Introduction to (trial based) economic evaluation

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Topics

1. Different concepts used clinical practice
2. Why/when performing economic evaluations?
3. Framing of a (trial based) economic evaluation
4. Data analysis, uncertainty and interpretation
5. Questions

References used for this presentation:
- Drummond M.F. Methods for the economic evaluation of health care programmes Oxford. 2015
- Neumann P. J. Cost-effectiveness in health and medicine. Oxford.2016

The King's Fund Ideas that change health care

SUMMARY

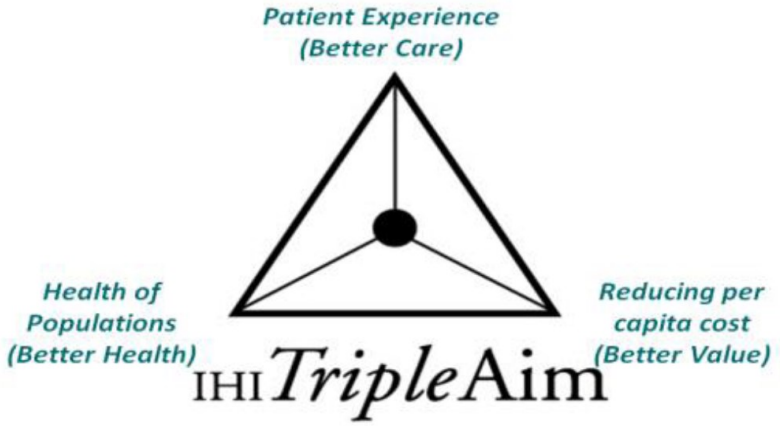
Better value in the NHS

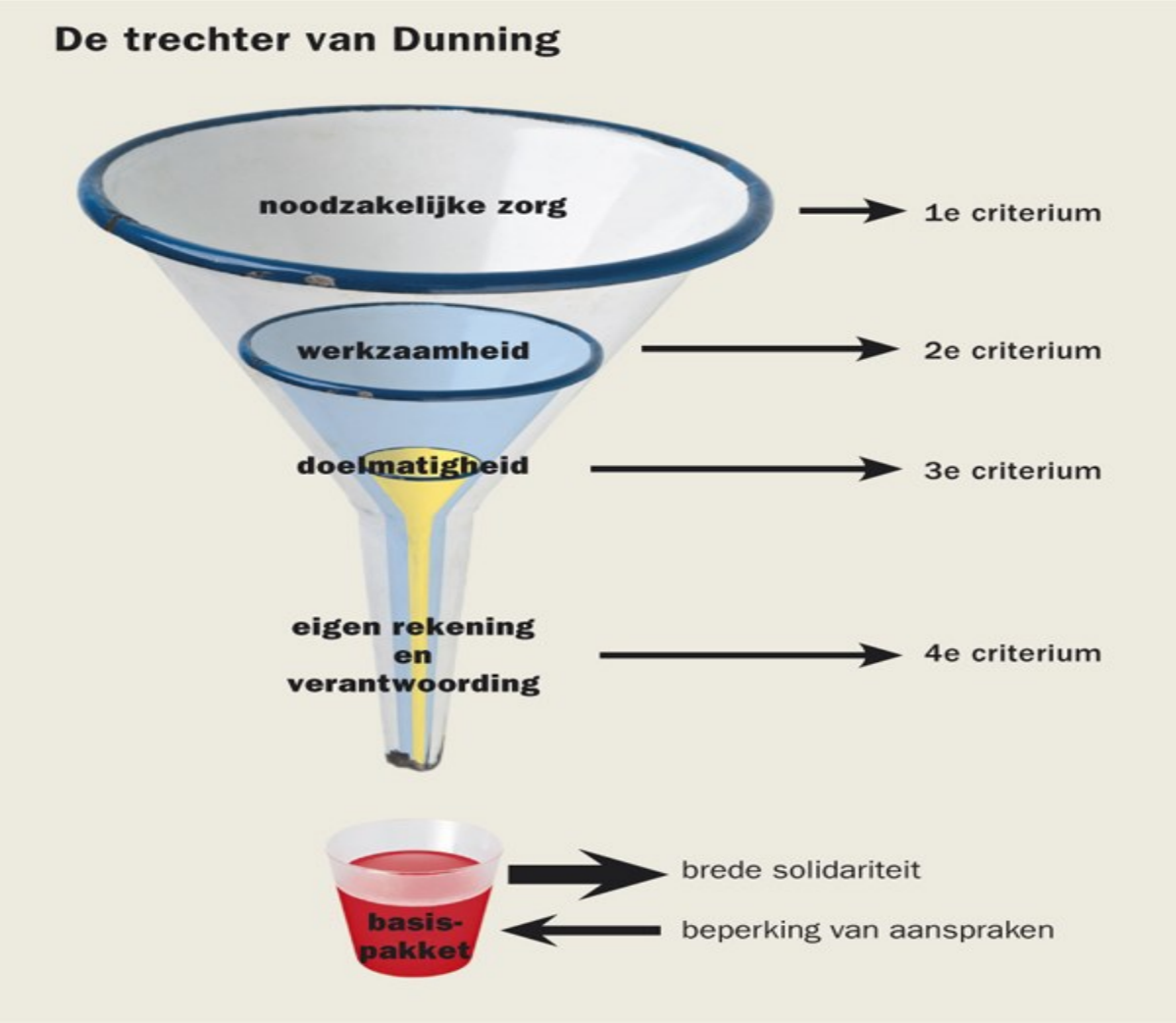
The role of changes in clinical practice

July 2015

Institute for Healthcare Improvement

IHI Triple Aim Initiative
Better Care for Individuals, Better Health for Populations, and Lower Per Capita Costs





Dunning: cardioloog AMC. Rapport 'kiezen en delen' 1991

Why a trial based economic evaluation?

RCT examines lack of existing evidence on a treatment effect: offers an early opportunity to determine estimates of cost- effectiveness

- Explanatory trials: does an intervention work under ideal circumstances (efficacy)?
- Pragmatic trials: does an intervention work in the "real world" (effectiveness) ?

