Early stage HTA

(reverse engineering applied to Health Economy)

Dr Leandro Pecchia
University of Warwick

HTA of Medical Devices

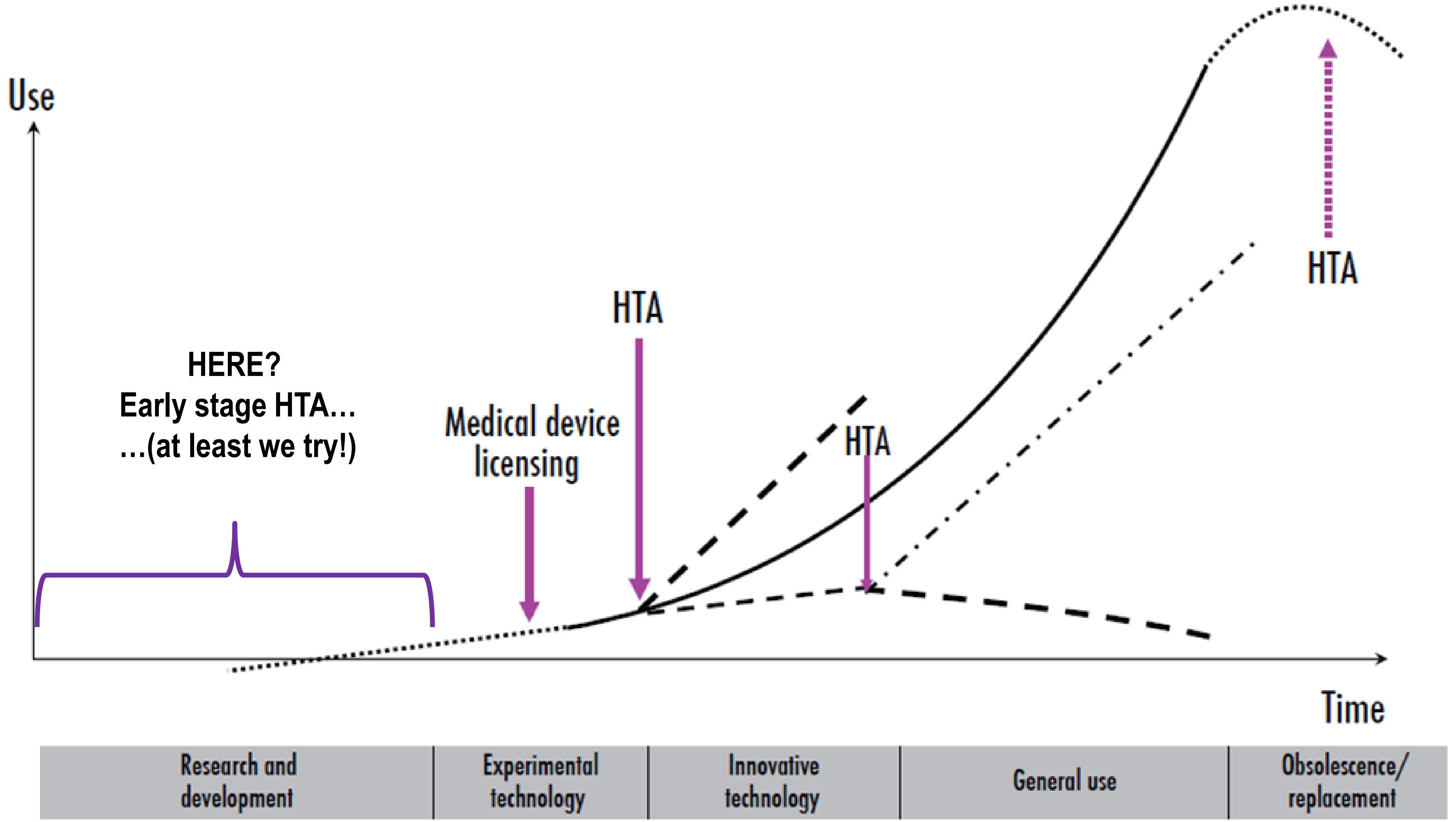
Medical devices vs Drugs

Devices	VS	Drug

…for MD, HTA should assess the whole process, not only the procurement and many mode dimensions than just cost-efficacy.
(MCDA?)

L Pecchia, MP Craven, "*Early stage Health Technology Assessment (HTA) of biomedical devices. The MATCH experience*". World Congress on Medical Physics and Biomedical 2012, 26-31 May 2012, Beijing, China.

HTA during design



*WHO web site (last access 15.09.2012): http://www.who.int/medical_devices/assessment/en/

Leandro Pecchia. l.pecchia@warwick.ac.uk

Health Technology Assessment (HTA)

- *Health Budget is limited, in some countries scarce. Introducing a new technology results in cutting another one.*
  - *Is our innovation worth of public money?*
  - *Is it worth of cutting budget to another health problem?*

- Health Technology Assessment (HTA) is the tool used by NHSs to answer those questions

- According to WHO *“the "problem" of the assessments is considered only when the technology is close to its placing on the market and not during R&D process”**

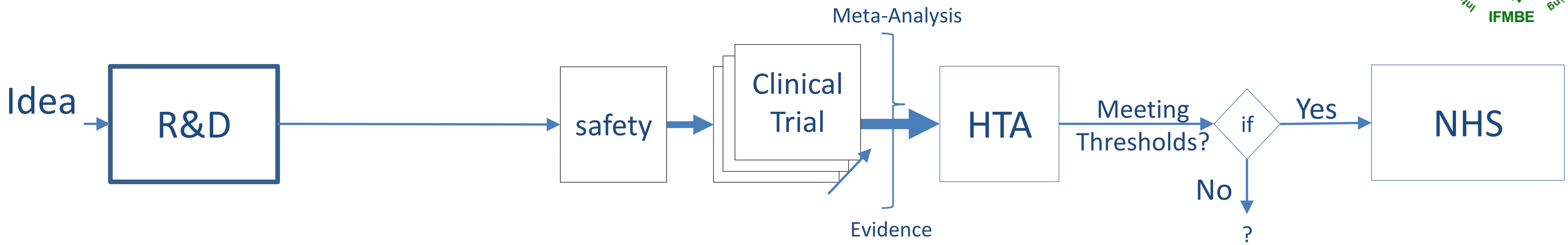
- Because of this “Tsunami”:
  - NHSs are increasing health-economic thresholds, in order to control public expenditure for health
  - New EU regulation on Medical Devices, will introduce pre-market assessment…
  - EU Commission developed the MAFEIP tool for the assessment of innovations in health

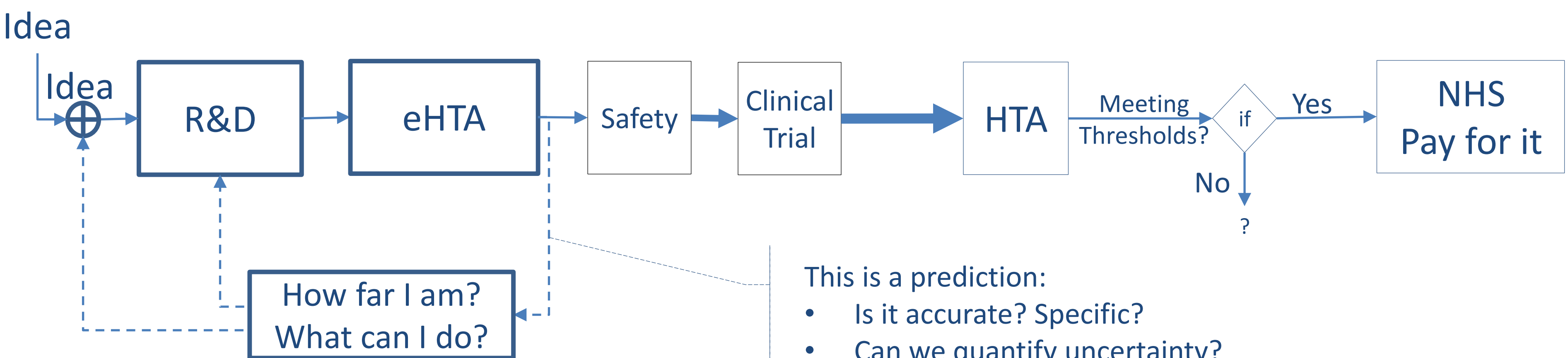
*WHO web site (last access 15.09.2012): http://www.who.int/medical_devices/assessment/en/

Early HTA

- We can consider "Market constrains/prospective" **during the R&D** (early stage HTA, premarket evaluation…), when **a small change may have a big impact**…
- The idea is to apply reverse engineering to health economic and back propagate this information to designers/developers to explore if it is possible to increase their impact (i.e. meet the cost-efficacy constrains)
- …let's see this concept within the context…

