# PHARMACOECONOMICS



## HANDLING THE RESULTS OF ECONOMIC EVALUATIONS

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# Learning outcomes



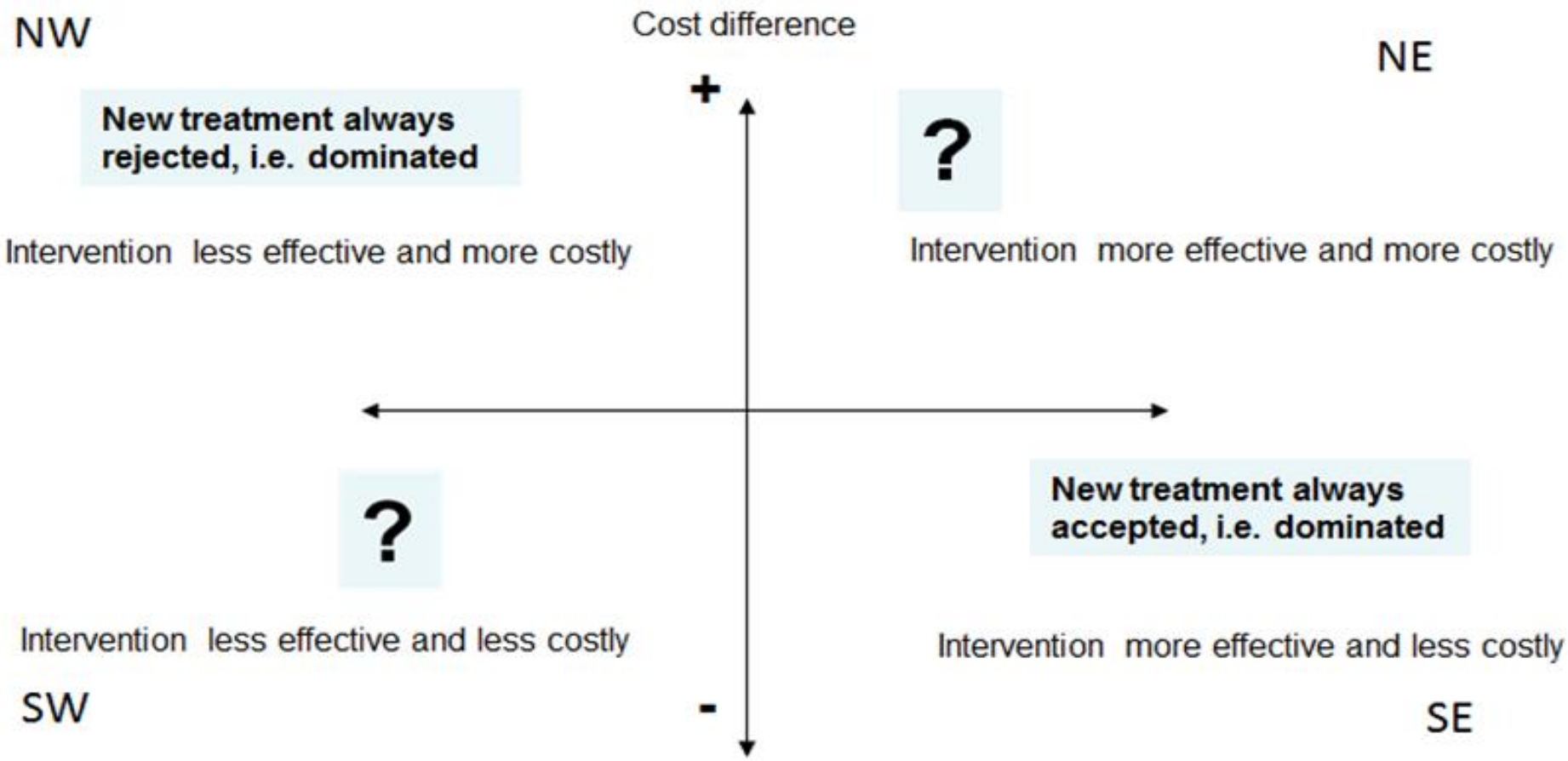
**By the end of this lecture, you would be able to:**

- Understand ways and techniques to handle the results of economic evaluations
- Understand what is sensitivity analysis
- Understand the Cost-effectiveness thresholds threshold
- Identify the power of economic evaluations to enable decision making

