

## HTA: BME prospective

**Dr Leandro Pecchia**

University of Warwick

*IFMBE HTA Division Chairman*



**IFMBE**  
HTA Division

WARWICK





## Career path:

- Since 2013: Assistant Professor in Biomedical Engineering, *University of Warwick, UK*
- 2011-2013: Research Fellow (RF2), *University of Nottingham, UK*
- 2009-2011: Research Fellow (RF1), *University Federico II of Naples, Italy*
- 2005-2009: PhD in Biomedical Engineering, *University Federico II of Naples, Italy*
- May 2005: BSc+MSc in Electronic Eng., *University Federico II of Naples, Italy*

## Research interests:

- Applied **Biomedical signal processing** and second level pattern recognition/data-mining
- Early stage **Health Technology Assessment (HTA)** and **User Need Elicitation** methods

## Main applications:

- Active/healthy ageing: chronic cardiovascular diseases and falls in elderly
- Disease Management Programs, patient pervasive monitoring and **Telemedicine**
- Behavioural Monitoring

## Director Applied Biomedical Signal Processing and Intelligent eHealth Lab

- established in 2014, 6 research studs, 6 associate Academics, 8 Visiting Researchers in 2016

## International Appointments

- Chair of the Health Technology Assessment Division of the International Federation of Medical & Biological Engineering (IFMBE)
- Chair of the Public Affairs WG of the European Alliance of Medical & Biological Engineering and Sc.
- Member of the WHO working group o HTA of Medical Devices
- Secretary of the European Parliament Interest Group on Biomedical Engineering [link](#)