Why a trial based economic evaluation?

Most ideal situation: clinical trial is largely pragmatic and corresponds with clinical practice→ real world conditions.

However: an RCT often has an an explorative character when it deals with new or innovative treatment/medicine
Disadvantages of an explorative trial for an economic evaluation:

- limited comparison
- limited external validity
- limited time-horizon

Still, for a large part, this can be solved with modelling techniques→ separate masterclass

When a (trial based) economic evaluation?

Objective: to support decision making surrounding a new treatment or new diagnostics within a context of limited resources

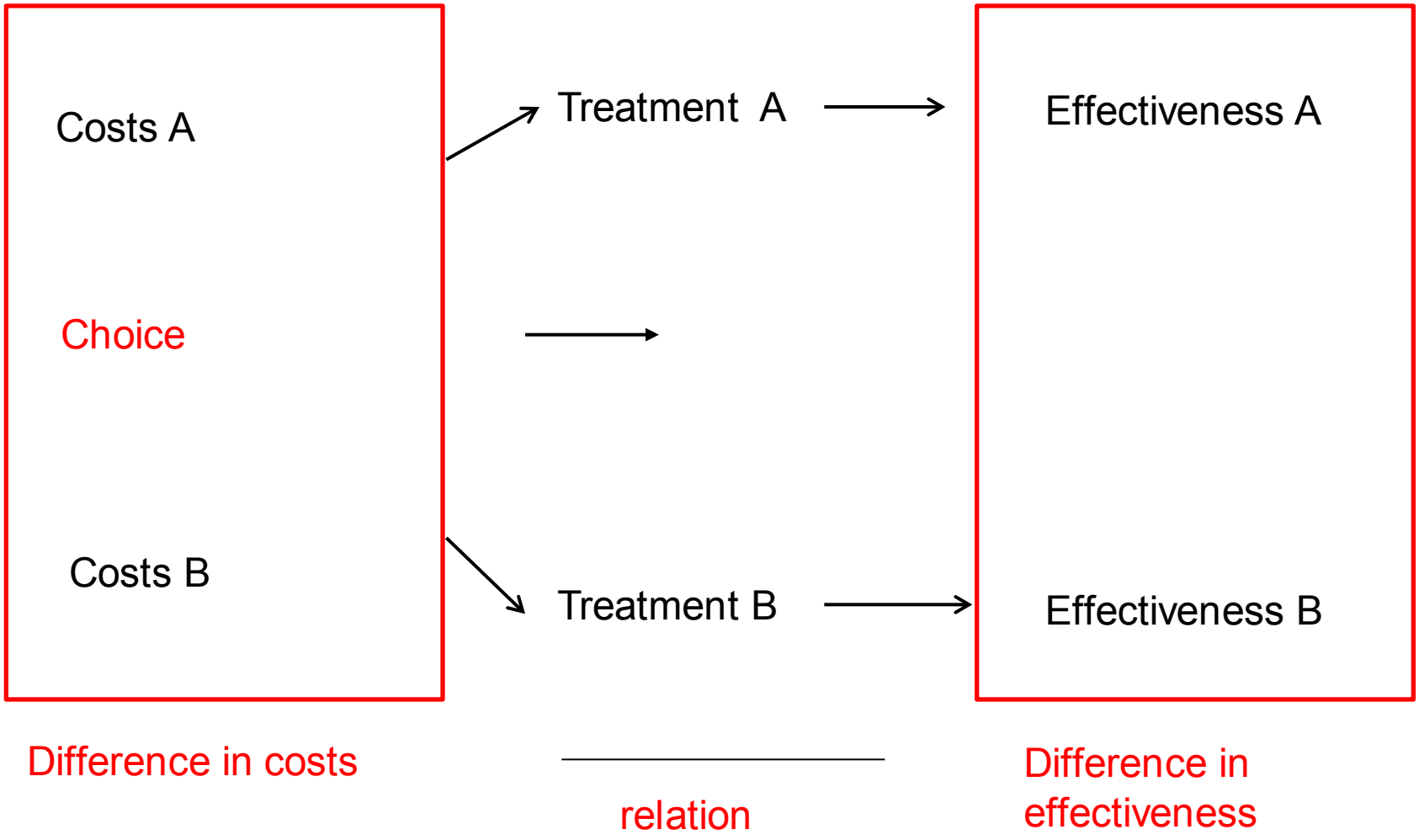
1. Decision problem?
2. Perspective?
3. Type of economic evaluation?

1. The decision problem

Economic evaluation provides a framework for assessing the costs and consequences of alternative programs or interventions

- Is a new intervention cost-effective compared to usual care?
- Is a treatment cost-effective for certain groups of patients?
- Is a treatment cost-effective within a certain setting? (hospital or general practitioner)?

Economic evaluation: always comparison!



2. Perspective

The perspective determines the categories of resource use included in the study

- Insurer perspective
- Healthcare perspective
- Institution perspective
- Patient perspective

Societal perspective (includes all perspectives): mandatory!!

3. Type of economic evaluation

Type	Costs	Health outcomes
Cost-analysis	Yes	None
Cost-effectiveness analysis	Yes	Natural units (life years gained; recurrence prevented
Cost-utility analysis	Yes	Quality Adjusted Life year (QALY)
Cost-benefit analyis	yes	Monetary unit

Steps in evaluation of effectiveness

1) Identification relevant effects

2) Measurement of effects/health related outcomes

3) Valuation of heath related outcomes: utility

4) Multiplication of utility with duration of the health related outcomes: QALY (in cost-utility analysis)

1) Identification of relevant effects

Cost-effectiveness analysis

- Clinical outcomes like symptom free days for asthma or life years gained or prevention of stroke
- Depending on the objective of a trial and specific to the clinical field.