# Decision and sensitivity Analysis

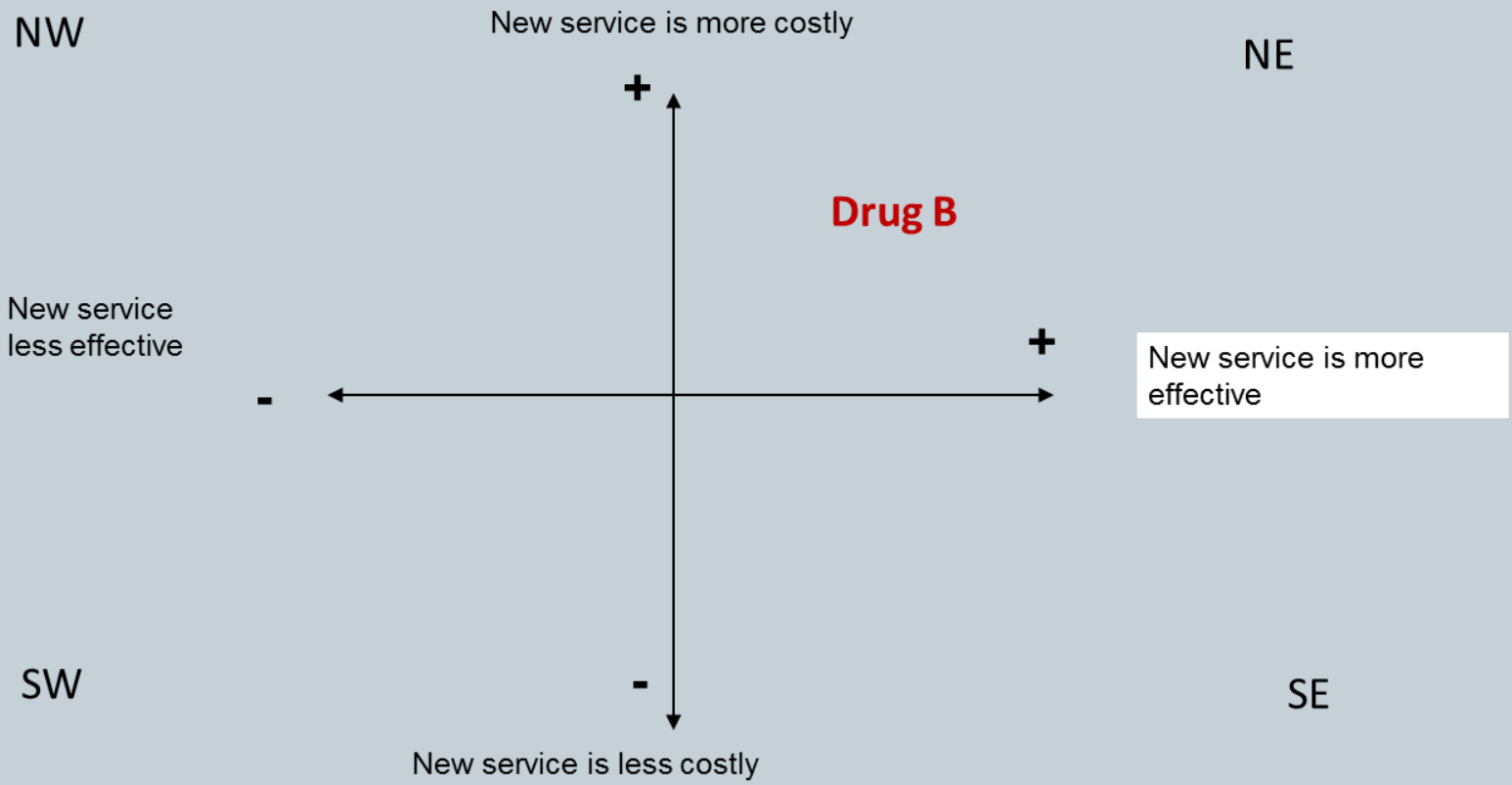


## Do you remember the cost effectiveness plane?



# Think of such case

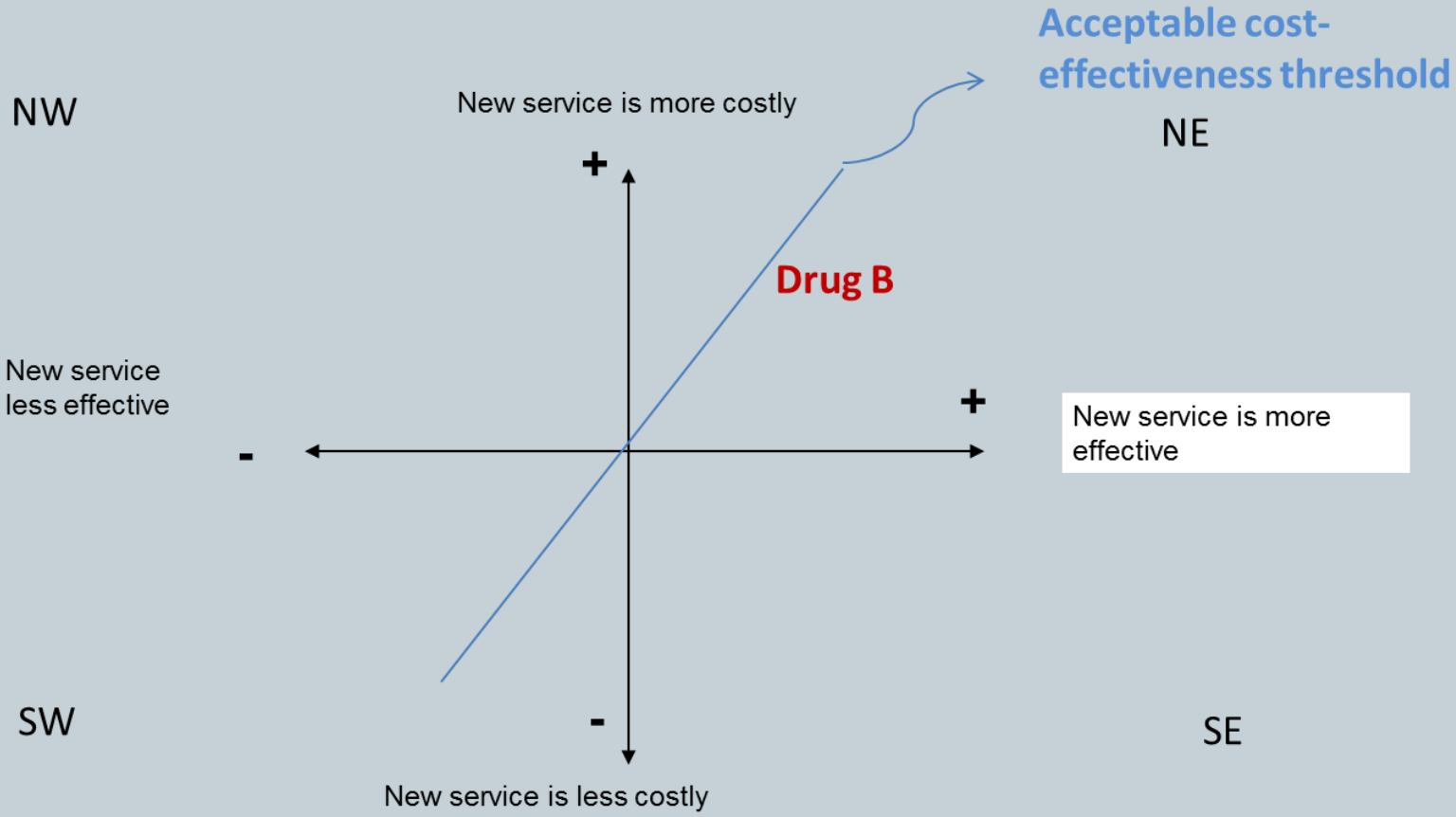


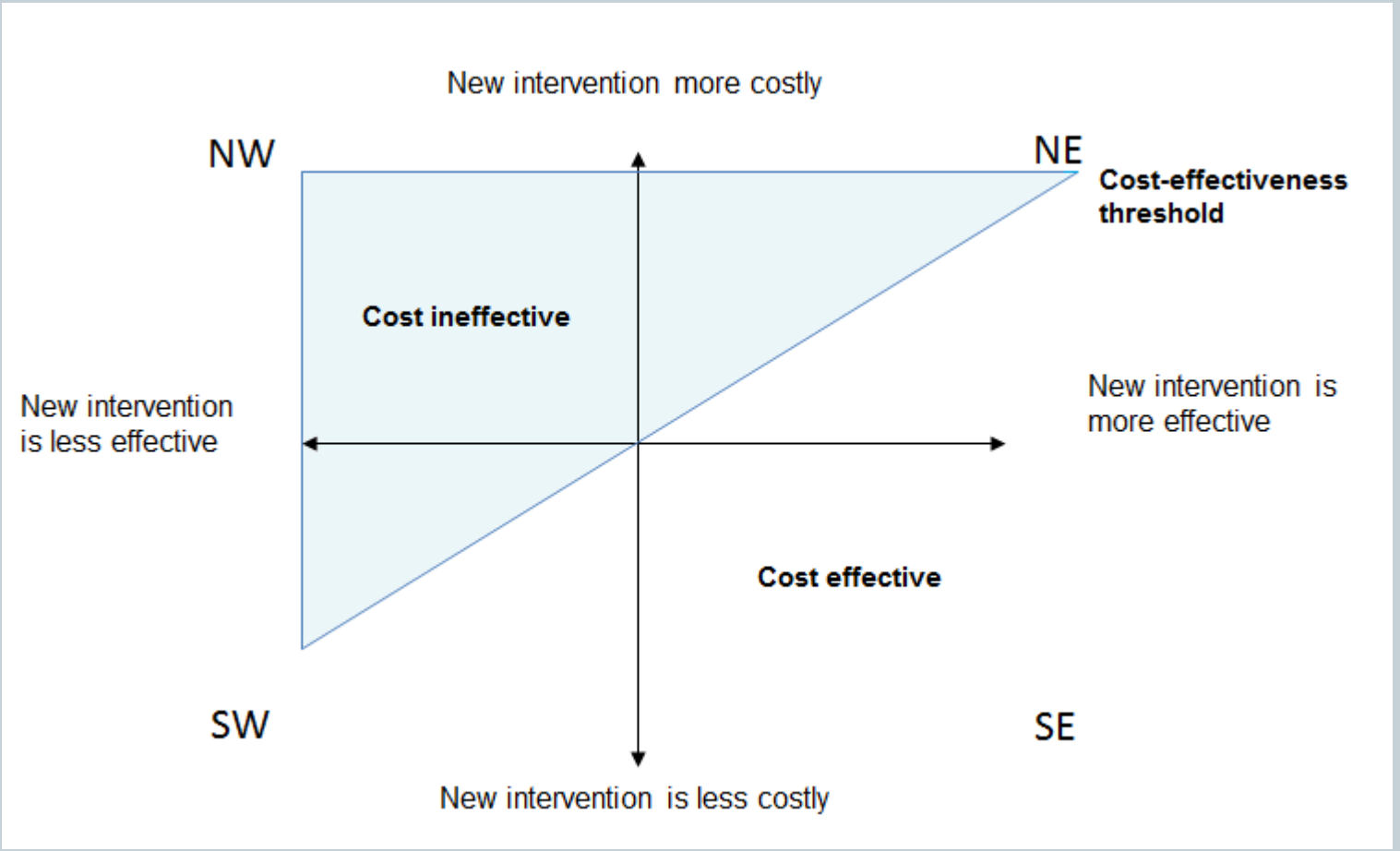


# How do we decide on whether to accept Drug B?



- Can we afford it?
  - Budget!!
- Can we justified ?
  - What are the consequences of accepting/not accepting it?
- The decision is not black and white unless we draw a line of acceptance


Acceptable cost-effectiveness threshold
NW
New service is more costly
NE
+
Drug B
New service less effective
+
New service is more effective
-
SW
-
SE
New service is less costly


New intervention more costly
NW
NE
Cost-effectiveness threshold
Cost ineffective
New intervention is less effective
New intervention is more effective
Cost effective
SW
SE
New intervention is less costly

# Remember ICER?



- Incremental Cost-effectiveness Ratio (ICER); the difference in costs between alternatives divided by the difference in outcomes measured

- If the ICER of the new intervention **<** than the acceptable cost-effectiveness threshold then the treatment should be adopted

  - Cost-effectiveness threshold is the value a decision maker is willing to pay for a unit of health gained (e.g QALY or LYG)

# Cost-effectiveness thresholds



- If the government uses a cost effectiveness threshold that is too high, this will promote inefficient uses of NHS resources.

- If however, the threshold is too low, then the most valuable interventions will not be adopted and thus this will not make the best use of available resources.

- E.g. In UK,