**WHO Consultant for Global Forum of Medical Devices (HTA)**

**European Parliament Interest Group on BME, secretariat**

**DG CONNECT Consultant for MAFEIP tool**

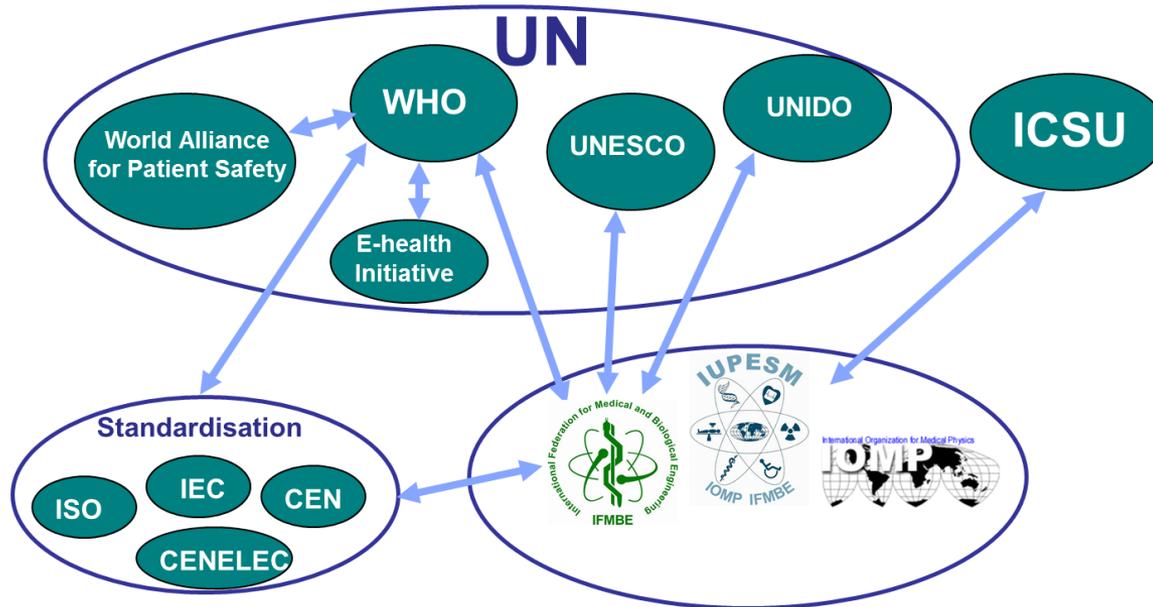
**Chairman of the IFMBE HTA Division**

**Chairman of the Public Affair Working Group of the EAMBES**

**Director of the Applied Biomedical Signal Processing and Intelligent eHealth lab, University of Warwick, UK**

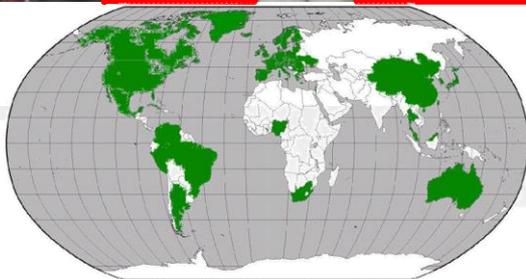


- The IFMBE was established in 1959 when a group of medical engineers, physicists and physicians met in the UNESCO Building, Paris, France to create an organization entitled IFMBE
- IFMBE is recognised as NGO cooperating with UN (WHO, UNESCO, UNICEF) and is part of an eco-system working to improve health world-wide:



# IFMBE: scientific society but very close to real problems

54 national, 7 transnational BME societies 120k members



## Divisions

- James C. H. Goh**, Singapore, IFMBE President
- Shankar M. Krishnan**, USA, IFMBE President Elect
- Kang Ping Lin**, Taiwan, Secretary General
- Marc Nyssen**, Belgium, Treasurer
- Ratko Magjarevic**, Croatia, Immediate Past President

### Clinical Engineering Division (CED)

#### Board Members

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  - Mladen POLUTA, Treasurer (South Africa, 2015-2021)
  - Saide CALIL, Elected Member (Brasil, 2012-2018)
  - Tony EASTY, Elected Member (Canada, 2012-2018)
  - Paolo LAGO, Elected Member (Italy, 2015-2021)
  - Ewa ZALEWSKA, Elected Member (Poland, 2012-2018)
  - Yadin DAVID, Coopted Member (USA, 2015-2018)
  - James WEAR, Coopted Member (USA, 2015-2018)

### Health Technology Assessment Division (HTAD)

#### Board Members

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- Members
- Patricia TRBOVICH, Secretary, Canada
  - Marjan HUMMEL, Treasurer, The Netherlands
  - Nicolas PALLIKARAKIS, Past Chairman, Greece
  - Mladen POLUTA, South Africa
  - Mario MEDVEDEC, Croatia
  - Lennart PHILIPSON, Sweden



Patricia TRBOVICH  
Canada  
*Treasurer (2012-18)*



Marjan HUMMEL,  
The Netherlands  
*Secretary (2015-21)*



Kalliroi STAVRIANOU,  
Greece  
*Member (2015-21)*



Rosanna TARRICONE,  
Italy  
*Co-opted Member (2015-21)*



Nicolas PALLIKARAKIS,  
Greece  
*Past-Chair (2012-18)*



Mladen POLUTA,  
South Africa  
*Member (2015-21)*



Mario MEDVEDEC,  
Croatia  
*Member (2015-21)*



Leandro PECCHIA,  
UK  
*Chair (2012-18)*



...?  
Patients, ONG...



Julie POLISENA,  
CANADA/CADHT  
*Collaborator*



Dan CLARK,  
UK/NICE/NHS  
*Collaborator*



Oriana CIANI,  
Italy  
*Collaborator*



Giuseppe Fico,  
Spain  
*Collaborator*

# EAMBES Council 2016-7



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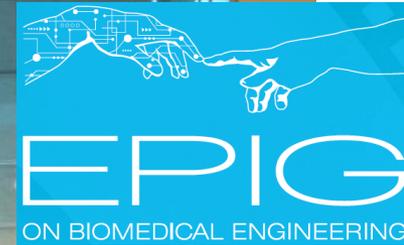
**Councillor of Education: Richard Reilly, Ireland**