Early HTA & R&D





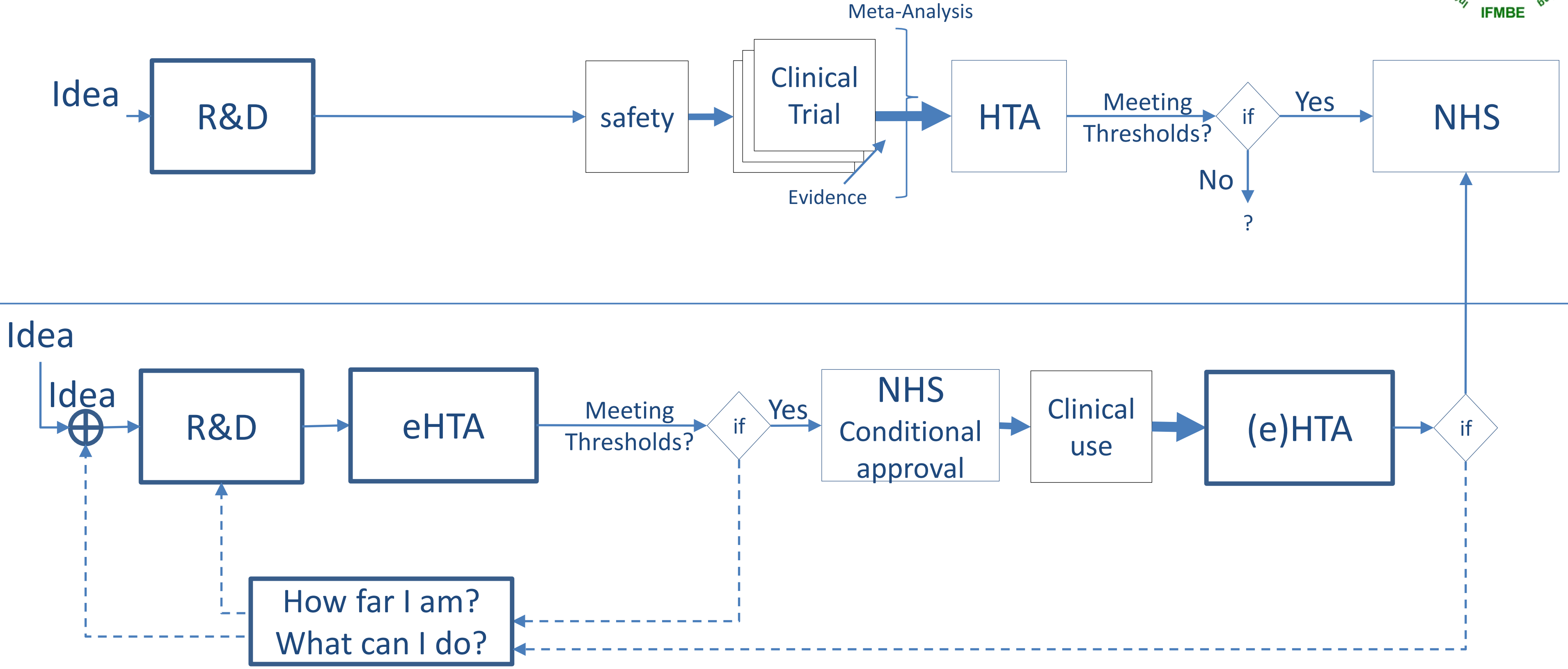
This is a prediction:

- Is it accurate? Specific?
- Can we quantify uncertainty?
- Is the model accurate? Properly dimensioned?
- Can we minimize overfitting?

This is a controller:

- Is the 'process' fully observable (i.e., am I measuring all I need?)?
- Is the 'process' controllable (i.e., can I change it?)?
- Is the closed-loop feedback stable (i.e., will I reach a consistent result?)?

Early HTA & R&D



Meta-Analysis
Idea
R&D
safety
Clinical Trial
Evidence
HTA
Meeting Thresholds?
if
Yes
No
?
NHS
Idea
Idea
R&D
eHTA
Meeting Thresholds?
if
Yes
NHS Conditional approval
Clinical use
(e)HTA
if
How far I am? What can I do?

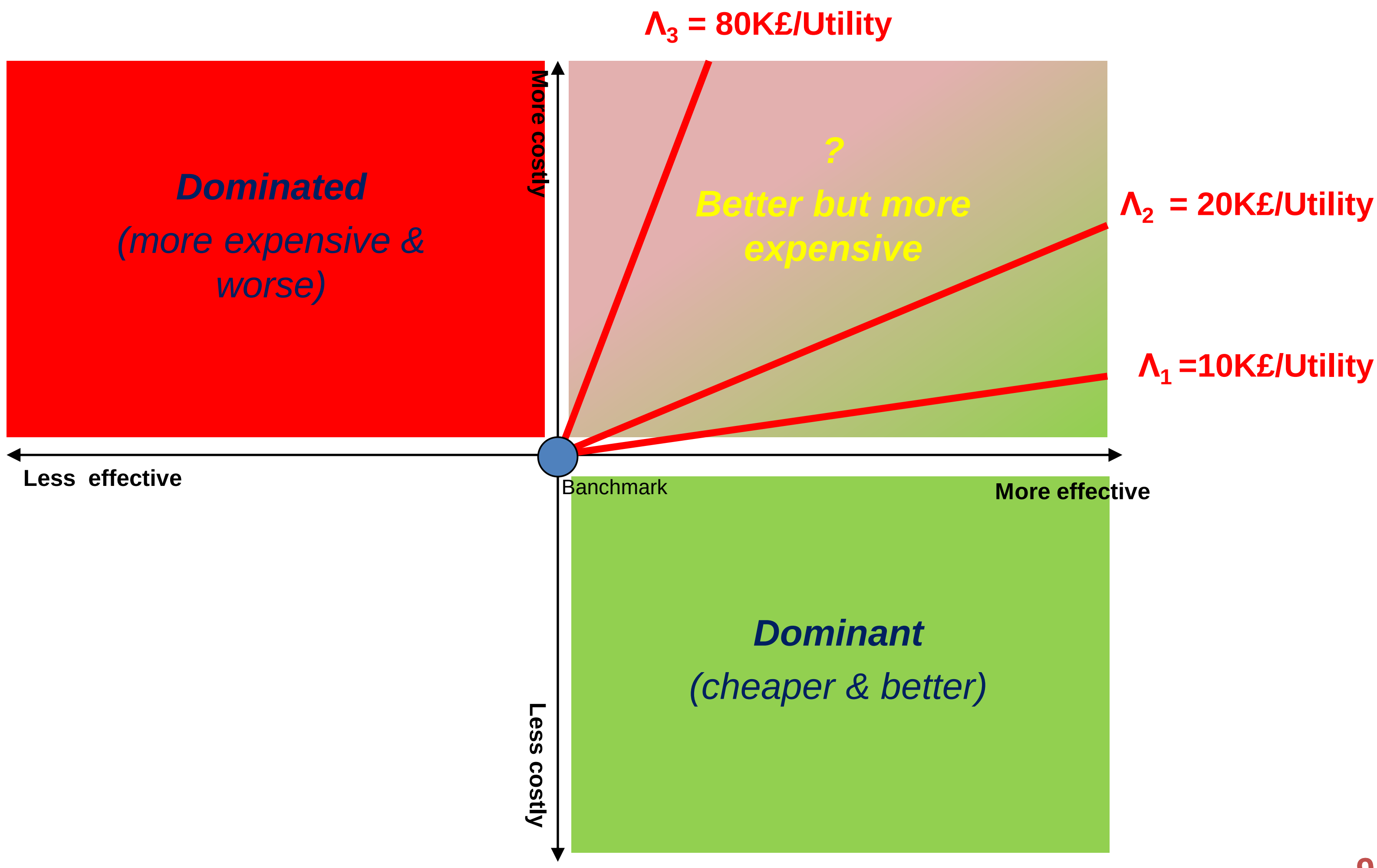
GOALS

eHTA methods/aims

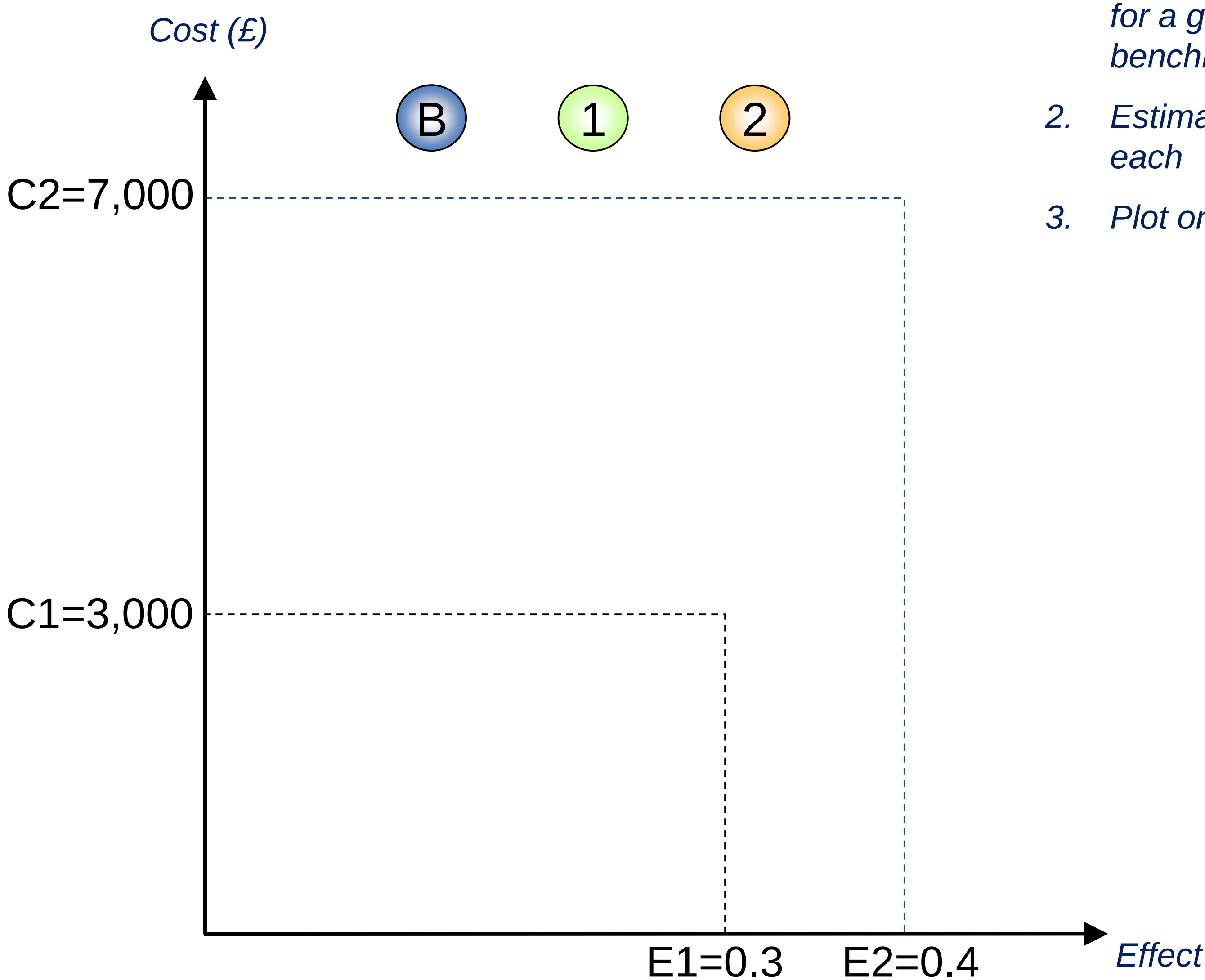
- **“Standard” methods of HTA limitation for Med. Dev. and early HTA**
- Methods and tools for early stage HTA:
    - **Headroom Analysis (HA):**
        - Assuming such a benefit for the patient, above the existing funded treatment…
        - …what is the maximum cost that the new device may have, to be cost-effective?
        - Is this worth of investing my resources? It there a reasonable ROI?
    - **Markov Models (MM):**
        - Assuming that my device will have this benefit (i.e. reduce ΔX% mortality)…
        - …will it be cost-effective, with a reasonable certainty?
        - May I simulate the scenario and infer, with statistical significance, its cost-effectiveness?