  - NHS funds services which cost <£20,000 to < £ 30,000per QALY

# Cost-effectiveness thresholds



- Other countries
  - Australia funds AU$69 900/QALY
  - New Zealand funds NZ$20 000/QALY
  - In the USA ($50 000/QALY)
  - In the Netherlands (€80 000/QALY)
  - In Canada (CAN$20 000 - $100 000/QALY).

**Why ?**

**There is a range rather than one fixed value?**

**Values and decisions might vary across countries or institutions?**

# Why?



- Because, judgements about the acceptability of an intervention is subject to many factors beside the budget and health needs in an area.

- factors including
- The degree of uncertainty surrounding the calculation of ICERs (due to the source of uncertainty around the data source)
- The innovative nature of the intervention (other innovative nature of intervention not captured by the health benefit measure)
- The particular features of the condition and population receiving the intervention

# Estimate of Cost-effectiveness threshold



- Defining what is an acceptable maximum value or threshold for ICER is difficult and controversial
  - How much is an extra QALY or life year worth? This is a value judgment.
  - It can be explored to some extent through techniques such as trying to identify what a patient or the public might be willing to pay to avoid an unfavourable outcome
  - Some countries use by common consent, e.g provide treatment in the form of coronary bypass grafting: then workout the cost £X per QALY, and so this establishes a baseline for our thinking about how much we value a QALY.

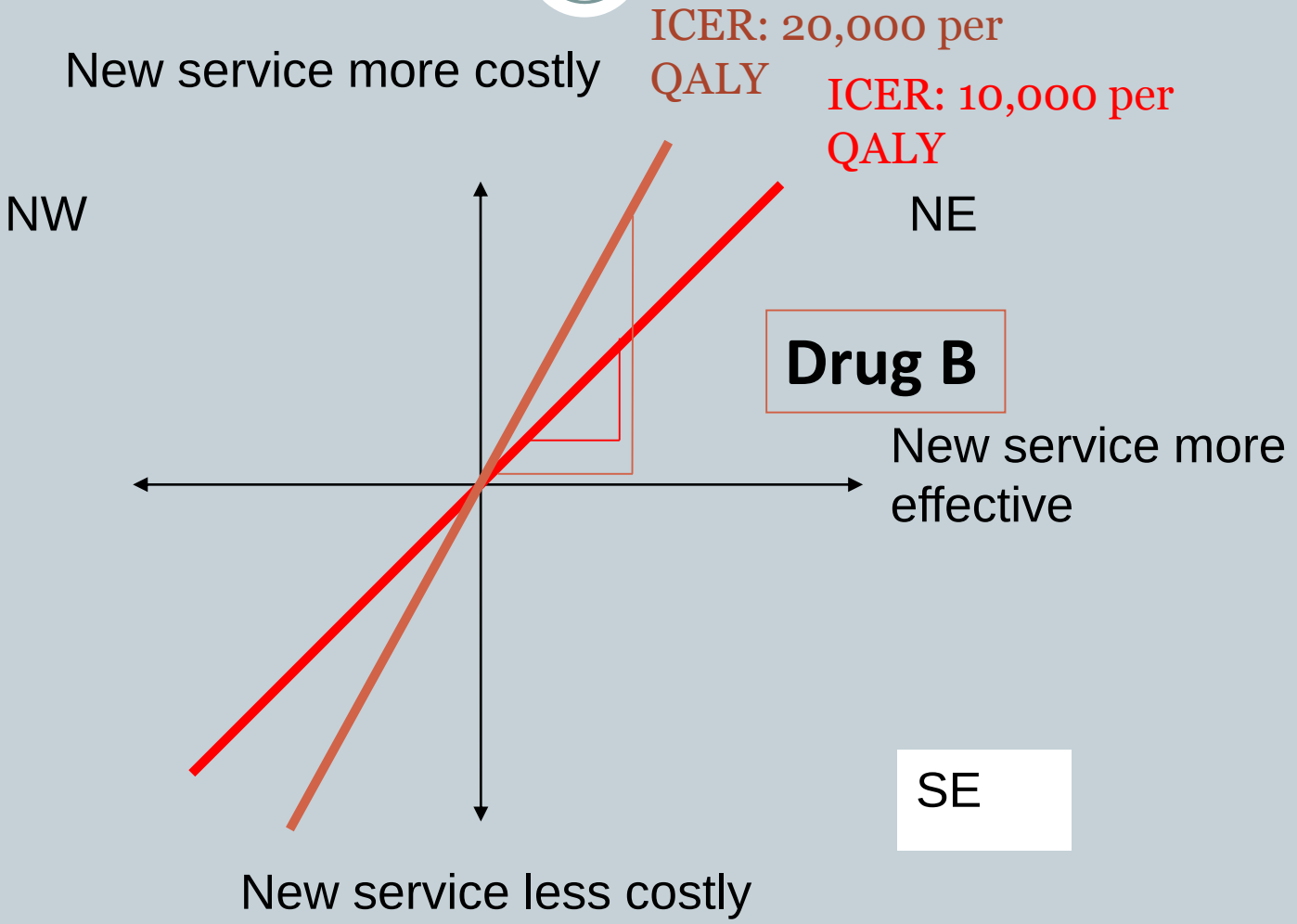
# Estimate of Cost-effectiveness threshold