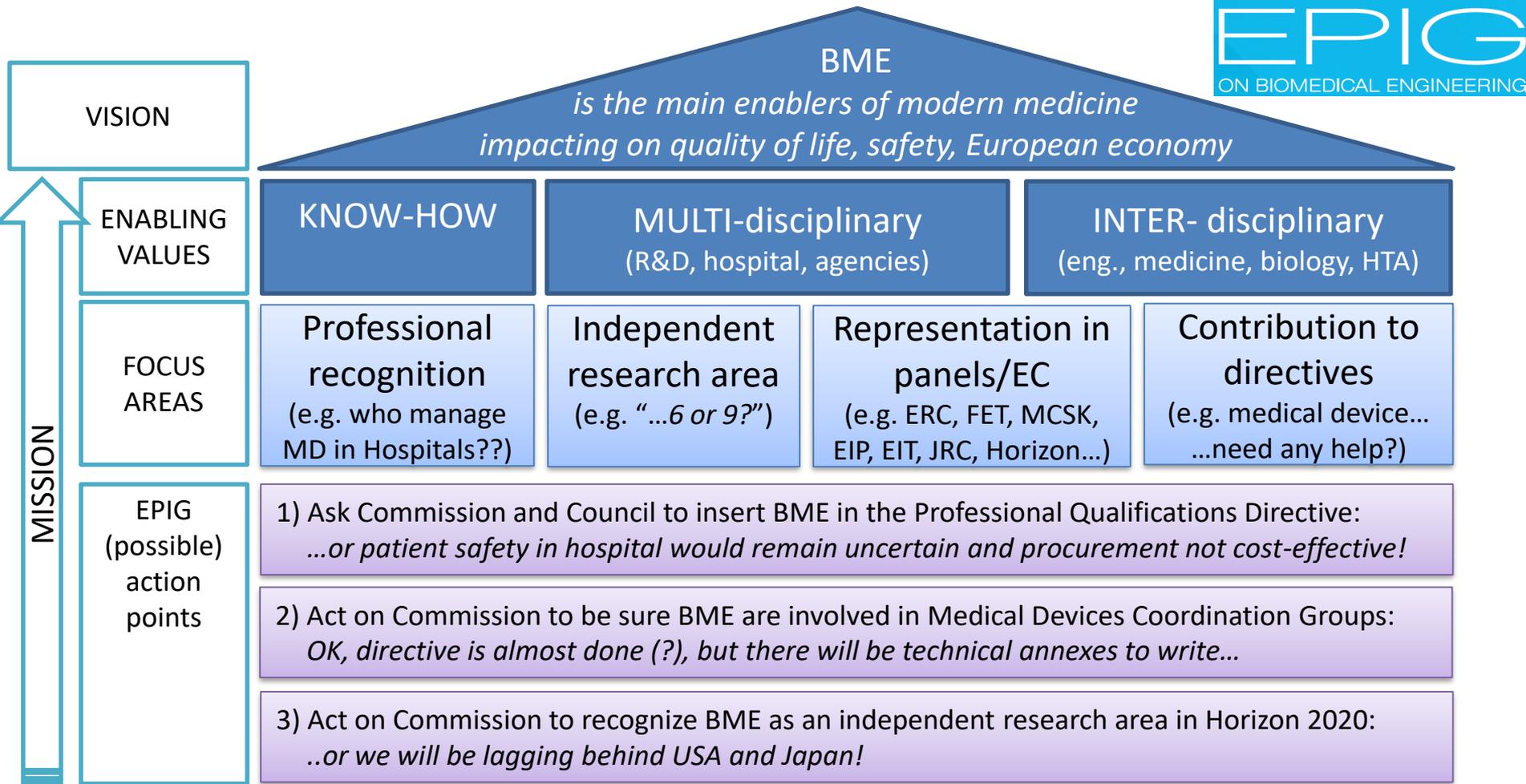
**Councillor of Institutions Karin Wardell, Sweden**