HTA

Willingness to pay

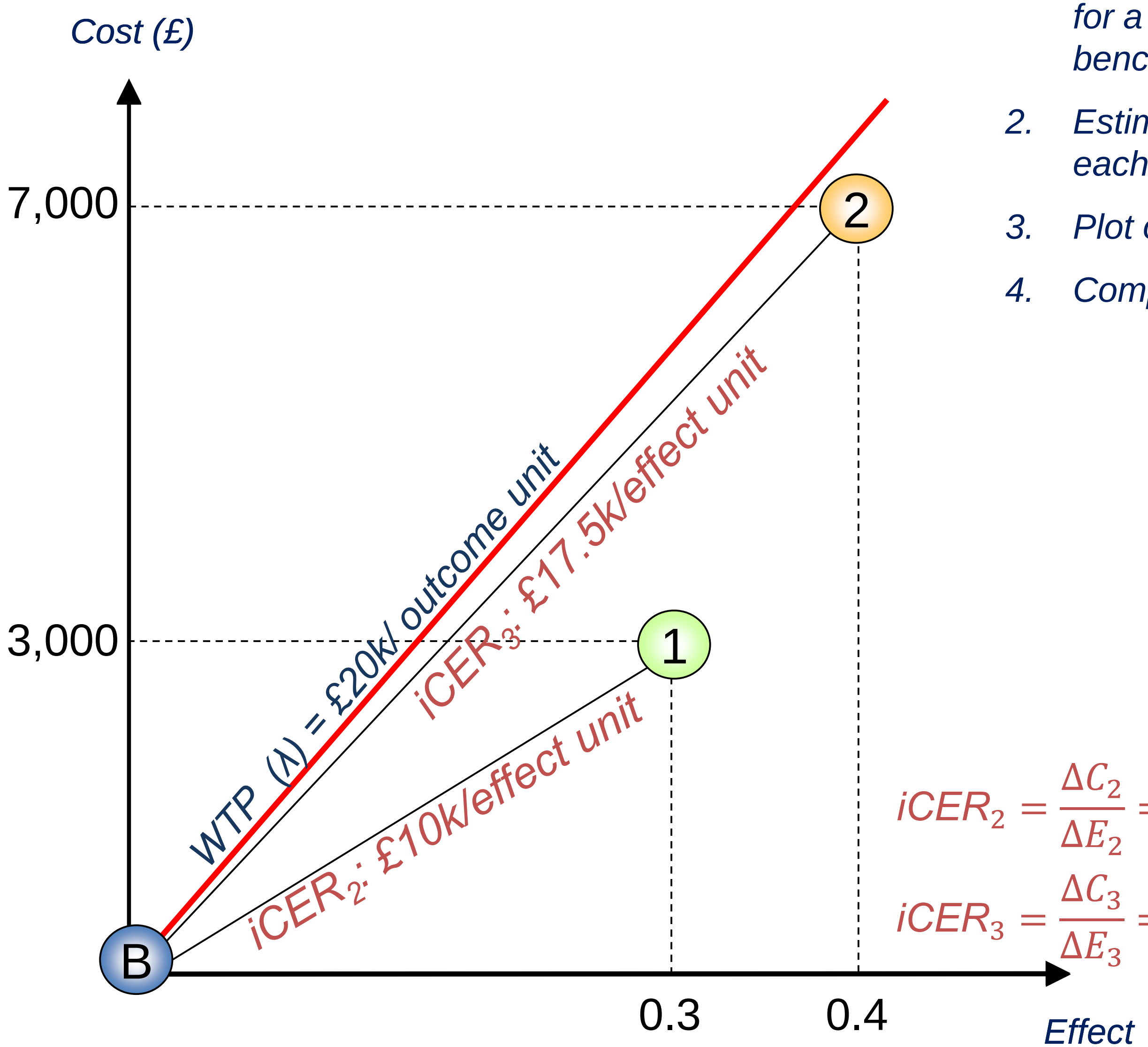


Leandro Pecchia. l.pecchia@warwick.ac.uk



1. *Identify all feasible treatment options for a given patient group, including the benchmark, if any*
2. *Estimate the costs and health effects of each*
3. *Plot on the cost-effect plane*

HTA
standard methods

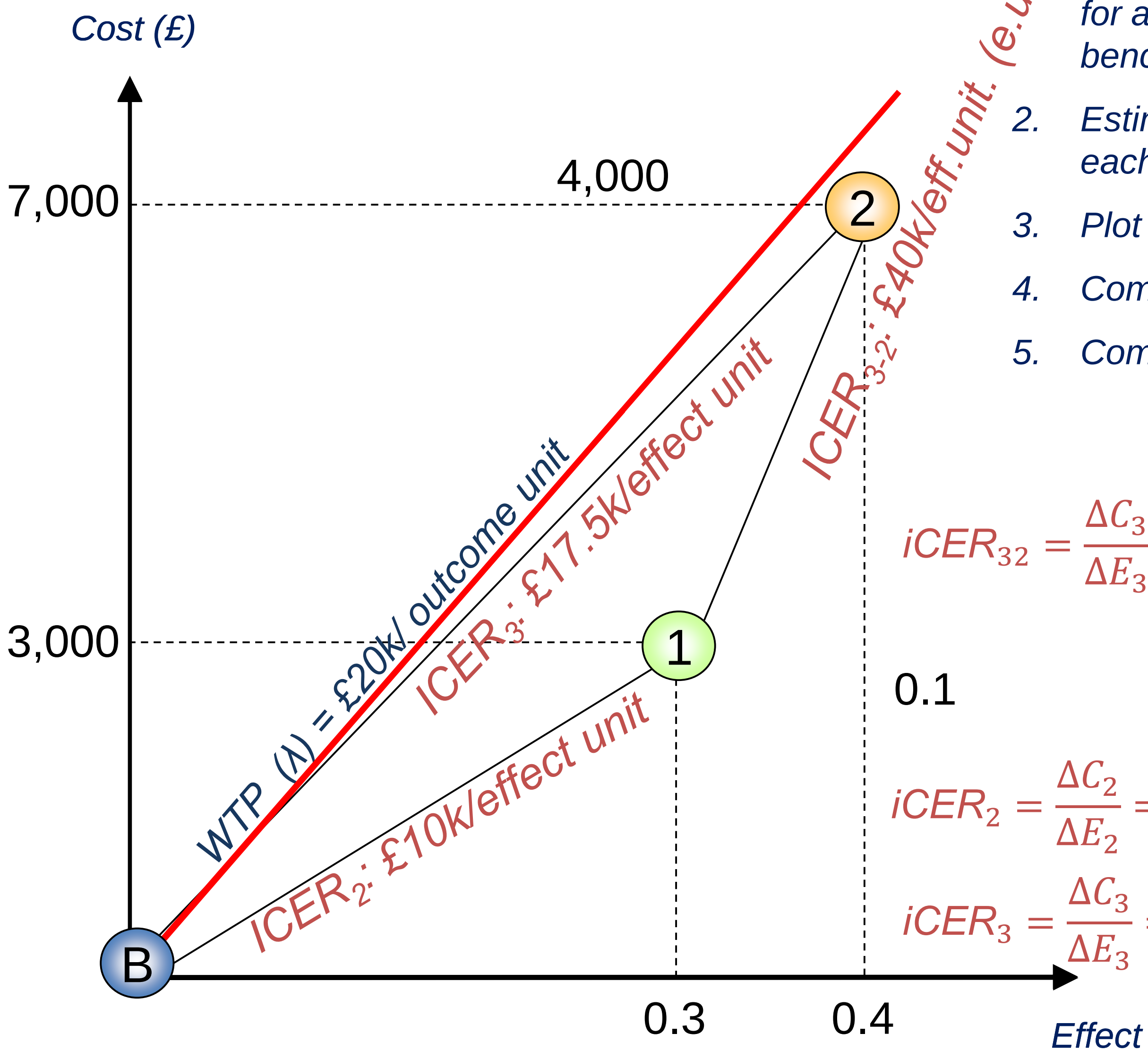


1. *Identify all feasible treatment options for a given patient group, including the benchmark, if any*
2. *Estimate the costs and health effects of each*
3. *Plot on the cost-effect plane*
4. *Compute and compare the iCERs*

$$iCER_2 = \frac{\Delta C_2}{\Delta E_2} = \frac{C_2 - C_B}{E_2 - E_B} = \frac{£3k}{0.3} = £10k/e.u.$$

$$iCER_3 = \frac{\Delta C_3}{\Delta E_3} = \frac{C_3 - C_B}{E_3 - E_B} = \frac{£7k}{0.4} = £17.5k/e.u.$$

HTA
standard methods



1. Identify all feasible treatment options for a given patient group, including the benchmark, if any
2. Estimate the costs and health effects of each
3. Plot on the cost-effect plane
4. Compute and compare the iCERs
5. Compare 1 with 2