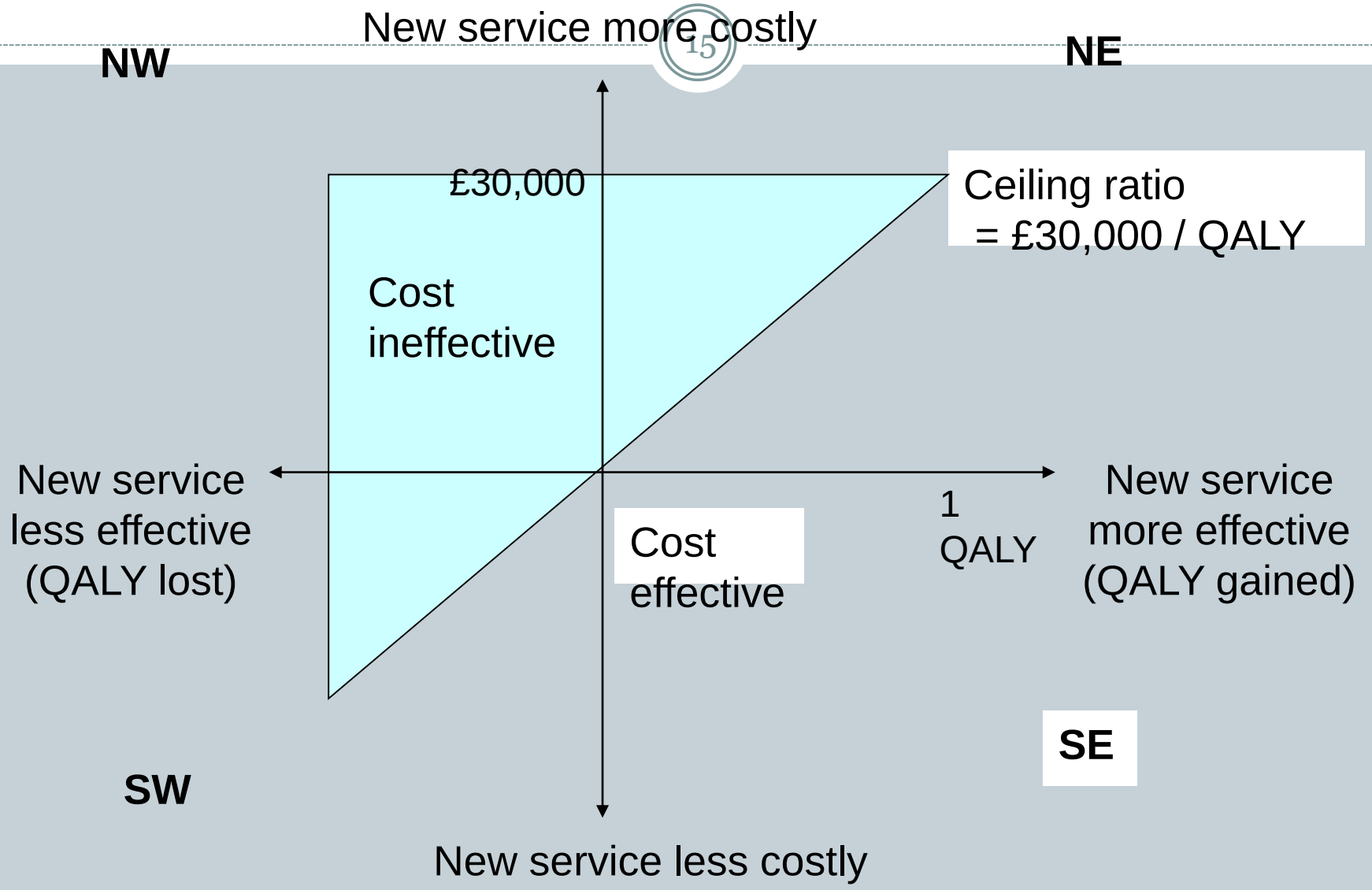


- Set the threshold equal to per capita Gross Domestic Product
- every member of society were to be given a fair share of nation's wealth, they would receive the per capita GDP. The maximum they could therefore spend on health gain in any one year would therefore be the per Capita GDP.
  - If expenditure exceeds this value either the nation is spending more than it earns or some people are receiving less than their fair share.
  - GDP = Gross domestic product; < GDP per capita (Very cost-effective); 1-3 x GDP per capita (cost-effective); > 3 x GDP per capita (not cost-effective)

# What do you explain here in this graph






New service more costly
NW
NE
£30,000
Ceiling ratio
= £30,000 / QALY
Cost
ineffective
New service
less effective
(QALY lost)
1
QALY
New service
more effective
(QALY gained)
Cost
effective
SE
SW
New service less costly

# Uncertainty in PE evaluation



- **Remember**
- All PE evaluations present means or proportions as outcomes e.g.
  - The mean reduction in blood pressure was 10mmHg
  - The mean cost was £8,500
- These results are all based on samples
- If the study was repeated on a different sample we would obtain a slightly different result

So!!