Cost-utility analysis

- Health related quality of life (utility) multiplied with duration: QALY

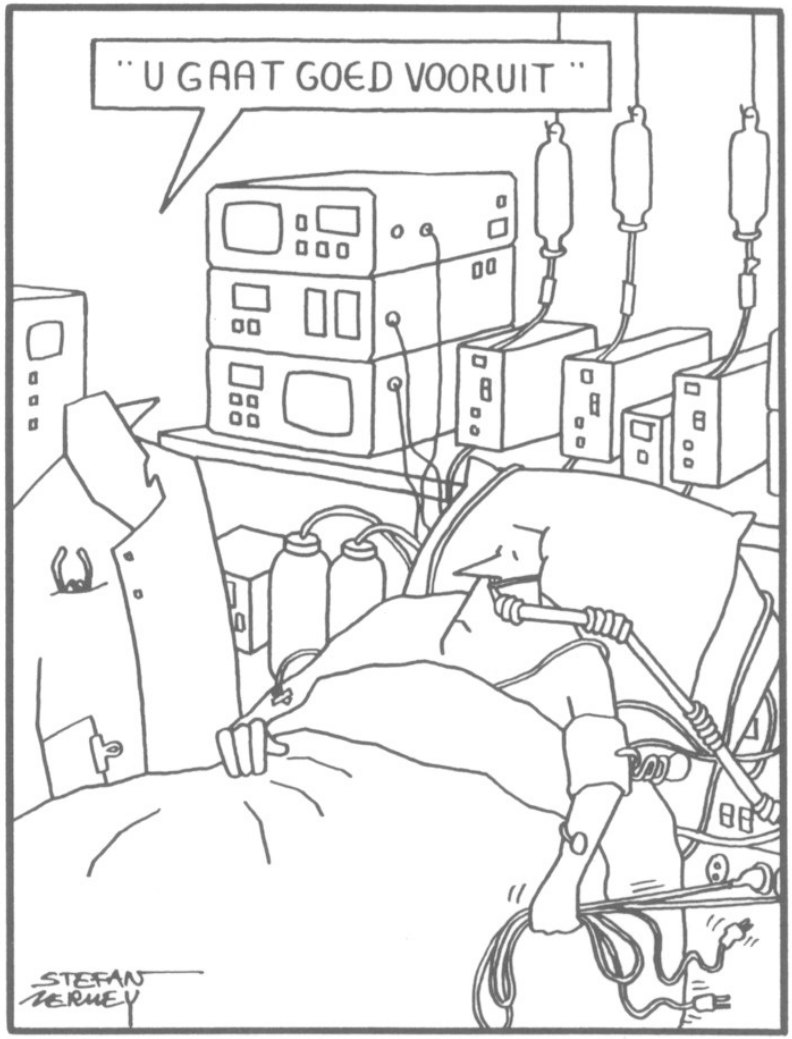
2) Measurement of clinical outcomes

Positive effects:

- Points reduction blood pressure (hypertension)
- Cases detected/prevented (screening and diagnostics)
- (diseasefree) survical (cancer)
- Prevention of an event (recurrence, heart attack etc.).

Negative effects:

- itching, rash
- nausea, pain
- infection
- mortality


"U GAAT GOED VOORUIT"
STEFAN VERMEY

2) Measurement of quality of life

Quality of life: no uniform definition or concept

What is health?

World health organisation (1948):
a state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity

This is a very broad definition and offers no clear guidance on the content of an instrument for measuring health

2) Measurement of quality of life

Health as a spectrum*

WHO (international classification of impairments, disability, and handicap 2001):

Disease	Impairment	Ability	Participation
Rheumatism	Pain	Limits walking	Role social / and usual activities

- Brazier J Measuring and valuing health benefits for economic evaluation. Oxford University Press. 2007

2) Measurement of quality of life

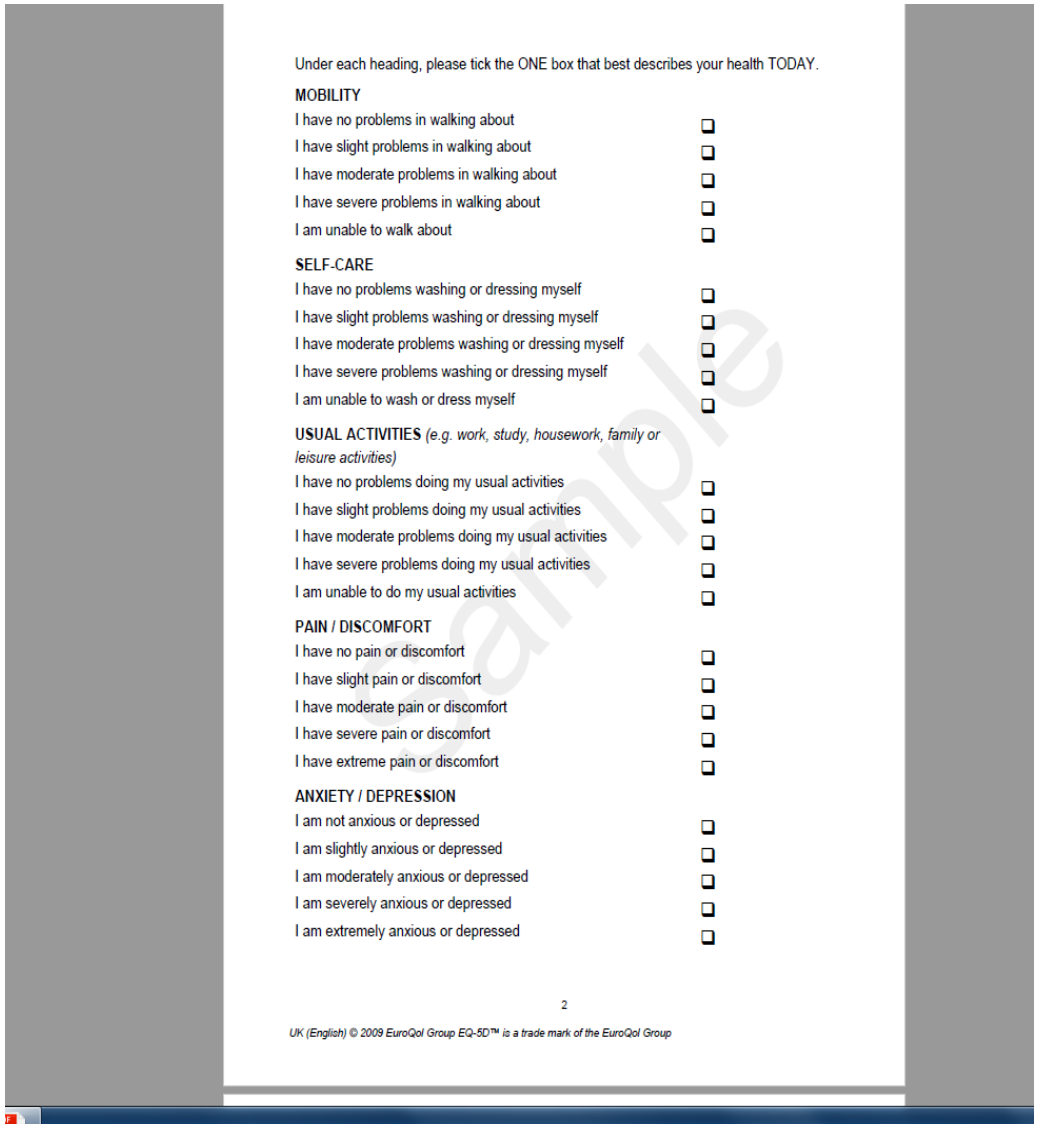
Different instruments:

Disease-specific questionnaires EORTC (cancer-specific); AFEQT- questionnaire (Atrial Fibrillation effect on quality of life)

Domain-specific questionnaires: State Trait Anxiety Inventory (STAI)

Generic quality of life questionnaires: EuroQol-5D; SF36

EQ-5Dimensions-5Levels



Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE

- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT

- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

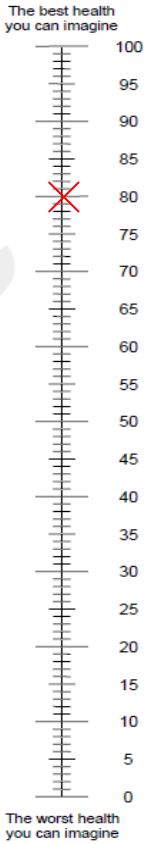
- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

2

EQ-5D-5L

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = 80



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EQ-5D-5L: example

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

- I have no problems in walking about ☑
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2

Health state

12212

What does it mean?

3) Valuation of quality of life

Why do we value health within an economic evaluation ?

- Weighing of different dimensions of quality of life in the endscore

Utility

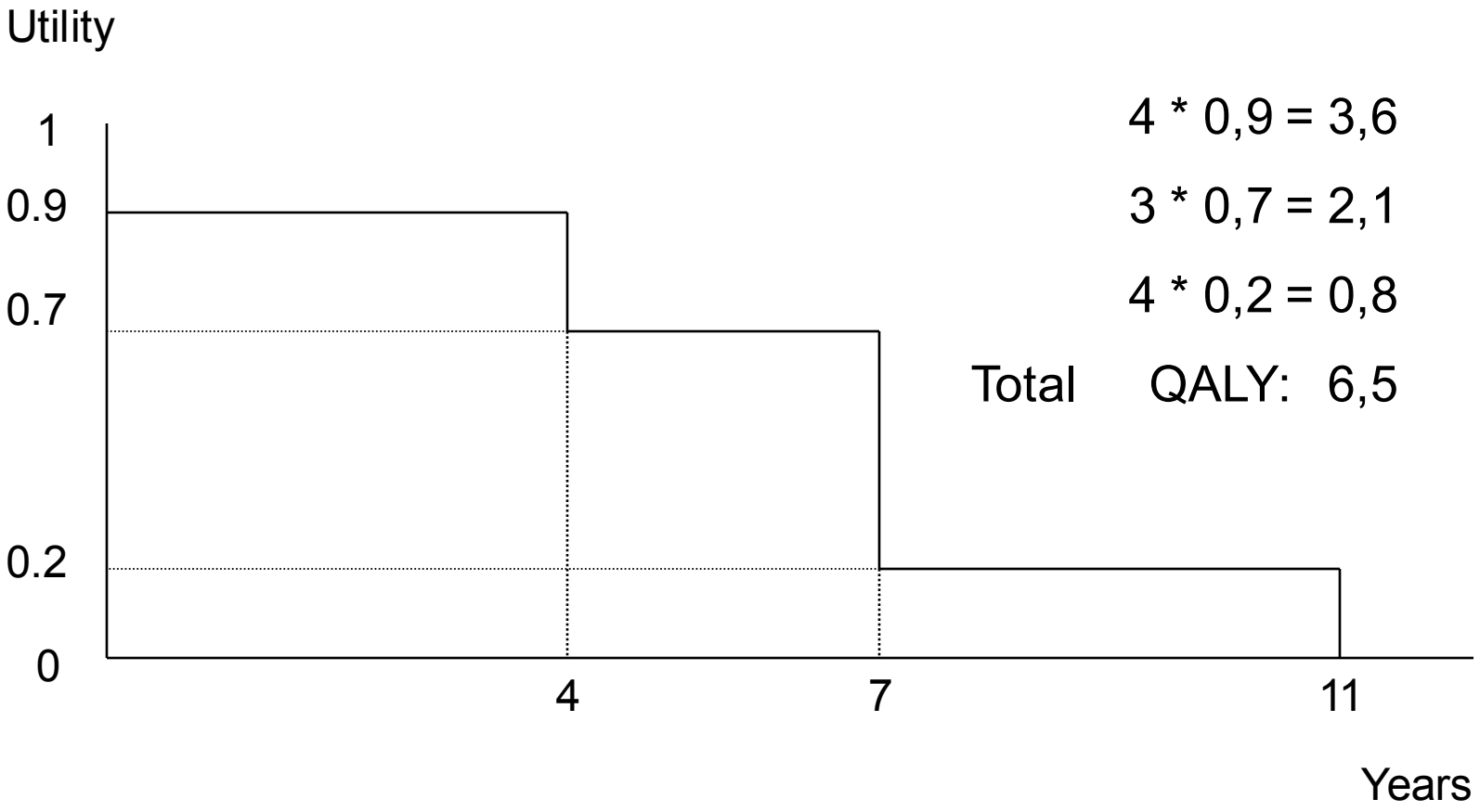
Assigning a weight to a certain health state, varying between:
0 (worst possible health state)
1 (best possible health state)