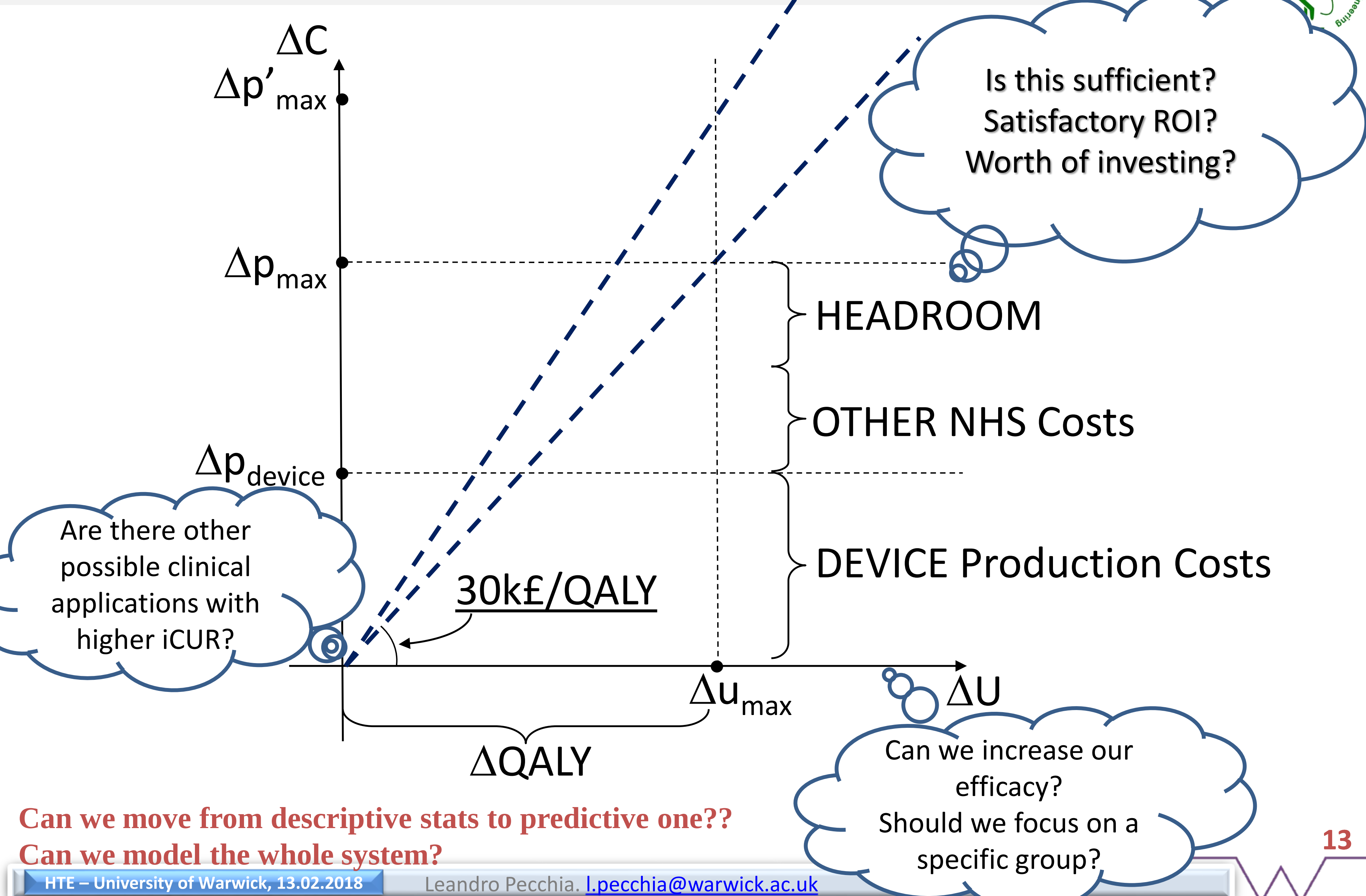
$$iCER_{32} = \frac{\Delta C_{32}}{\Delta E_{32}} = \frac{C_3 - C_2}{E_3 - E_2} = \frac{£4k}{0.1} = £40k/e.u.$$

$$iCER_2 = \frac{\Delta C_2}{\Delta E_2} = \frac{C_2 - C_B}{E_2 - E_B} = \frac{£3k}{0.3} = £10k/e.u.$$

$$iCER_3 = \frac{\Delta C_3}{\Delta E_3} = \frac{C_3 - C_B}{E_3 - E_B} = \frac{£7k}{0.4} = £17.5k/e.u.$$

Method 1

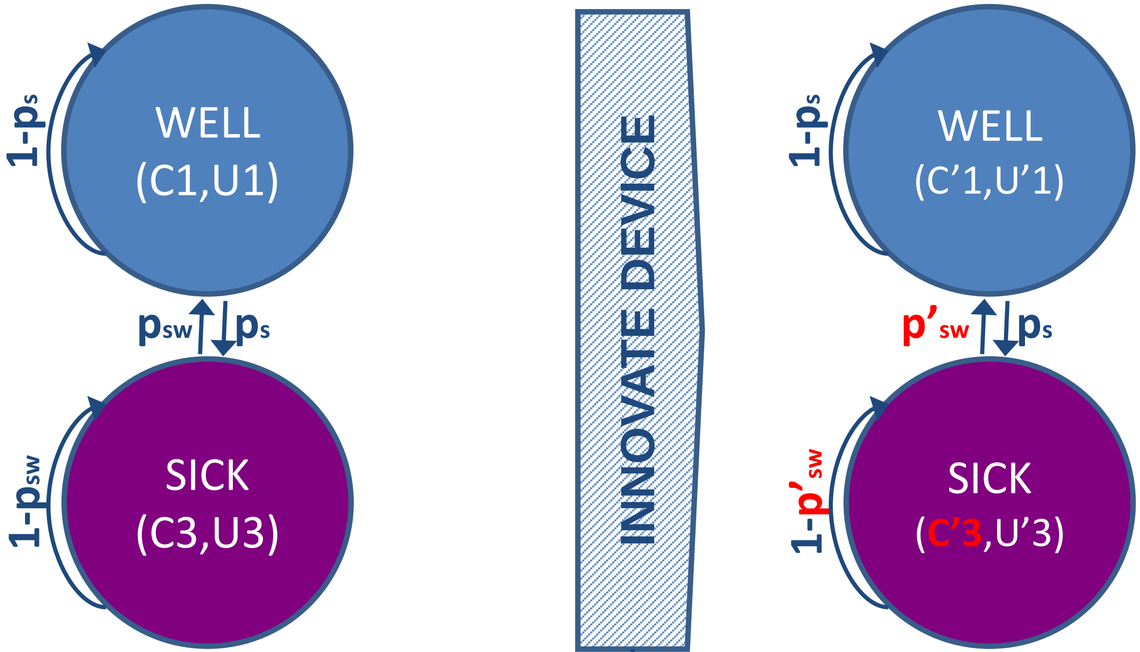
Headroom Analysis



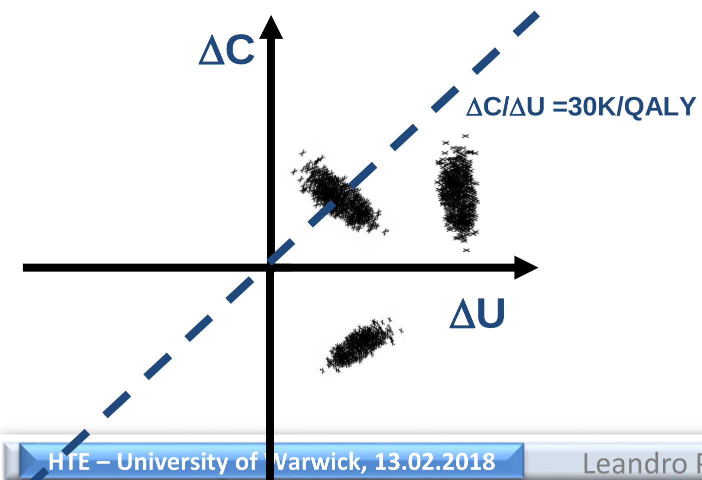
Can we move from descriptive stats to predictive one??
Can we model the whole system?

2 states Markov Models

disease/sick



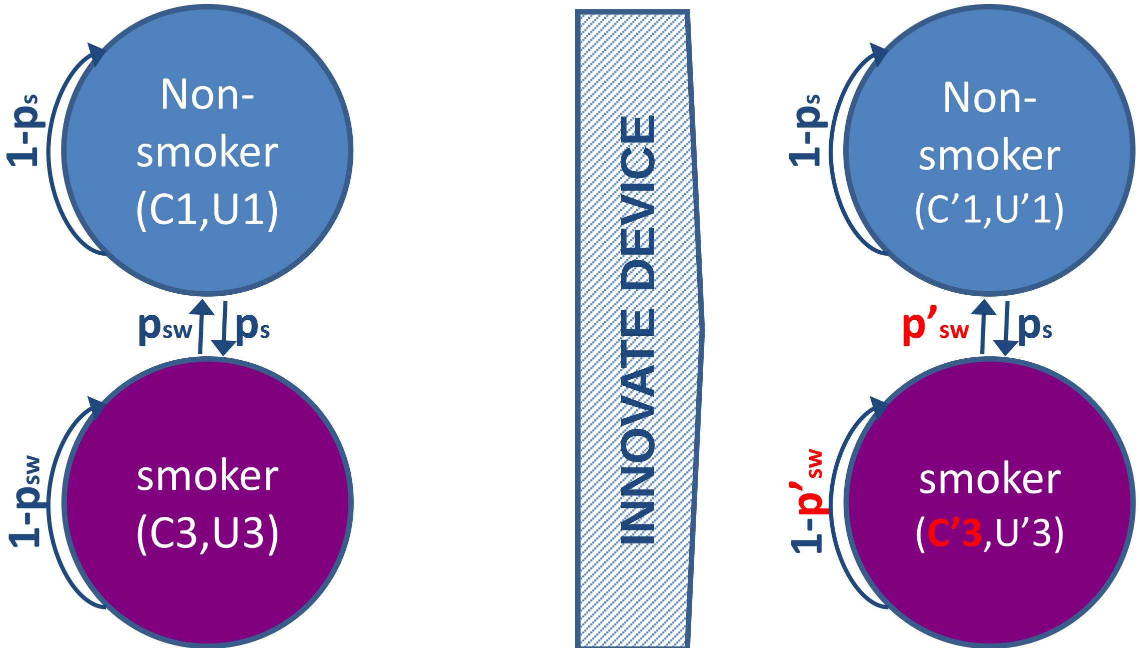
↑ heal ($p'_{sw} > p_{sw}$); ↑ costs ($C'_3 > C_3$)