We need to estimate the boundaries within which the population (real) value is likely to lie (sensitivity analysis)

# Last time we stopped at the notion of



- No matter how well-executed or comprehensive an economic evaluation, the data on costs and outcomes will inevitably contain various degrees of uncertainty and potential bias.

- *Once the ICER has been generated in the primary incremental economic analysis (base case analysis), it is necessary to assess the robustness of these ICER*
  - *Robustness refers to the sensitivity of the ICER to uncertainties in the data*

- **Sensitivity analyses are performed to test the robustness of study results and conclusions when these underlying assumptions or estimates are varied.**
  - This process reveals the degree of uncertainty, imprecision, or methodological controversy in the evaluation.

# Sensitivity Analysis



- A standard approach to manage uncertainty in PE evaluations
- A tool that tests the robustness of PE evaluation results and conclusions by holding other evaluation parameters constant, the study results are recalculated. E.g. different discounting rates
- If changing the values of specific variables does not substantially alter the results, you will have more confidence in the original findings
- Sensitivity analysis enhances extrapolation of the results (What does this mean?).

# Source of uncertainty



- Sensitivity analysis involves varying parameter estimates across a range and observing how this will impact the conclusion results
- Uncertainty may rise from
  - Diagnosis:
  - Natural history of the disease:
  - Treatment efficacy and effectiveness:
  - The development of adverse events:
  - Resources consumed by treatment  options:

- Effectiveness is concerned with what benefits/costs are associated with a new therapy when it is used in the real world whereas efficacy is concerned with measuring the benefit of therapy in controlled conditions (i.e. RCTs)
  - In RCTs, patients are more monitored and where the comparator may not be the one used in the clinical trial.
- There is often little evidence available about effectiveness, and we are forced to make *assumptions*
  - These assumptions should be reasonable, and should be transparent, so that they can be challenged.

# Sensitivity Analysis



- *Health Economists like to take into account the possible extremes (i.e. SD or CI) in the analysis rather than the mean*

# Uncertainty and variation in PE evaluations



- Variations in the outcomes (previous slide)
- Variations exist also around the estimated cost of the intervention
- *Mean (95% CI) usage costs for*
  - *Medicines £30K (10, 50)*
  - *Hospitalisations £20k (10, 30)*
  - *GP visits £30K (10,50)*
  - *Equipment for monitoring £10K (5,15)*

# Types of sensitivity analysis



- One way-sensitivity analysis
  - Varying each uncertain component individually to assess the effect of each on the results of analysis
- Multiway sensitivity analysis
  - Varying two or more components at the same time
- Threshold analysis
  - Identifying the critical value of parameters above or below which the conclusions of the study will change
- Probabilistic sensitivity analysis
  - Each parameter (e.g. cost and outcome) has a predefined distribution (range)
  - A computer simulation is run where different values from these ranges are selected randomly, thus resulted in generating different values of incremental costs, outcomes, and ICER that are plotted in a cost effectiveness curve (CEAC)

# Example



- The health care provider was able to purchase antibiotic C at a much lower price ICER must be recalculated with this new cost information.
- Calculate the new ICER
- What are the types of sensitivity analysis
- Plot it on the cost-effectiveness plane

| Analysis | Cost to treat 100 patients | | Effectiveness (%) | | Incremental effectiveness | Incremental cost | ICER |
|---|---|---|---|---|---|---|---|
| | Antibiotic C | Antibiotic A | Antibiotic C | Antibiotic A | | | |
| **Base case** | 8000 | 7000 | 80 | 75 | | | |
| **Antibiotic C** | 6800 | 7000 | 80 | 75 | | | |

# Think of this situation too



- For instance if a study assumes a rate of relapse of duodenal ulcers after treatment of 5% at one year, what happens if the relapse rate were to be actually 2.5%, or 10%?

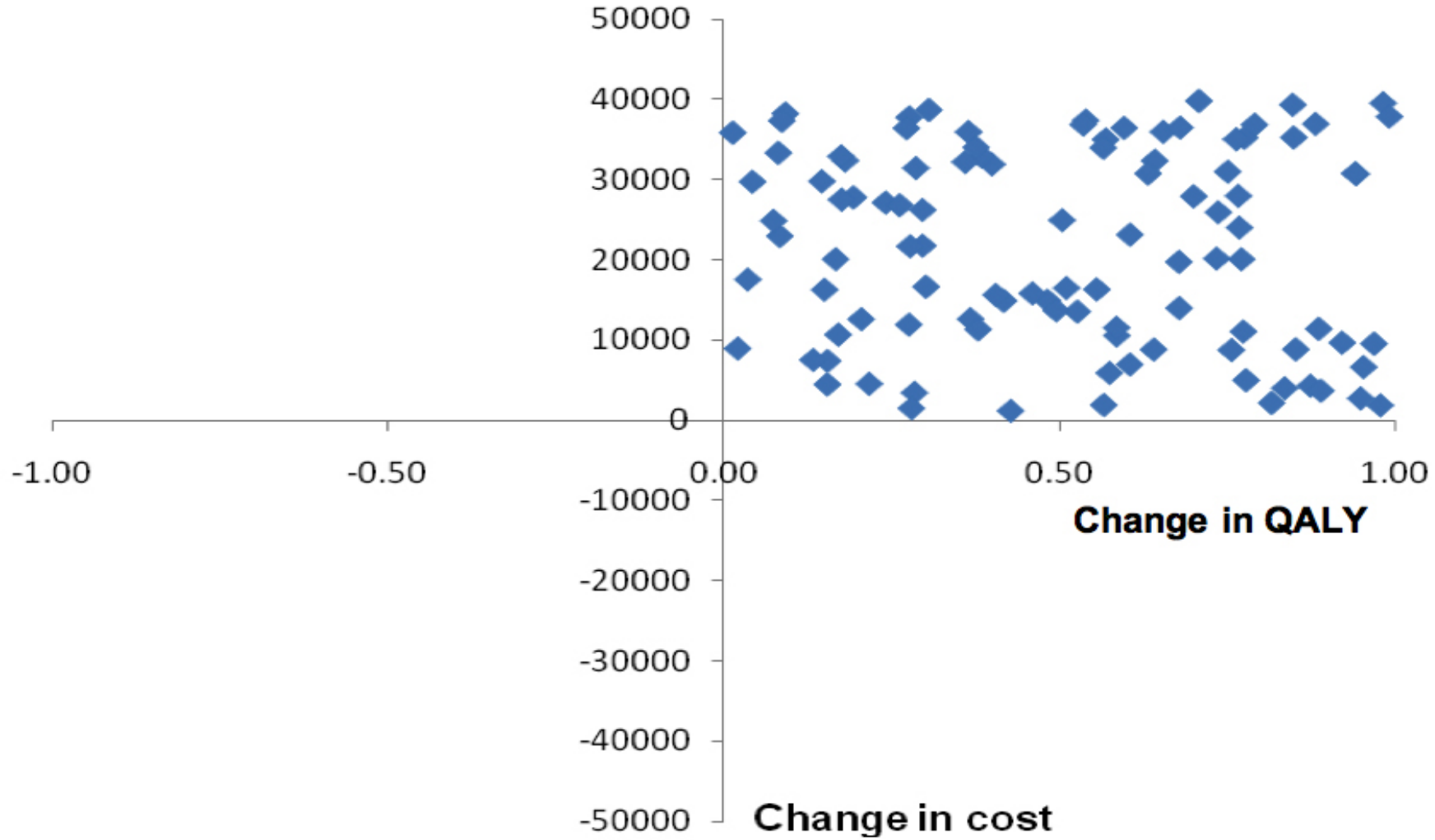
- This might drastically affect the outcome of a study.