Valuation of the Dutch EQ-5D-5L health state

Complete health	=	1.000
• Mobility (level 1)		-0
• Selfcare (level 2)		-0.06
• Daily activities (level 2)		-0.039
• Pain (level 1)		-0
• Anxiety/mood (level 3)		-0.069

- So, health state **12212:** **Utility = 0.832**

4) Qol*time: Quality Adjusted Life Year



Steps in evaluation of costs

1) Identification: relevant resource use

2) Measurement of resource use (Quantity)

3) Valuation: unit costs per resource item (Costs)

4) Total costs: Q*C

1) Identification resource use

	Societal perspective	Health Care perspective
Costs within health care	All costs directly related to prevention, therapy, care etc.	Same
	Indirect medical costs	Same
Costs of patients & family	- Travel costs - Costs of informal care - Out-of-pocket costs etc.	-
Costs in other sectors	- Education/law etc. - Productivity loss	

Example cost analysis

	H+ group given standard prophylactic treatment (n=296)		H– group given no prophylactic treatment (n=307)		€ Difference in costs: H- group minus H+ group* (95% CI)
	Resource use	Mean costs (€)	Resource use	Mean costs (€)	
In-hospital costs					
Duration of hospitalisation					
None	--	--	50%	0	
Day care (0 nights)	45%	162	27%	82	–80 (–105 to –55)
24 h (including 1 night)	27%	174	12%	76	–98 (–137 to –60)
Long stay (including ≥2 nights)‡	18%	257	3%	49	–208 (–275 to –137)
Long stay inpatients (including ≥2 nights)§	9%	765	8%	560	–205 (–833 to 245)
Materials					
1 L 0·9% NaCl intravenous bags	1·60	4·50	0	0	–4·50 (–5 to –4)
Sequelae of intravenous hydration					
Extra hospitalisation days (24 h)	0·06	37	0	0	–37 (–72 to –11)
Extra in-hospital specialist consultations	0·04	2·31	0	0	–2·31 (–4 to –1)
Extra in-hospital diagnostics (ECG, ultrasound, laboratory)	0·02	0·88	0	0	–0·88 (–1 to 0)
Outside hospital costs within 35 days					
Renal diagnostics					
Blood tests	0·14	0·88	0·13	0·78	–0·01 (0 to 0)
Urine tests	0·13	2·26	0·09	1·38	–0·88 (–2 to 0)
Ultrasound exams	0·07	4·30	0·04	1·30	–4 (–5 to –1)
Other					
General practitioner consultation	0·19	3·67	0·25	6·13	2·5 (0 to 6)
Productivity loss (h)¶	1·3	50·50	0·44	16·80	–34 (–77 to 0)

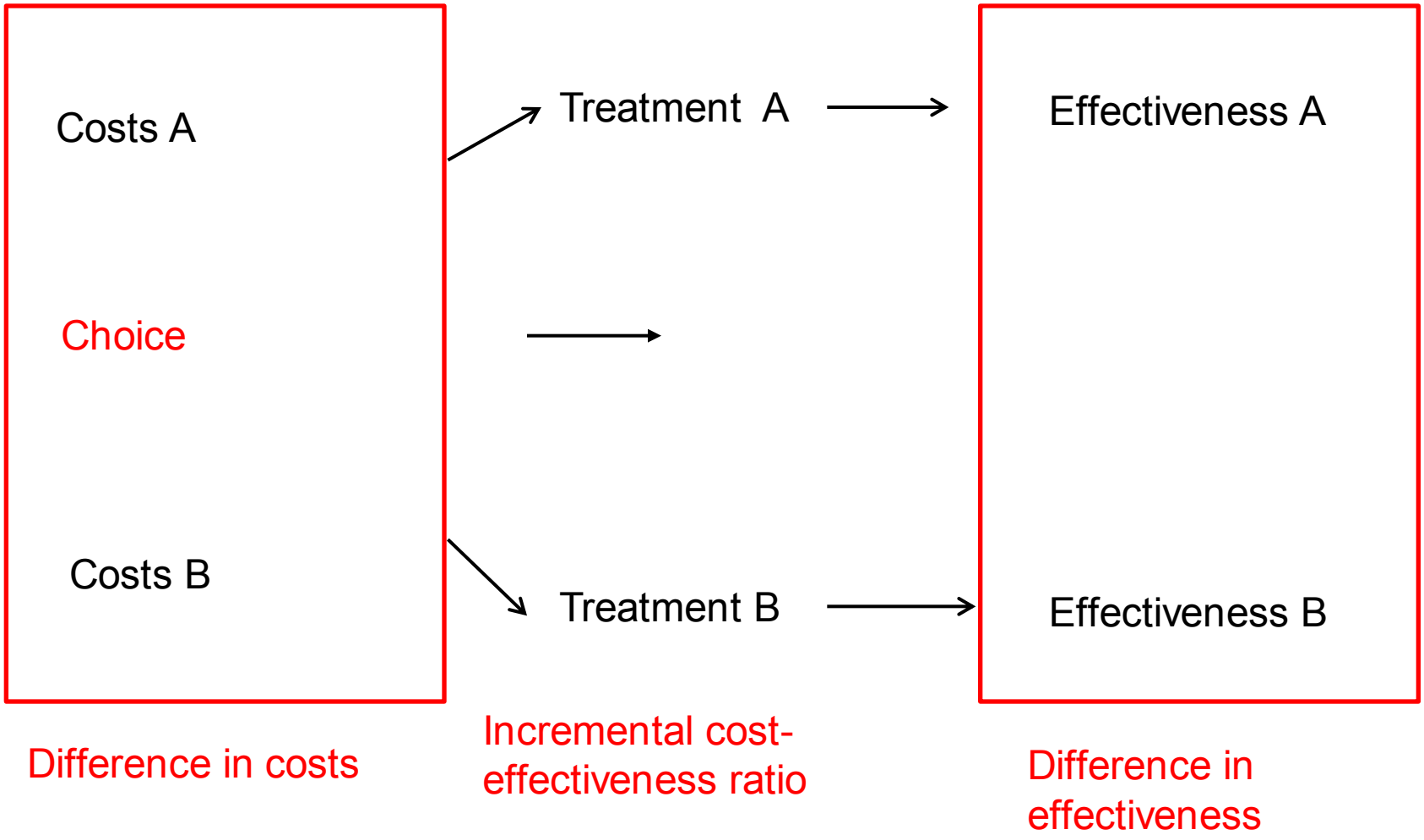
Resource use is given as % of patients using the resource or as mean number of units used per patient. Mean total costs were €1455 for the H+ patient and €792 for the H– patient (mean difference H– minus H+: €–663, 95% CI –1234 to –191). For unit prices see appendix p 6. All cost prices were indexed to the year 2015. Major renal events did not incur extra costs. ECG=electrocardiogram. *Obtained from the bootstrap analysis. †50% of the non-hydrated group was not hospitalised at all surrounding the contrast procedure and therefore incurred no hospitalisation costs. ‡Hospitalisation of patients specifically admitted for the procedure. §Hospitalisation of patients admitted for other reasons, before referral for the contrast procedure. ¶Productivity loss was calculated as the number of hours patients were absent from work multiplied by the gross wage per hour for men and women.