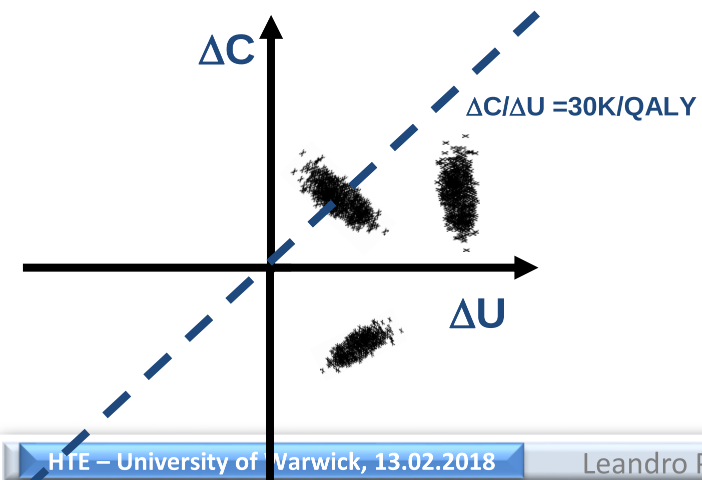
MM

2 states Markov Models

smoker/non-smoker

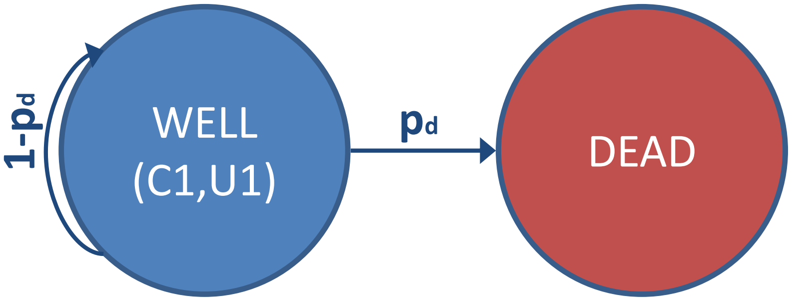


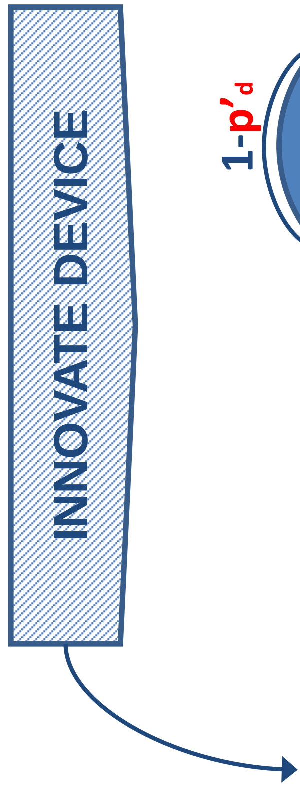
↑ heal ($p'_{sw} > p_{sw}$) ↑ costs ($C'_3 > C_3$)

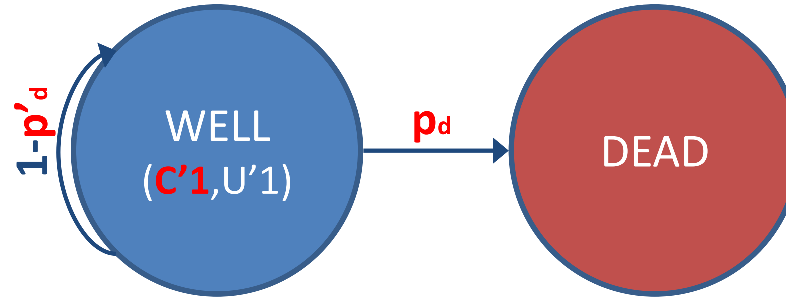


2 states Markov Models

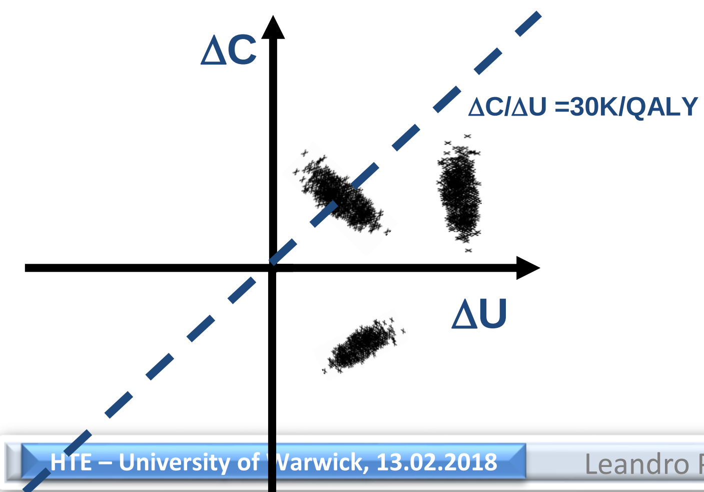
disease/dead







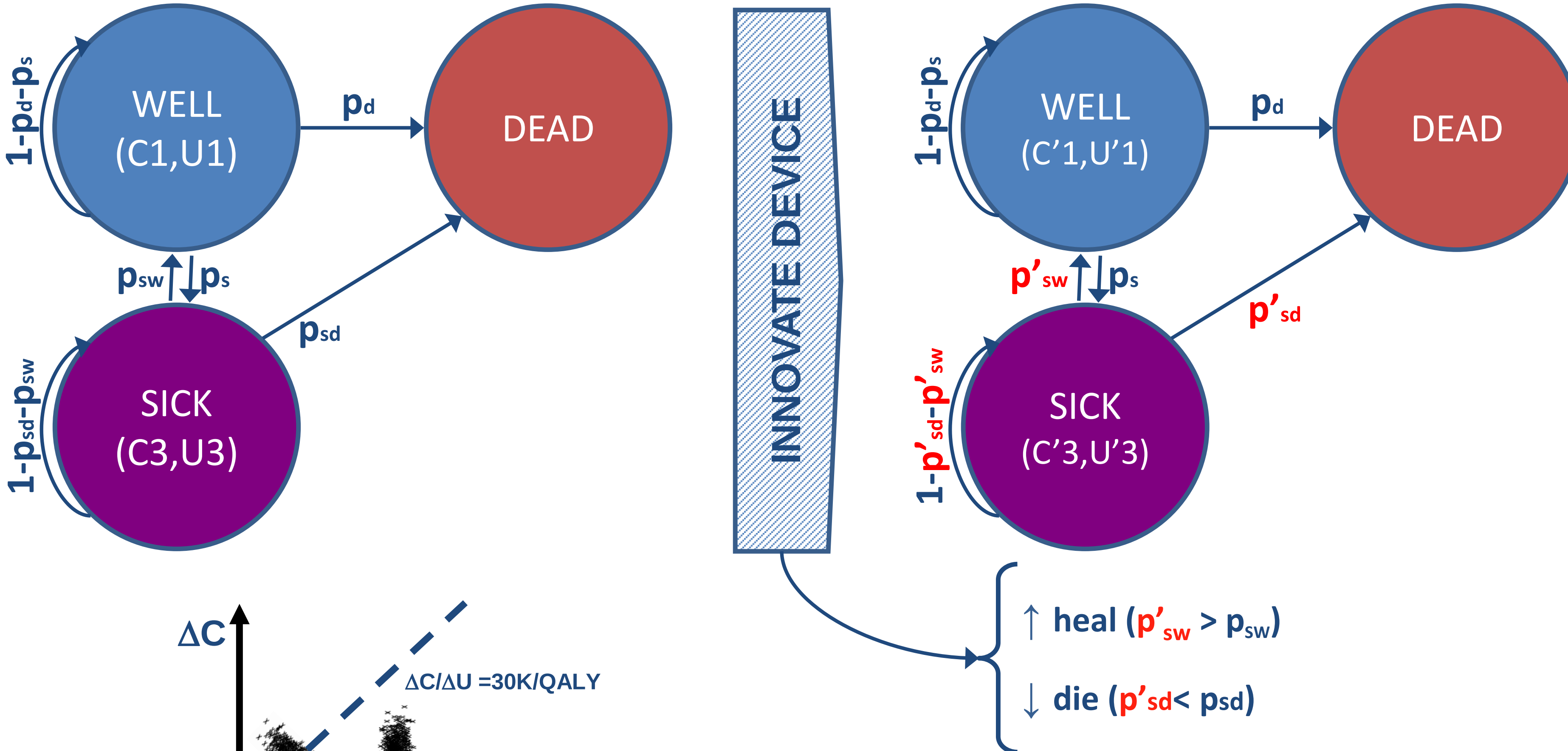
↓ die ($p'_d < p_d$); ↑ costs ($C'_1 > C_1$)