# Variations not only in outcomes



- How many different extreme values are there? (need to take into account all permutations)
- Therefore never just one point on an CE plane
- Plotting a single point on an CE plane is overly simplistic.
- When plotting an ICER it is necessary to take into account the variation in the accuracy of both the estimated costs and outcomes.

# Sensitivity analysis would look like this



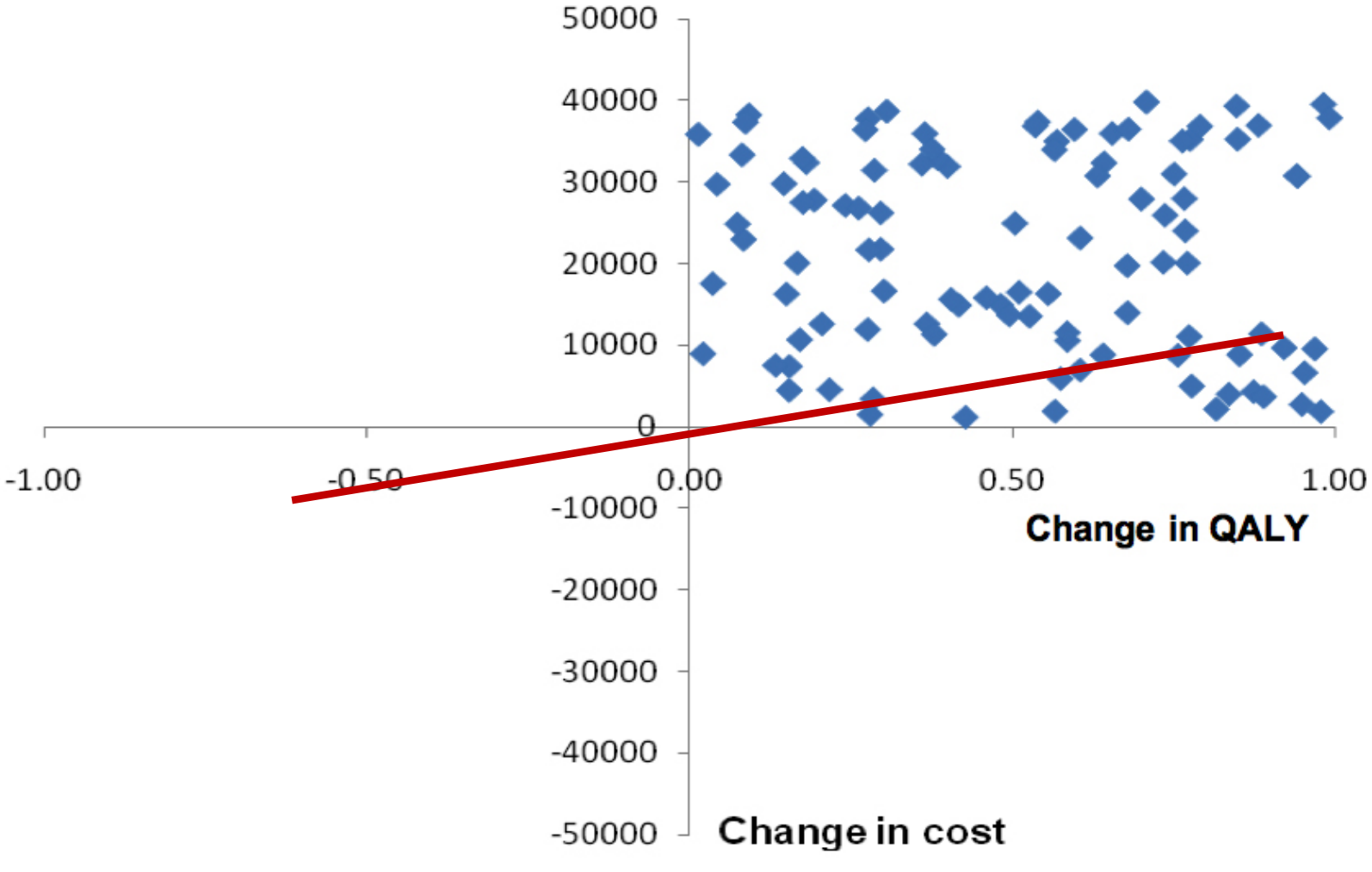
- Any good economic study will challenge their assumptions, by varying them in a *sensitivity analysis*.
- This explores the extent to which a conclusion is dependent on an assumption.
- A sensitivity analysis clarifies what are the critical assumptions and confirm that the results of the evaluation are robust, despite changes in the assumption.

- It is important for any PE evaluation to report the methods used for the sensitivity analysis
- The results of analyses should always be included in the results