Articles

Prophylactic hydration to protect renal function from intravascular iodinated contrast material in patients at high risk of contrast-induced nephropathy (AMACING): a prospective, randomised, phase 3, controlled, open-label, non-inferiority trial

Estelle C Nijssen, Roger J Rennenberg, Patty J Nelemans, Brigitte A Essers, Marga M Janssen, Marja A Vermeeren, Vincent van Ommen, Joachim E Wildberger

Economic evaluation: always comparison!



Incremental cost-effectiveness ratio

- *Clinical outcome:*
  - Costs per recurrence avoided
  - Costs per asthma free days
  - Costs per life years gained

} Cost-effectiveness analysis

- *Valuation quality of life:*
  - Costs per QALY

} Cost-utility analysis

Different ratio's within a study possible!!

Calculation cost-effectiveness ratio

Example 1	Costs	QALYs	Ratio
Care as usual A	16.000	7	
New intervention B	16.600	7.02	
Incremental (B-A)	€600	0.02	€30.000 investment /QALY gain

Example 2	Costs	QALYs	Ratio
Care as usual A	3.075	4	
New intervention B	3.000	3.95	
Incremental (B-A)	- €75	-0.05	€1500 savings /QALY loss

Interpretation of the ICER's

New intervention has (compared to the alternative):	Lower effectiveness -0.05 QALY	Higher effectiveness +0.02 QALY
Lower costs -€75	€1500 savings per QALY loss **What do we decide?**	Dominance: always accept
Higher costs +€600	Inferior: always reject	€30.000 investment per QALY gain **What do we decide?**

Data analysis, uncertainty and interpretation

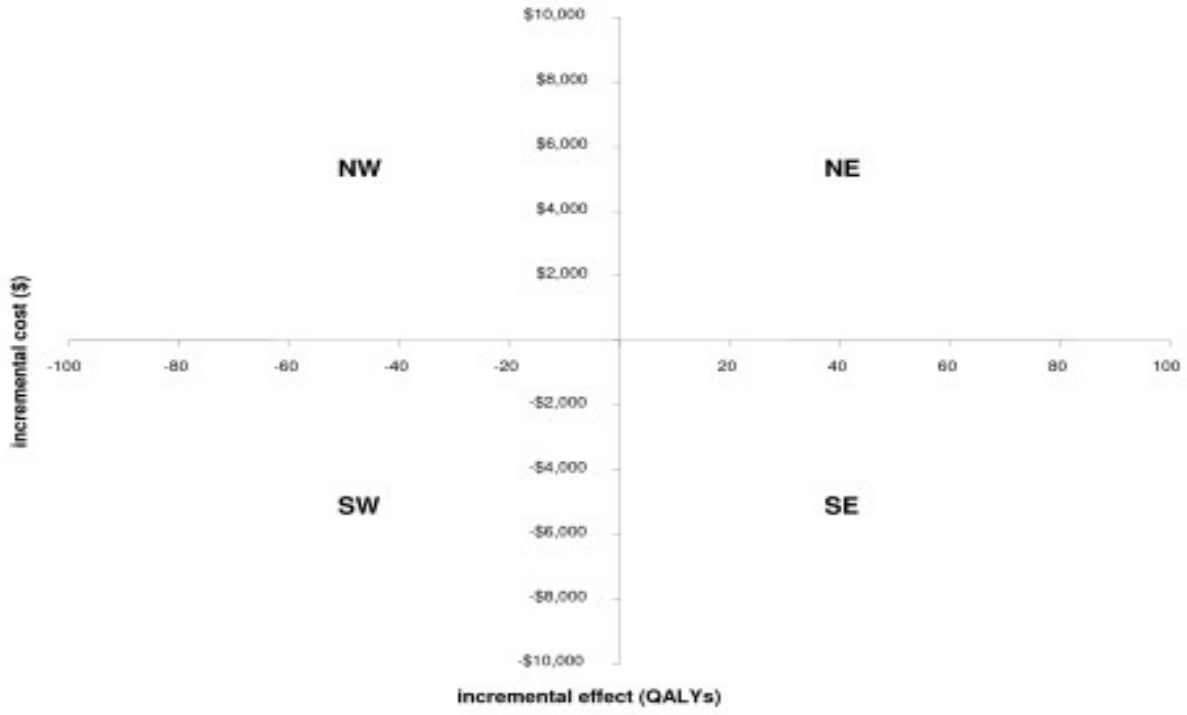
Uncertainty (more in separate module “uncertainty”):

What is the chance that a new intervention is cost-effective?