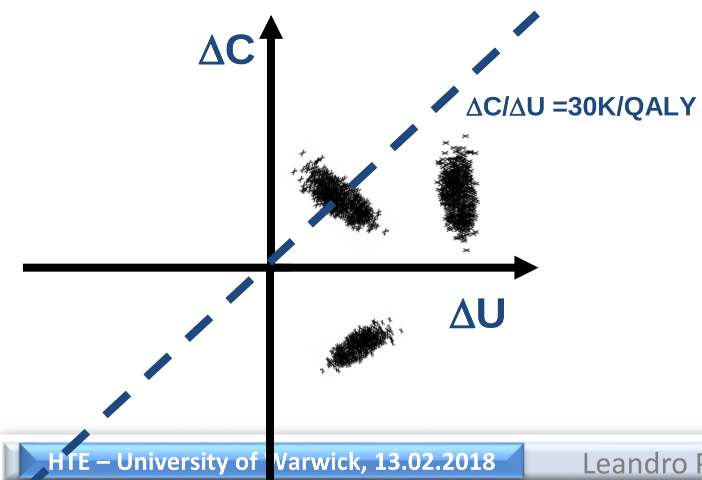


MM

4 states Markov Models

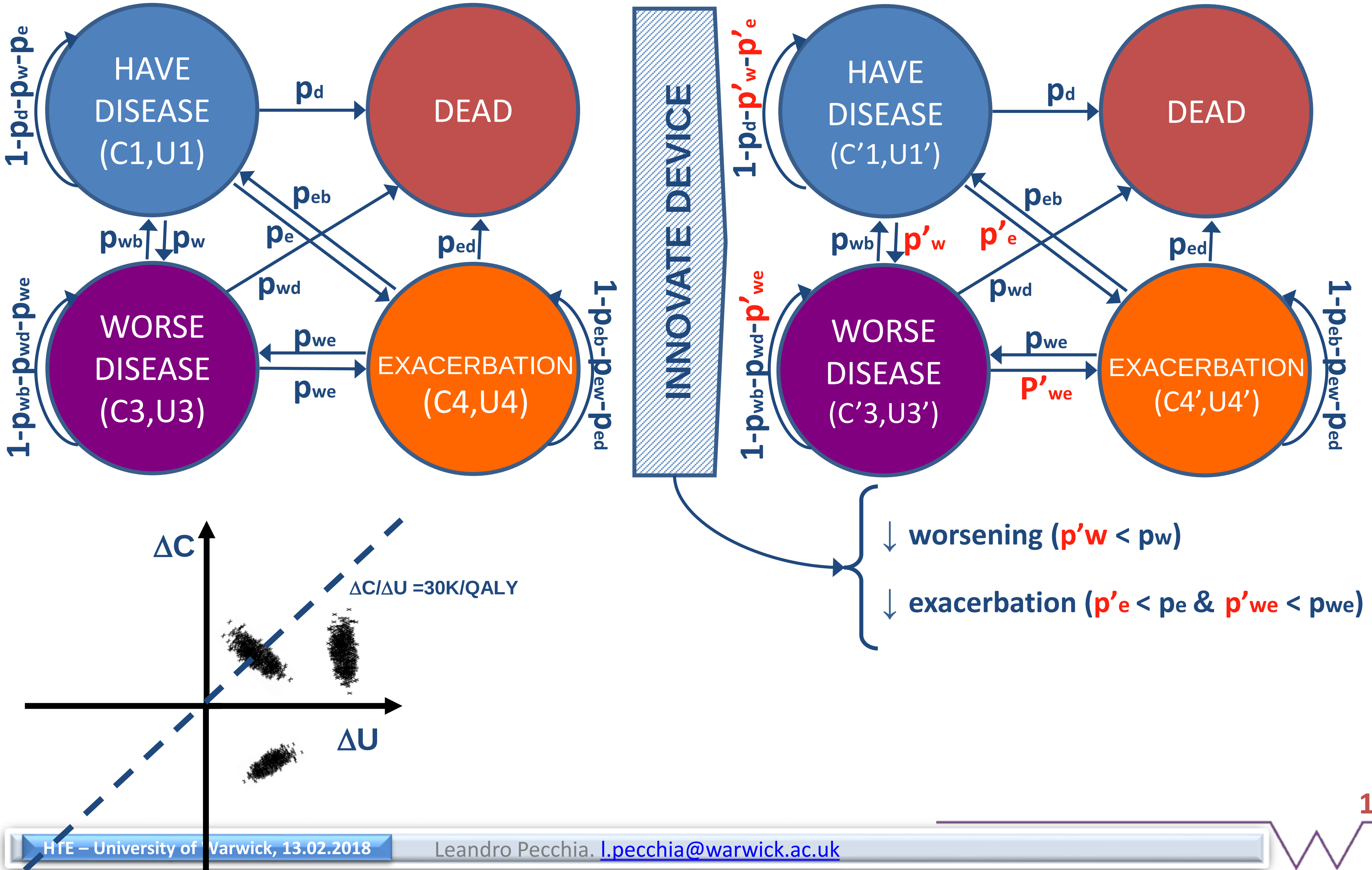
disease/worsening/exacerbation/dead





4 states Markov Models

disease/worsening/exacerbation/dead



↓ worsening ($p'_w < p_w$)

↓ exacerbation ($p'_e < p_e$ & $p'_{we} < p_{we}$)

CASE STUDY
Physiological monitoring and biomedical signal processing for fall prevention in elderly

Leandro Pecchia

Applied Biomedical Signal Processing and Intelligent eHealth (ABSPIE) Lab
University of Warwick
The United Kingdom

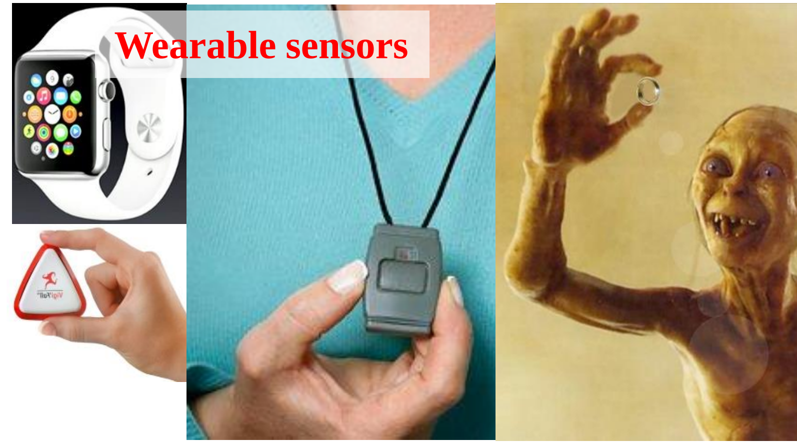
State of the art

- Falls are underestimated:
  - Hospital reports focus on hospitalization cause, which are falls consequences (i.e. hospitalised hip fracture)
  - …no specific DRG for fall.
- Falls are caused by the ***complex and dynamic interactions*** between
  - ***Intrinsic risks*** *(subject dependent)*: balance/gait, dizziness, hypotension
  - ***Extrinsic risks (circumstances dependent)***: rising from chair/bed, unsupervised toileting
  - interpreting physiological changes into the context is crucial, but really complex

	Main aim	Methods	Tools
Prevention	↓risk of falling	• Risk assessment • Intervention • Monitoring (loop)	• Physical tests/assessment scale (also ICT) • Physical training, drug revision, home interventions (risk minimization)… • High risk referred to local fall clinics/GP
Detection	↓falls harms	• Monitoring • Automatic warnings	• Ambient sensors • Wearable sensors (mainly accelerometers and gyroscopes)
Prediction	Avoid next fall	• Risk assessment • Monitoring • Intervention	• Ambient sensors to detect exposure to extrinsic risk factors • Wearable sensors (mainly accelerometers and gyroscopes)

State of the art

- Today, technology-based fall prediction and detection focuses on:
  - early detection of falls or circumstances that may result in a falls (i.e. rising from bed)



- Limits:
  - Additive technologies (useful only for falls) => costly interventions!
  - Elevated number of false positives
  - Obtrusiveness: few elderly are willing to wear devices, or to be “spied”, “just for a fall”

Warwick approach: physiological monitoring

Three case studies in which biomedical signal processing was applied to falls:

- **Fall prevention (Risk of fall assessment):**
  - Cross sectional study investigating association between depressed HRV and risk of falling in 3 months
  - 167 hypertensive subjects assessed at the base line and monitored for 12 months
  - Results: a depressed HRV is associated with an increased risk of falling

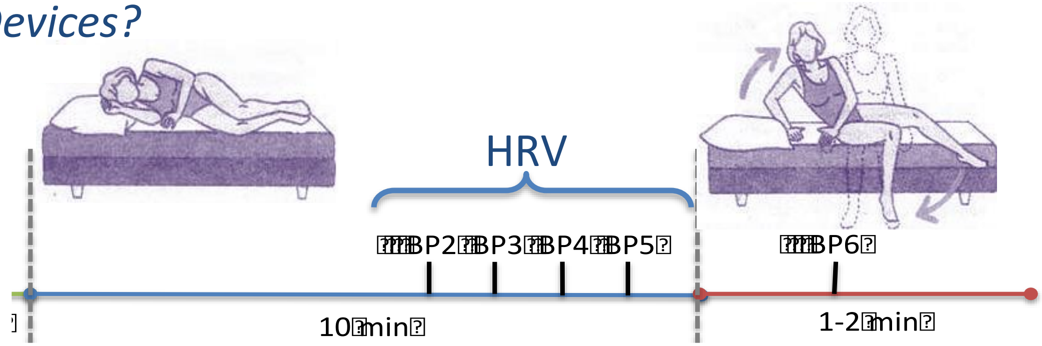
- **Fall detection:**
  - Proof of concept: ECG was measured in simulated falls
  - 30 healthy subjects
  - Result:
    - 4 ECG features resulted significantly changed when the subject was laying
    - An automatic classifier detected satisfactory simulated falls

- **Fall prediction (predicting BP drops due to standing hypotension basing on HRV)**
  - Proof of concept: ECG was measured during active standing from a bed and a mathematical model to predict major BP drops was developed and tested
  - 30 healthy subjects
  - Result: the model predicts significant BP drops (acc 80%, sensit. 92.5%, spec 90%).

Study design

A significant number of indoor falls happen while rising from beds/chairs, mainly because of postural hypotension.
Research question: is it possible to predict blood pressure drops by monitoring HRV?

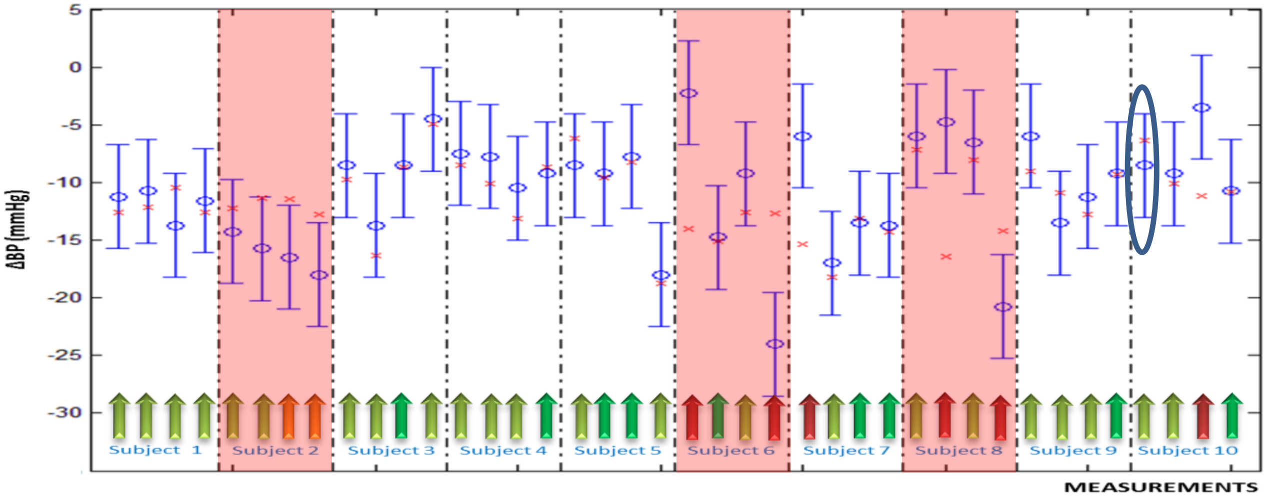
To What Extent it is Possible to Predict Falls due to Standing Hypotension by Using HRV and Wearable Devices?