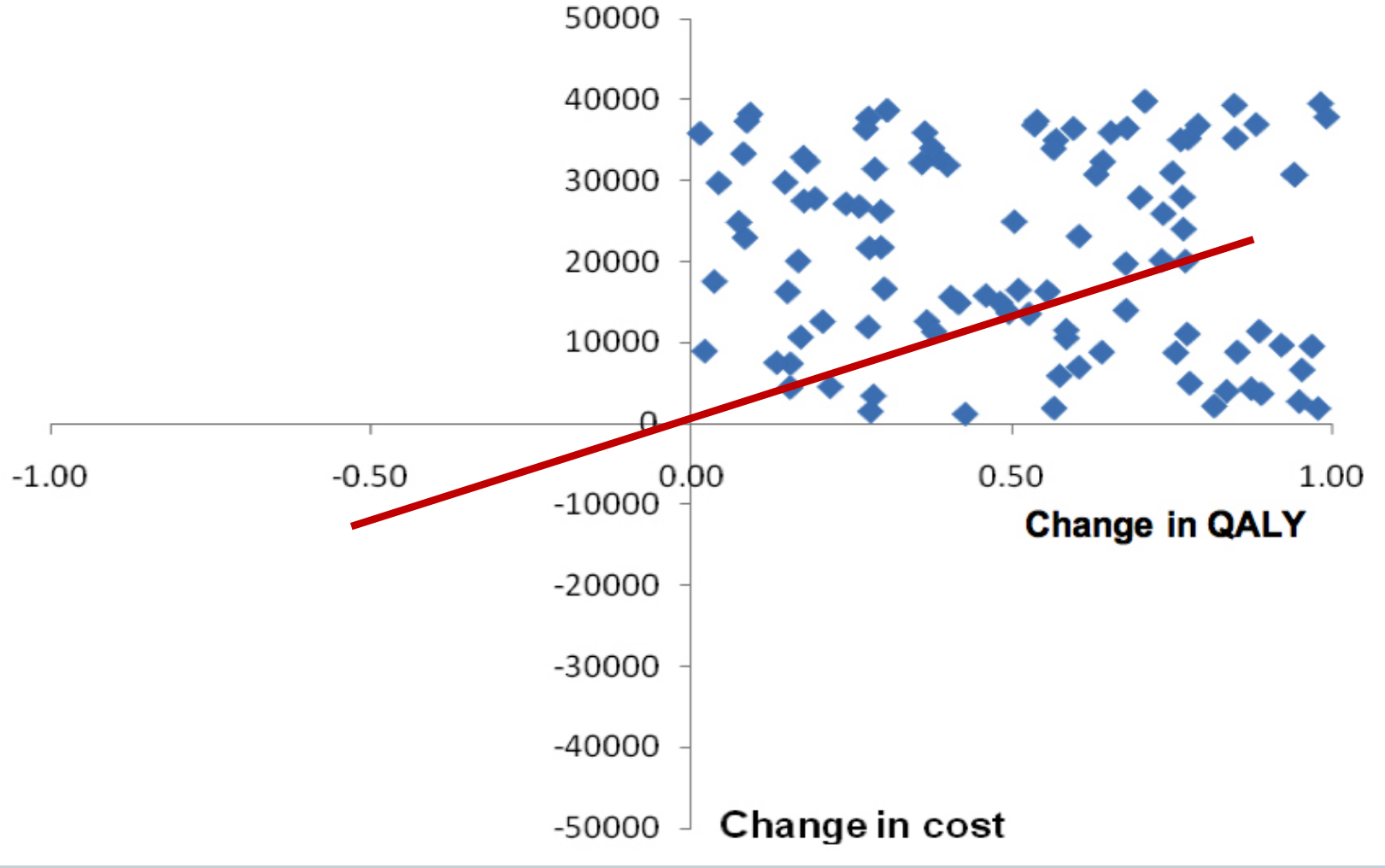
- This is important to determine the likelihood of acceptance for an intervention

  - *This is determined from the proportion of points below different thresholds*

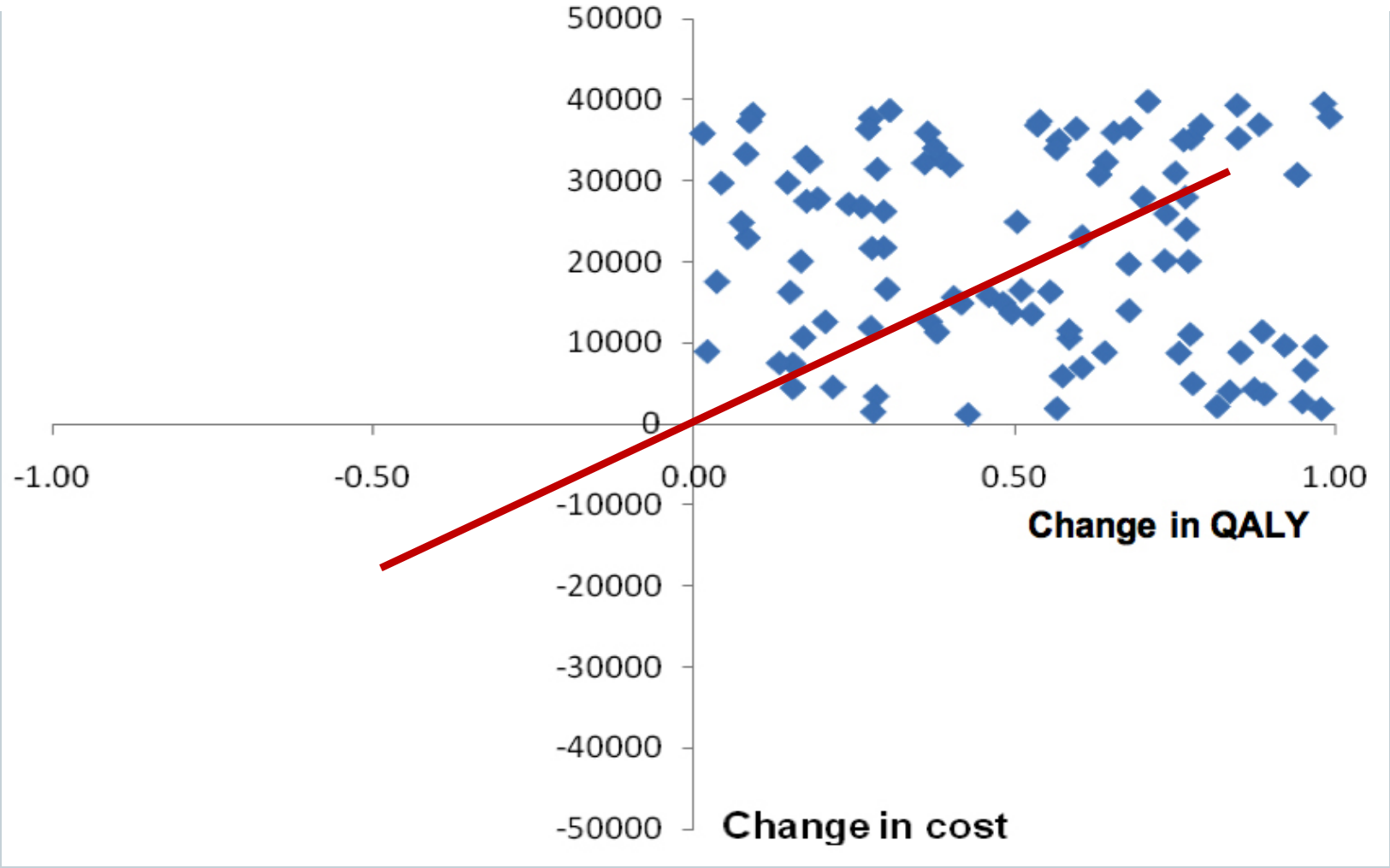
# What is the proportion of points demonstrate a Cost per QALY < 10,000?