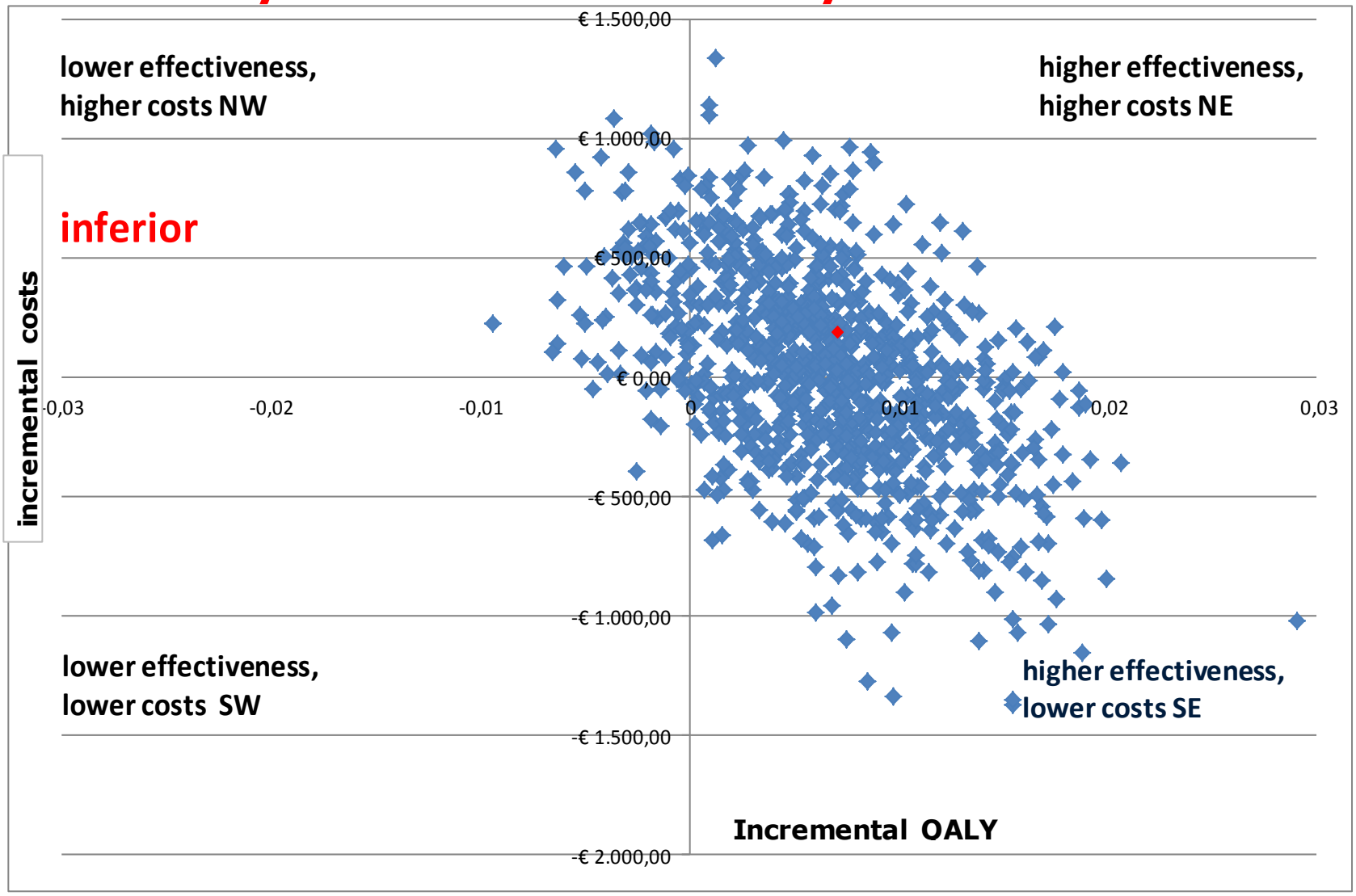
What is de uncertainty surrounding the CE-ratio?

