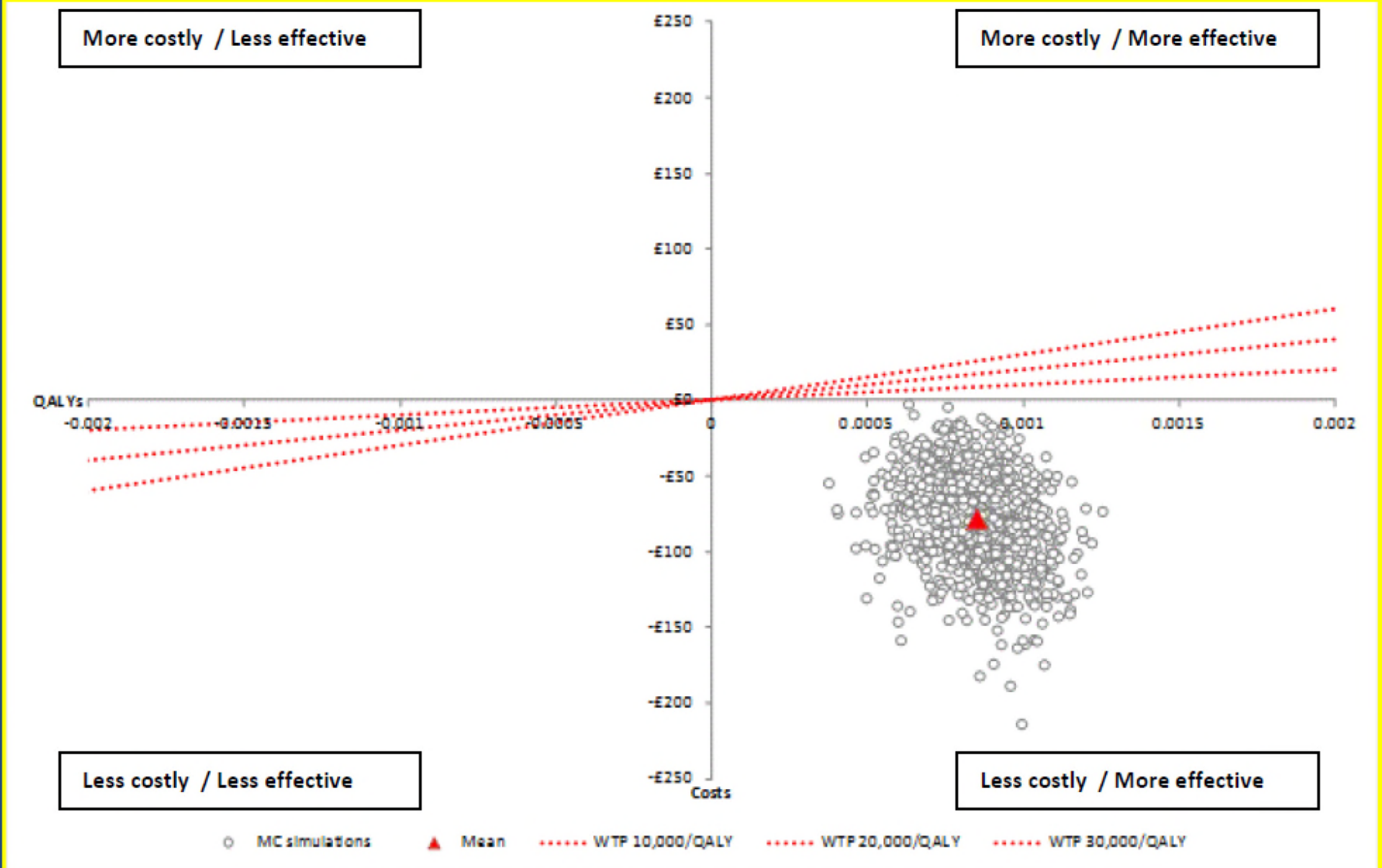
- Deterministic , one-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were used to reflect any uncertainty in the parameter inputs used in the model
- A cost-effectiveness acceptability curve (CEAC) was constructed and analysis of covariance methods (ANCOVA) were used to determine the proportion of variance in the incremental costs and QALYs saved explained by parameter uncertainty

Parameters	Sensitivity analysis	Distributional assumptions
Utilities	One-way and PSA	Beta distribution
Unit costs	PSA	Gamma distribution
Cost of home monitoring	One-way	
Effectiveness	One-way	
Resource use – hospital	PSA	Gamma distribution
Resource use – non hospital	PSA	Poisson distribution

Results

- Detailed results have been embargoed until published.
- Home monitoring was estimated to be both cost-saving and more effective than current practice for breast cancer patients undergoing adjuvant chemotherapy with EC90.

Cost-effectiveness plane



Where next

- Phase 2 of SBRI grant
  - Expand model to cover other cancers and treatments and assess cost-effectiveness
  - Inform design of future RCT

Thank you