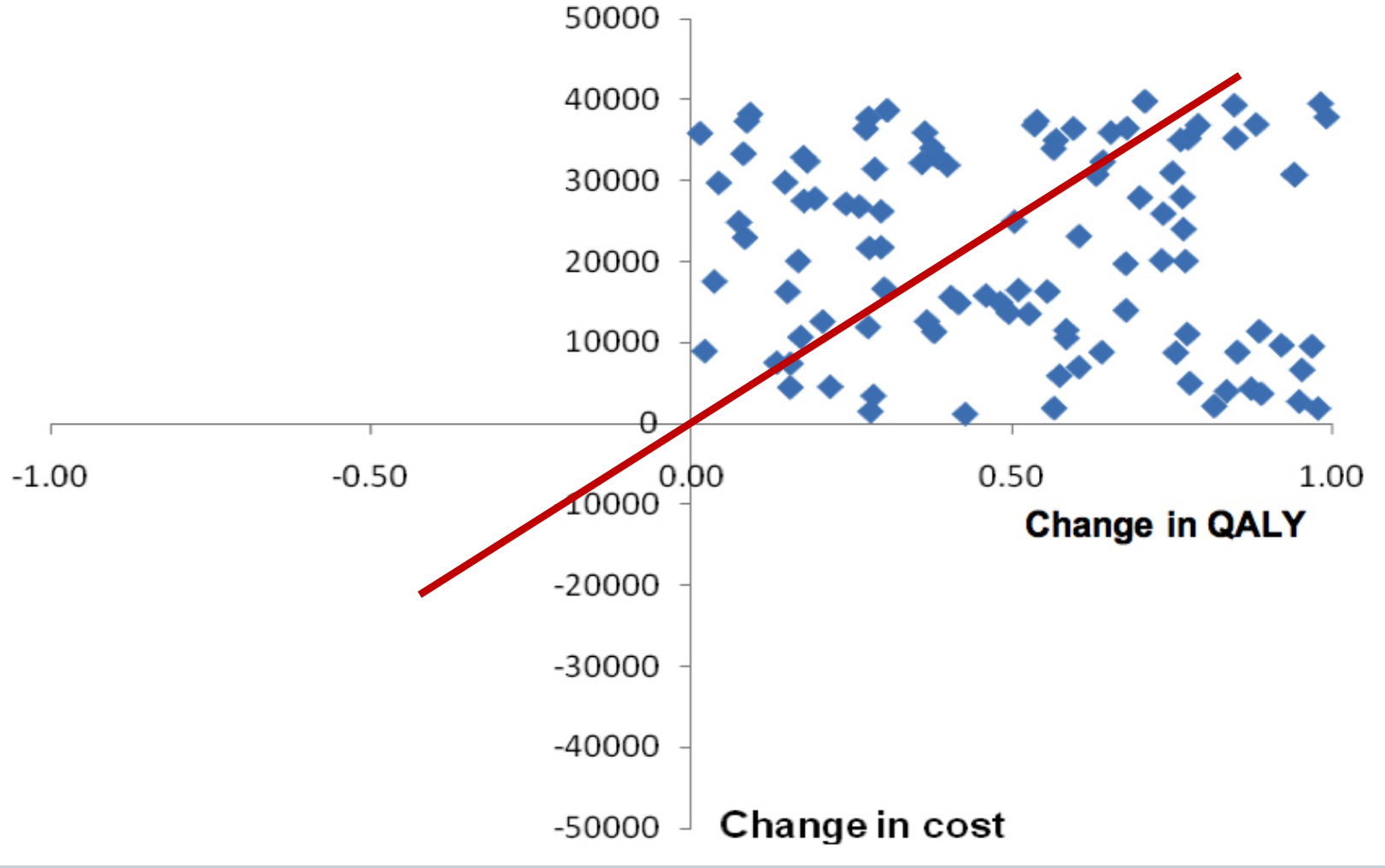
# What is the proportion of points demonstrate a Cost per QALY < 20,000?



# What is the proportion of points demonstrate a Cost per QALY < 30,000?



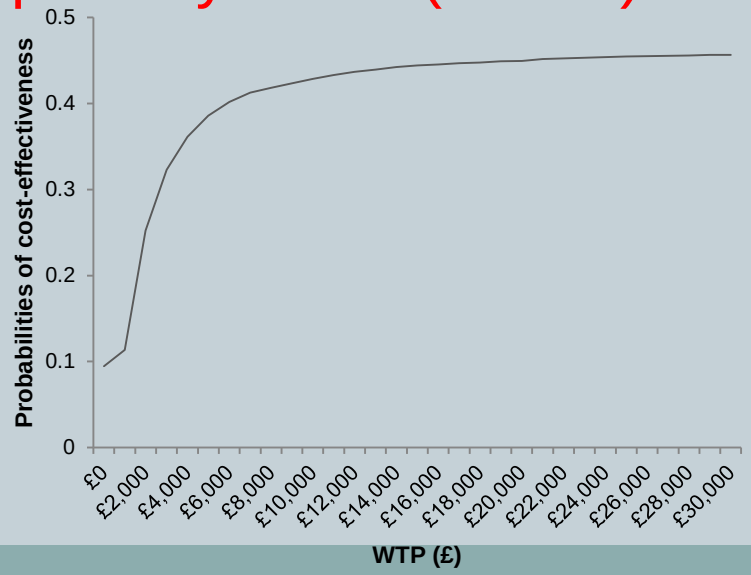
# What is the proportion of points demonstrate a Cost per QALY < 40,000?



# Likelihood of acceptance for an intervention (being cost effective)



- Proportion of points under the cost-effectiveness threshold = likelihood of the intervention being cost effective
- If we plot proportion of points under the cost-effectiveness threshold against the cost-effectiveness threshold this would give the cost effectiveness acceptability curve (CEAC)



- In the CEAC curve, the probability that intervention is more cost-effective than control group for a range of the decision-maker's WTP(λ) for an extra LYG or QALY are presented.
  - The CEAC is constructed by plotting the proportion of the incremental cost-effect pairs (y-axis) that were cost-effective for a range of λ values (x-axis). These proportions are calculated by dividing the number of the incremental cost-effect pairs, lying to the south and east of a ray with a slope equivalent to λ in the cost-effectiveness plan, over the total number of cost-effect pairs.
  - This process is repeated numerous times with different values of λ (in the UK ranging from 0 to £30,000)

# Summary



- Health economics used to make decisions regarding which interventions to accept
- We accept interventions proven to be the most cost effective use of health resources
- In order to decide this we need to consider
  - **Accepted value of health gain (cost-effectiveness threshold)**
  - **Uncertainty around cost effectiveness estimate (sensitivity analysis)**
  - **Likelihood of being cost effective (CEAC)**

# Example: screening for colorectal cancer



| program | incremental cost (JDs) | Incremental Life-years gained | ICER |
|---|---|---|---|
| Every 2 years, age 55-74 | 800,000 | 400 | |
| Every 1.5 years, age 55-74 | 700,000 | 300 | |
| Every Year, age 55-74 | 1,400,000 | 500 | |
| Every year, age 50-74 | 1,700,00 | 500 | |

CE threshold = 3000 JDs per life year gained

Which of these we should adapt ?