Costs/effect data often skewed: non-parametric bootstrap analysis

Data analysis and uncertainty



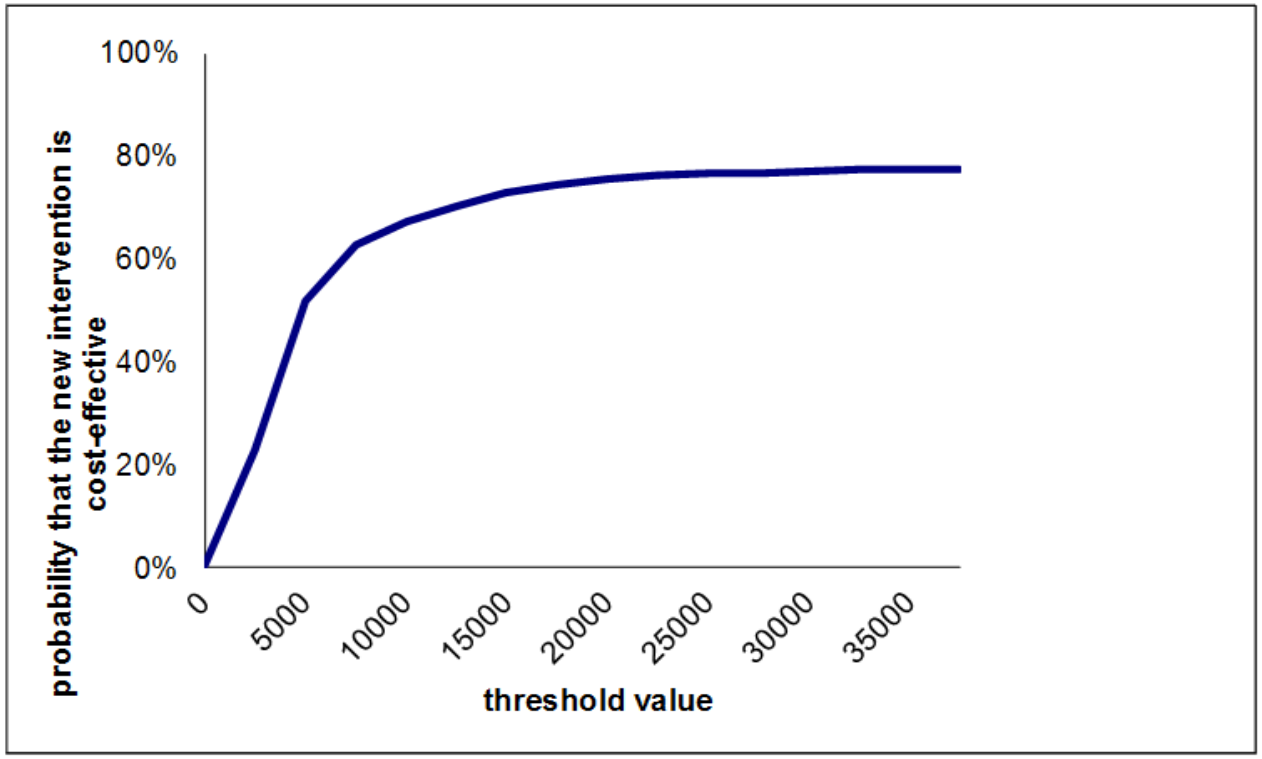
Data analysis and uncertainty



Data analysis and uncertainty

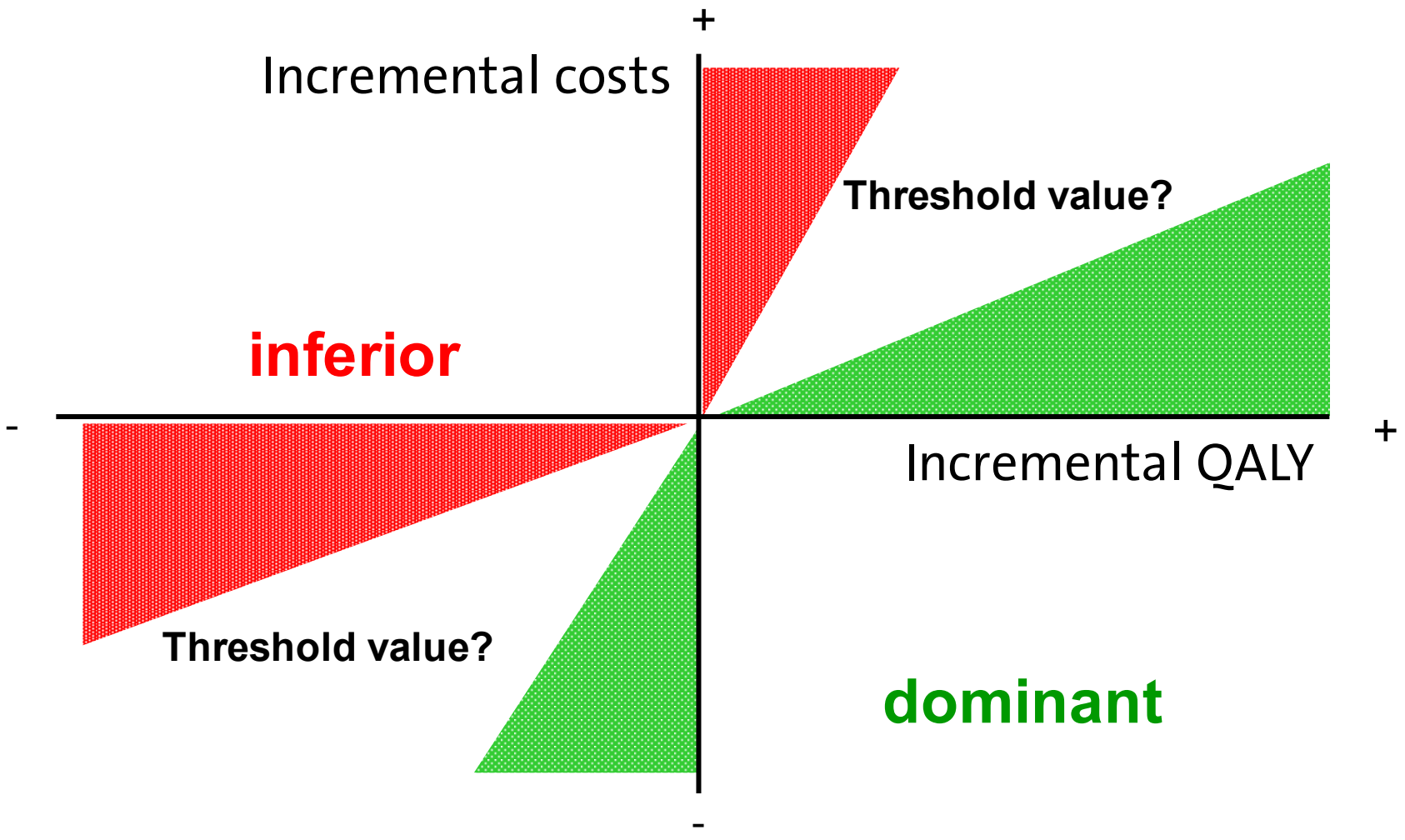
Decision uncertainty can be graphically displayed in an:

Acceptability curve: shows the probability that the new intervention is cost-effective across a range of threshold values.



Threshold value= societal willingness to pay for a gain in effectiveness or QALY

Data analysis, uncertainty and interpretation



What is an acceptable threshold value for a QALY?

- Netherlands: €80,000/QALY with a high disease burden (RVZ 2006)
- UK: varies between £ 30.000 to £ 45.000 per QALY

- So:
  - No fixed value!
  - Other considerations also count: (public) opinion, ethical, legal aspects

Final points

Time horizon

- Should capture all relevant events (as long as the follow-up of the RCT) BUT

- Extrapolation of results beyond the follow-up of a trial often necessary→ lifetime

In short

– Trial based economic evaluations are complements to economic evaluations that use decision analytical modeling.