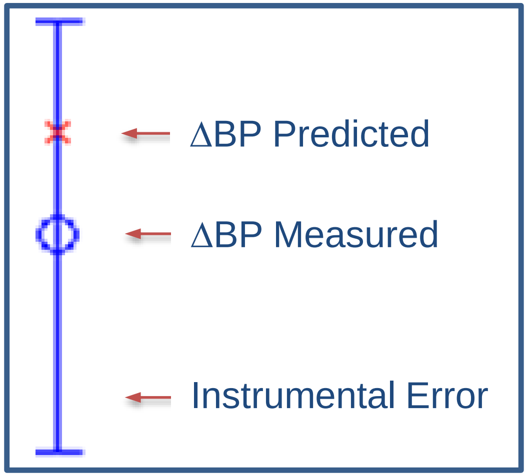


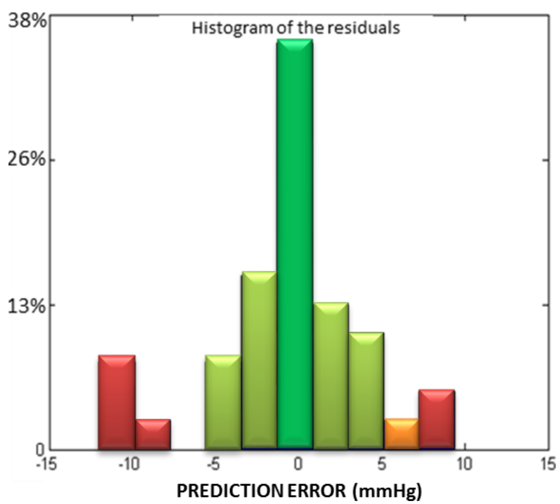
↓BP
ΔBP= BP6-average (BP2:BP5)
ΔBP =f(HRV) [??]

HRV → **Predictive Model** **ΔBP = *f*(HRV)** → ΔBP

Lab model performance: efficacy in the best case







87% rate of correct prediction *(error<4.5 mmHg)*

The majority of errors are from few identifiable subjects:
(75% or errors from the same 3 subjects: 2, 6 and 8 in figure)
=> the rate of correct prediction can go <u>up to 93%</u>

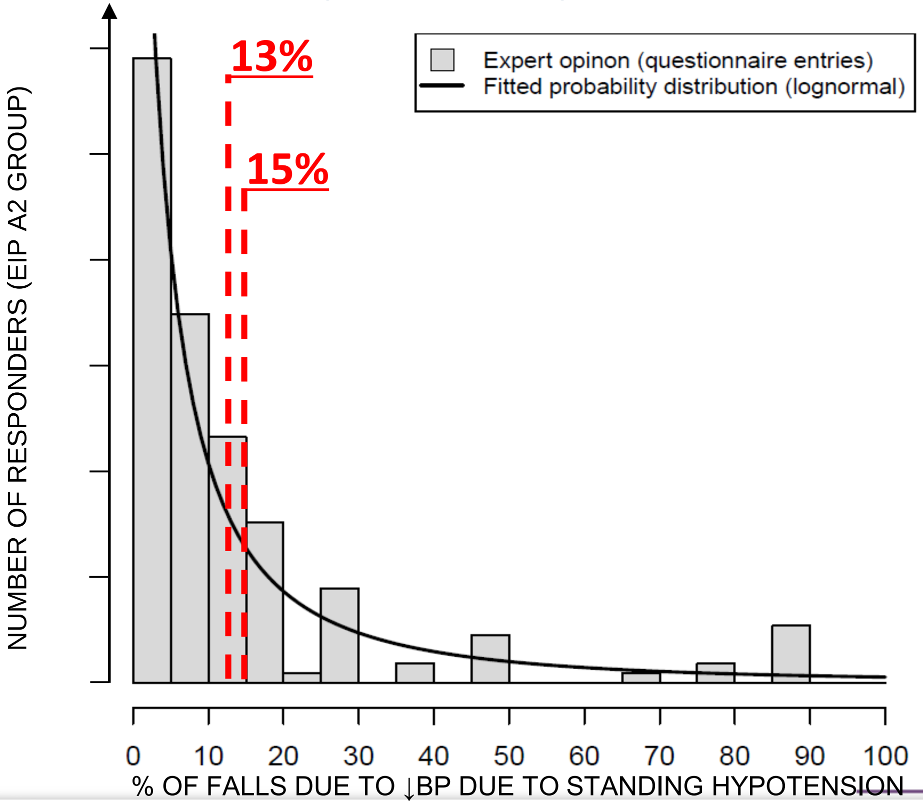
**Patent Application (No RM2014A000504), "Method to predict falls", filed the 5th of September 2014*

Next steps?

- Those results opened new questions:
  - What % of falls are due to ↓ΔBP?
  - What % of falls can we expect to be predictable?
  - Can we estimate the minimum efficacy we have to reach to be cost-effective?
  - Can we estimate the max reimbursable cost for the device?
  - Can we estimate the uncertainty of all those estimations?

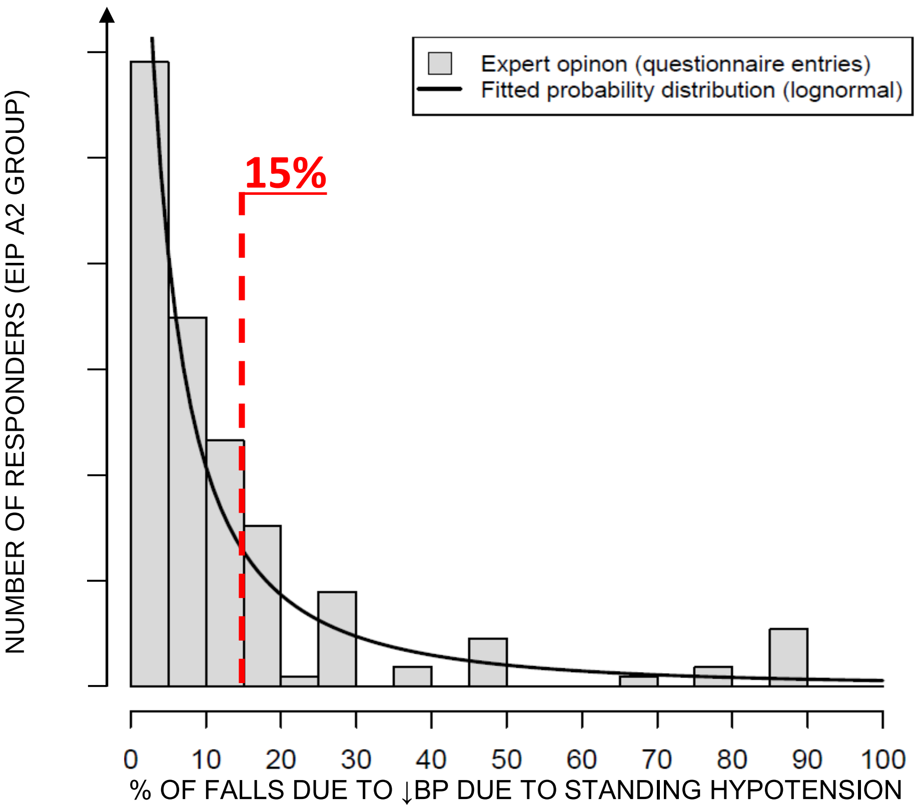
Next steps?

- Those results opened new questions:
  - What % of falls are due to ↓ΔBP?
    - *Interviewed EIP Experts*
    - *Fitted their answers with a statistical distribution*
    - *Calculated its mean value (15%)*
  - What % of falls can we expect to be predictable? *The 87% of 15%→ 13%*



Next steps?