**Councillor Societies and clinical collaboration: Andreas Melzer, UK**

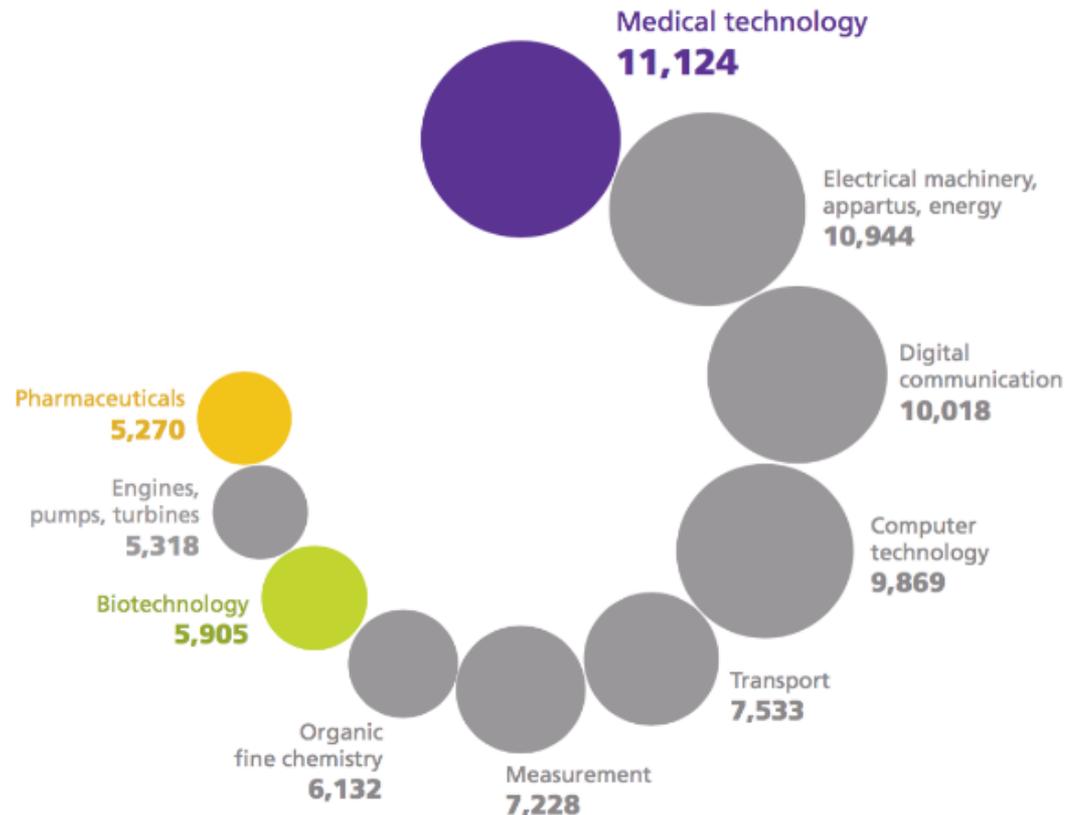






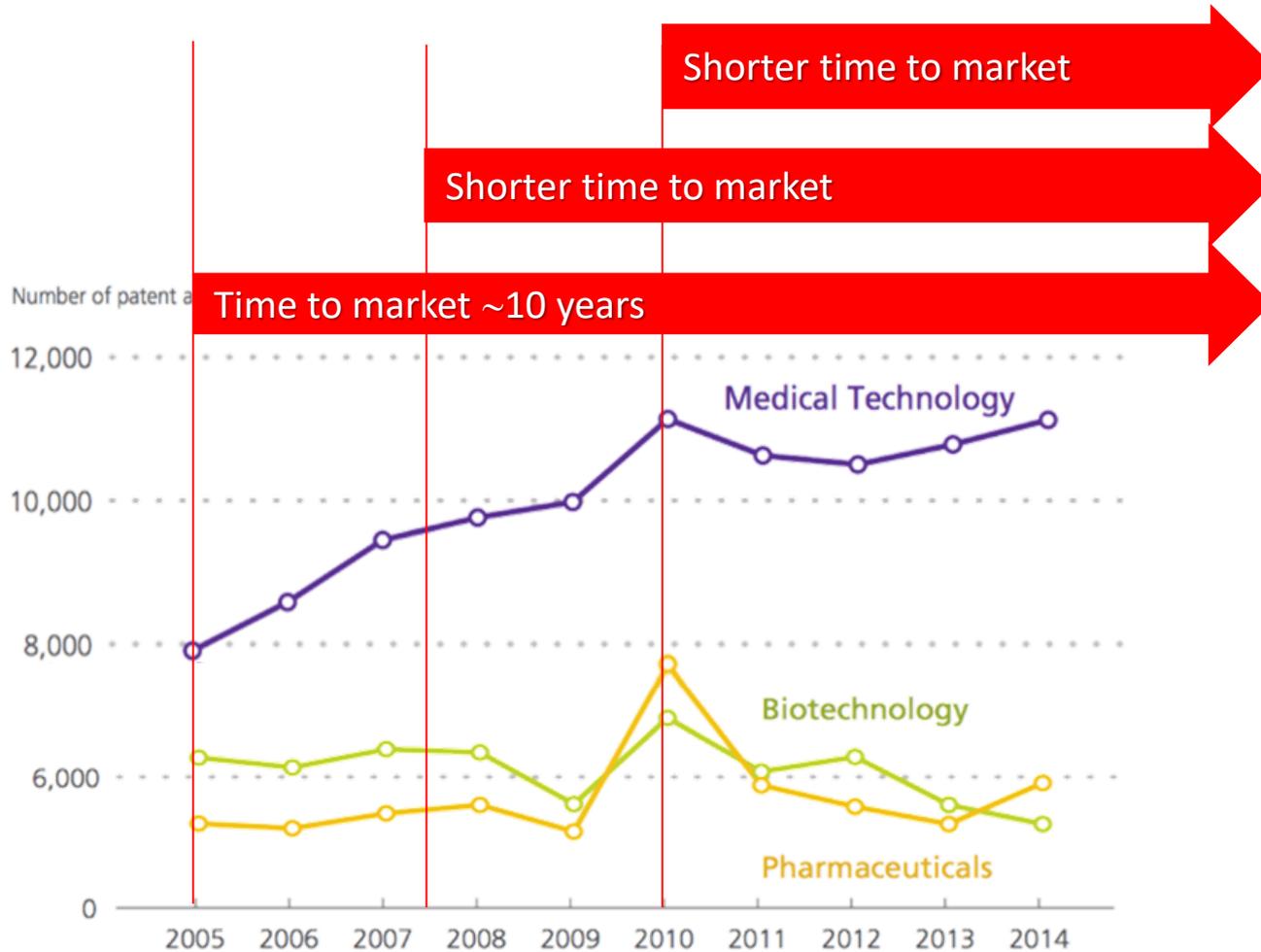
# BME outcomes in 10 years

## Medical Technologies are 1<sup>st</sup> for IP



\*MedTech Europe, *The European Medical Technology Industry. In Figures. Brussels, 2015.*

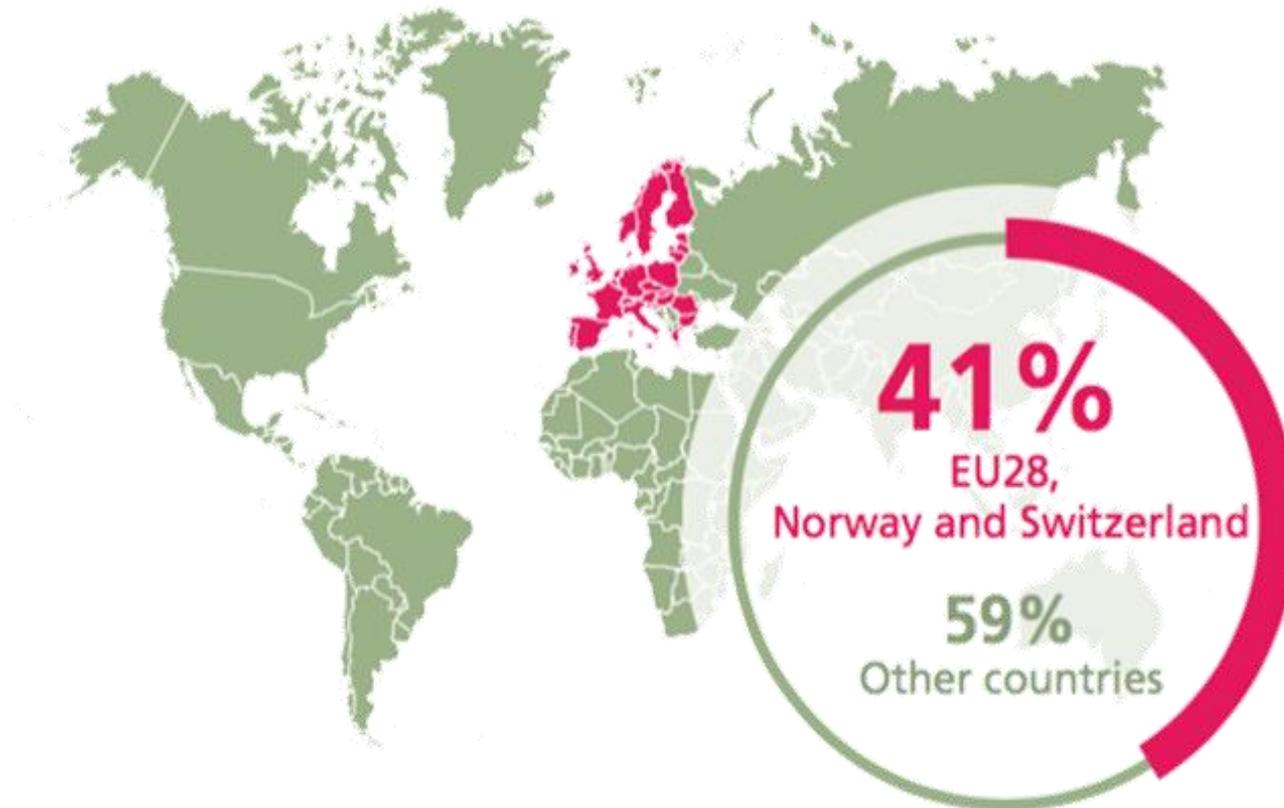
# BME outcomes in 10 years



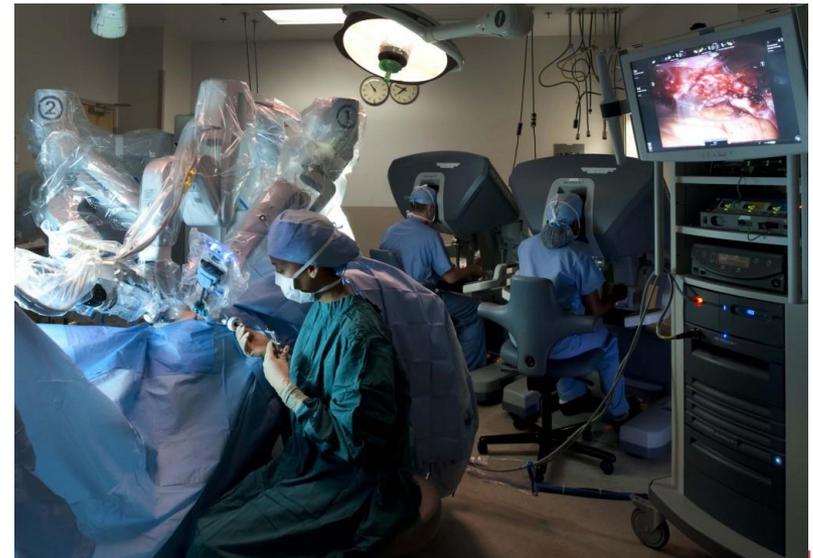
\*MedTech Europe, *The European Medical Technology Industry. In Figures. Brussels, 2015.*