- The model: two stages Markov Model
- The data

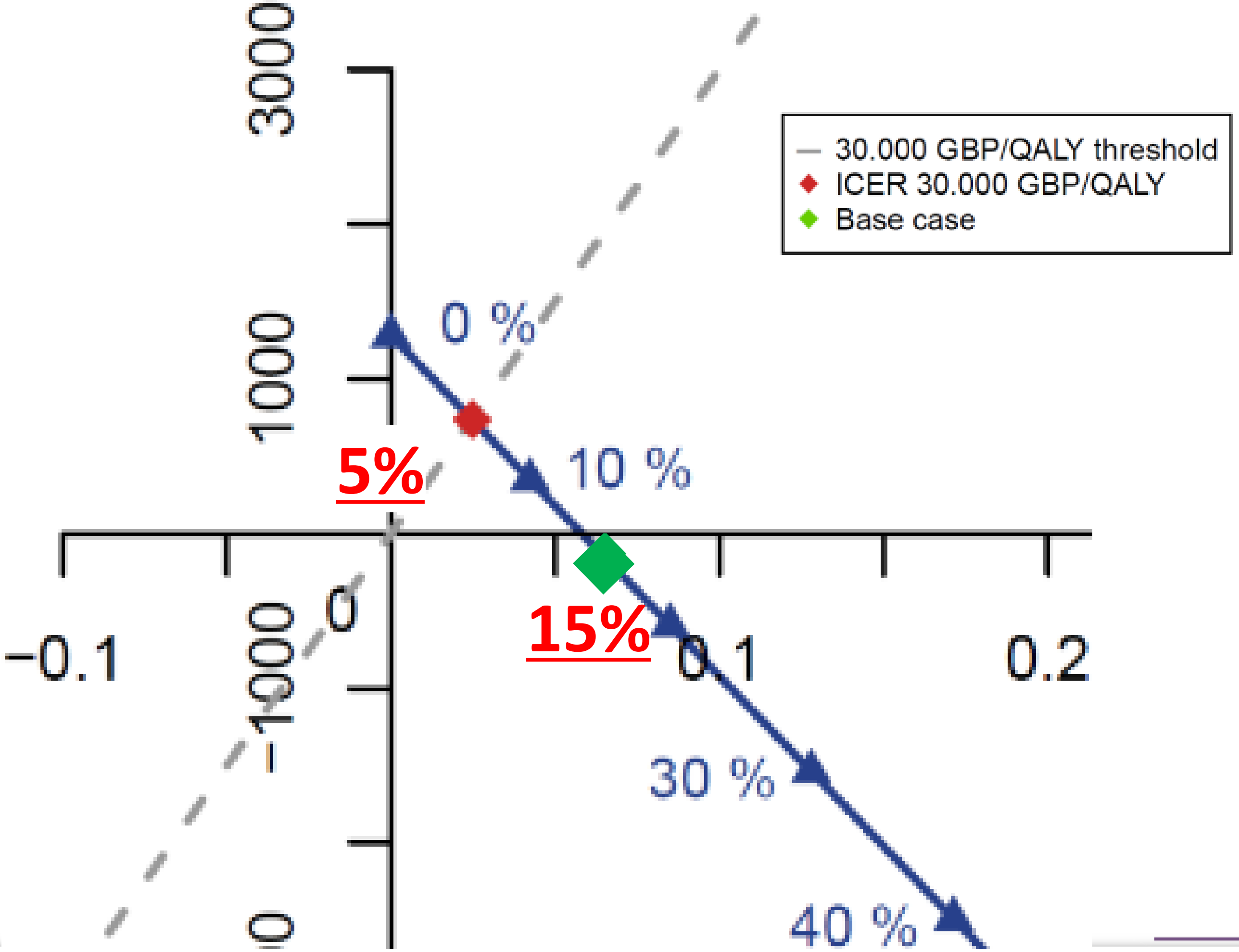


Discount factors (NICE, 2008)		
	Costs	3.50%
	Effects	3.50%
Alive transition probabilites (mainly UK-DH, 2009)		
	Incidence (current care scenario)	0.3
	'Recovery' (current care scenario)	0.7
	Incidence (intervention scenario) (15% of 30%=0.25)	0.2541
	'Recovery' (intervention scenario)	0.7459
Relative risks (mortality) (human mortality database)		
	Deteriorated health (current care scenario)	1.373
	Baseline health (intervention scenario)	1
	Deteriorated health (intervention scenario)	1.373
Resource use weights (various sources)		
	Baseline health	0
	Deteriorated health	3674.92
HRQoL weights (Thiem et al., 2014 & EuroQol)		
	Baseline health	0.811
	Deteriorated health	0.7553
Cost of intervention (by analogy – REFINE-study)		
	GBP per user per year	130.00

- The tool:
  - http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing&pg=mafeip

Next steps?

- Those results opened new questions:
  - Can we estimate the minimum efficacy we have to reach to be cost-effective?
    [min cost of the device/service £1.5k] => 5%



Next steps?

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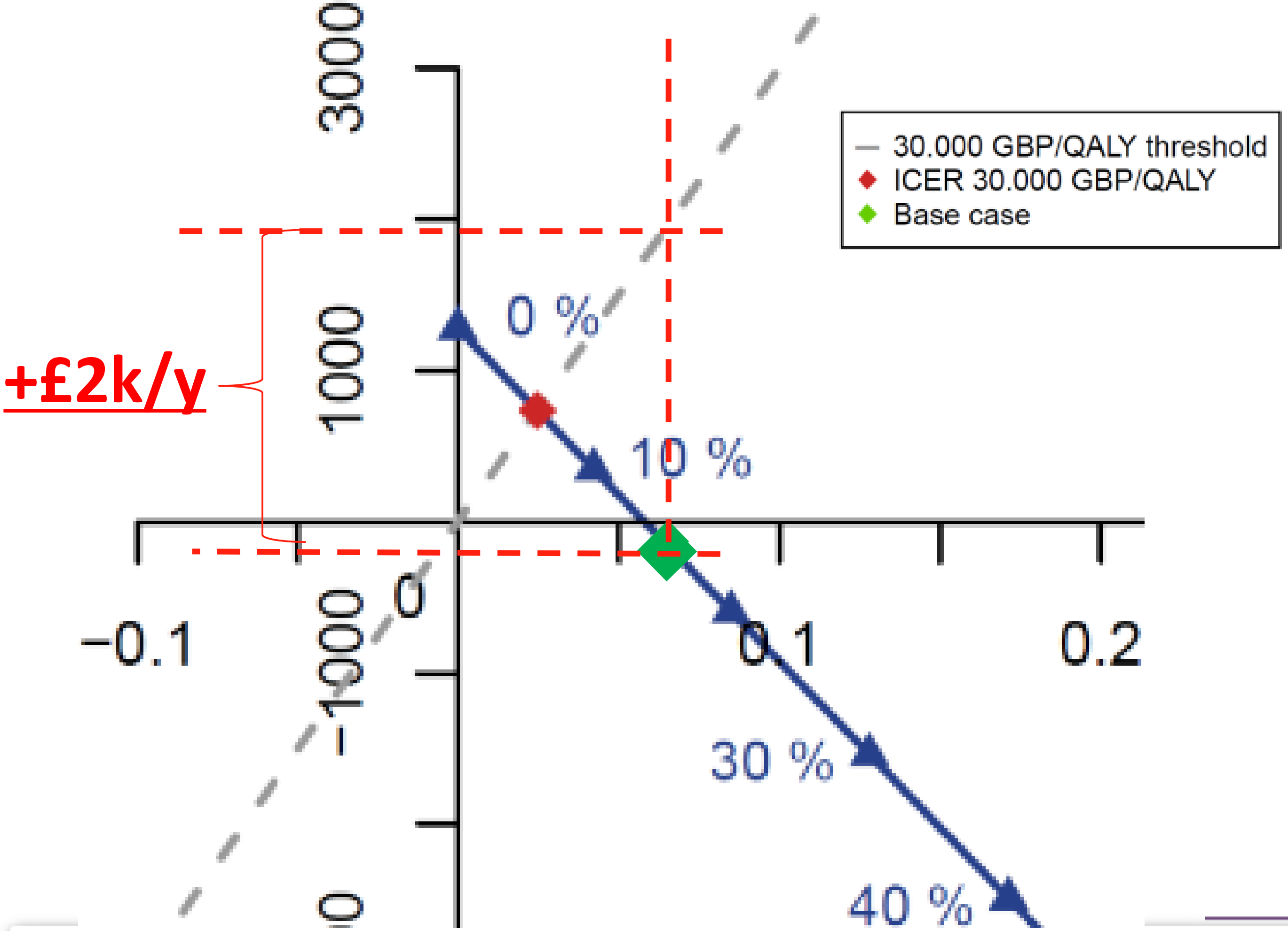
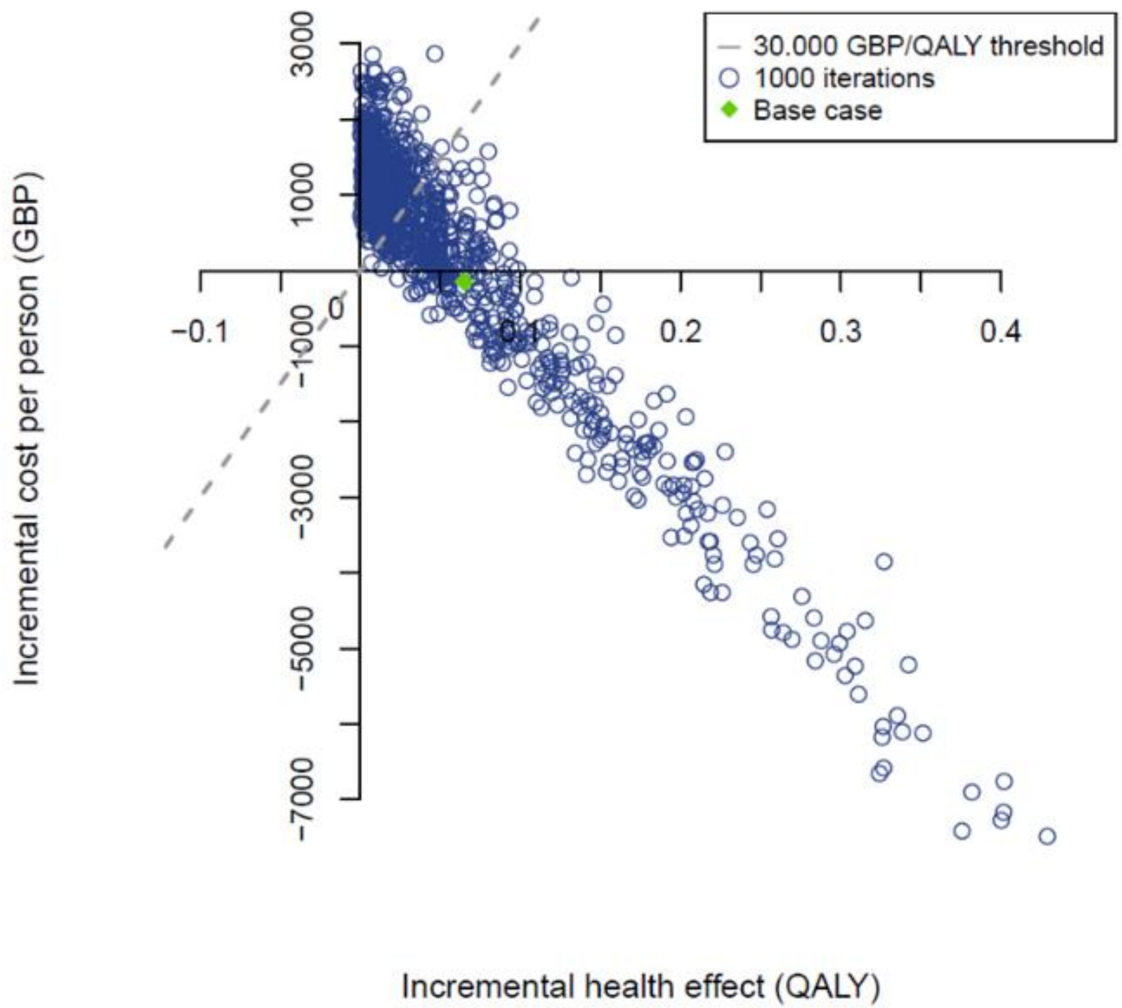


Next steps?

- Those results opened new questions:
  - Can we estimate the uncertainty of all those estimations?



What did we learn from this case study?

- The proof of concept gave the efficacy of the device in the best case
- The best possible evidence (No trials/meta-analysis available) was gattered (survey & stats)
- Estimated the cost-effectiveness of the disruptive innovation
- Calculated the max reimbursable cost
- Performed a sensitivity analysis to estimate the uncertainty.

Exercises

- **4-state Markov Models (MM)**: the MATCH tool (University of Nottingham)
  - http://www.nottingham.ac.uk/match/research/tools/markovtoolmain.html
- **Headroom Analysis: the MAFEIP** tool (JRC European Commission)
  - **http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing&pg=mafeip**

The group!

Rossana Castaldo

Luiss Montesinos Silva

Tim Siu Wang

Dr Paolo Melillo
Second University of Naples

Dr Giovanna Sannino
Italian CNR

Dr Christian Boehler
European Commission JRC

Applied Biomedical Signal Processing and Intelligent eHealth (ABSPIE) Lab University of Warwick