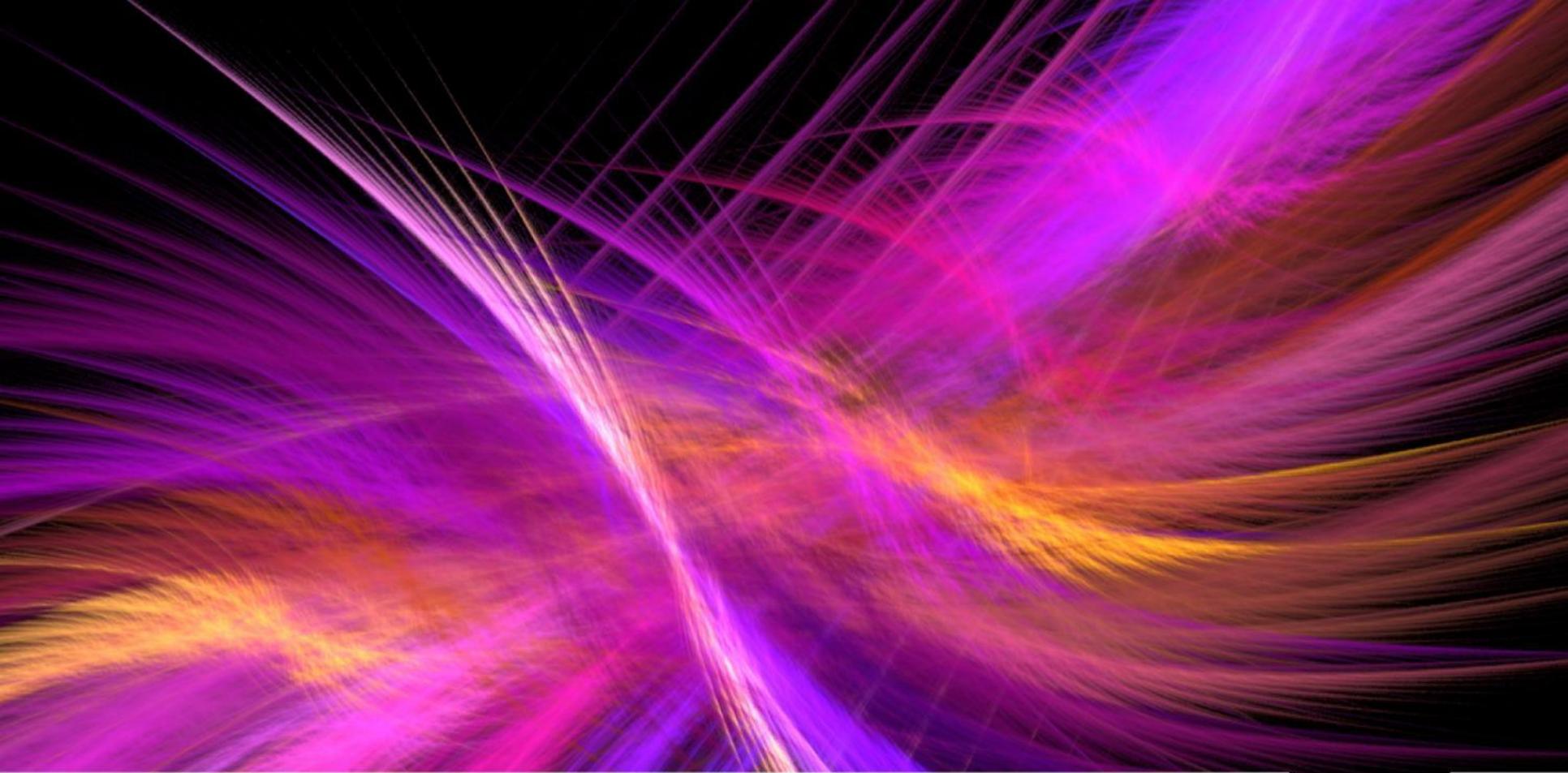
# BME outcomes in 10 years

41% of Patents from EU



# BME impact





# HTA: into

Dr Leandro Pecchia – 14/1/2016



- *Introduce the concept of Market*
- *Discuss why healthcare is not an ideal market (...why we need HTA?)*
- *HTA recall*
- *Early stage HTA*

- *BMEs are increasingly involved in HTA, collaborating with economists, medical doctors, nurses, pharmacologists, patients, healthcare managers.*
- *BMEs contribution to HTA is peculiar because **BMEs are involved also in the design** of health technologies and particularly medical devices*
- *The **European Economic and Social Affairs Committee's (EESC)** of the **European Commission** stated recently that:*
  - *“**Biomedical Engineering is not simply a subset of modern medicine. Modern medicine predominantly secures important advances through the use of the products of biomedical engineering**”\**

\* EESC, *Promoting the European single market combining biomedical engineering with the medical and care services industry*, 23<sup>rd</sup> April 2015, <http://www.eesc.europa.eu/?i=portal.en.ccmi-opinions.32831>

- **Health Technology**, according to WHO definition, refers to any application of organized knowledge and skills in the form of medicines, medical devices, vaccines, procedures and systems developed to solve a health problem and improve quality of life.
- **Health technology assessment (HTA)** refers to the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology. The main purpose of conducting an assessment is to inform a policy decision making.
- *“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” (WHO\*)*

\*WHO web site (last access 15.09.2012): [http://www.who.int/medical\\_devices/assessment/en/](http://www.who.int/medical_devices/assessment/en/)

## What is a market?

“human beings have unlimited wants but limited resources with which to meet those wants. Given the limited resources, human beings constantly make decisions that require trade-off.”

- **Market:** The term market refers to a situation where buyers (consumers) and sellers (producers) interact (directly or through intermediaries) to trade goods and services.
- **Supply** is the total amount of a product (good or service) that producers (sellers) are willing and able to sell at a specified price.
- **Demand** is the total amount of a good or service that consumers are willing and able to purchase at a given price.
- **Market forces** of supply and demand represent the aggregate influence of self-interested buyers and sellers on prices and quantities of goods and services offered in a market: demand and supply interact to determine prices of goods and services being exchanged.

## What is it a ideal market?

### A market is ideal under several conditions (perfect competition):

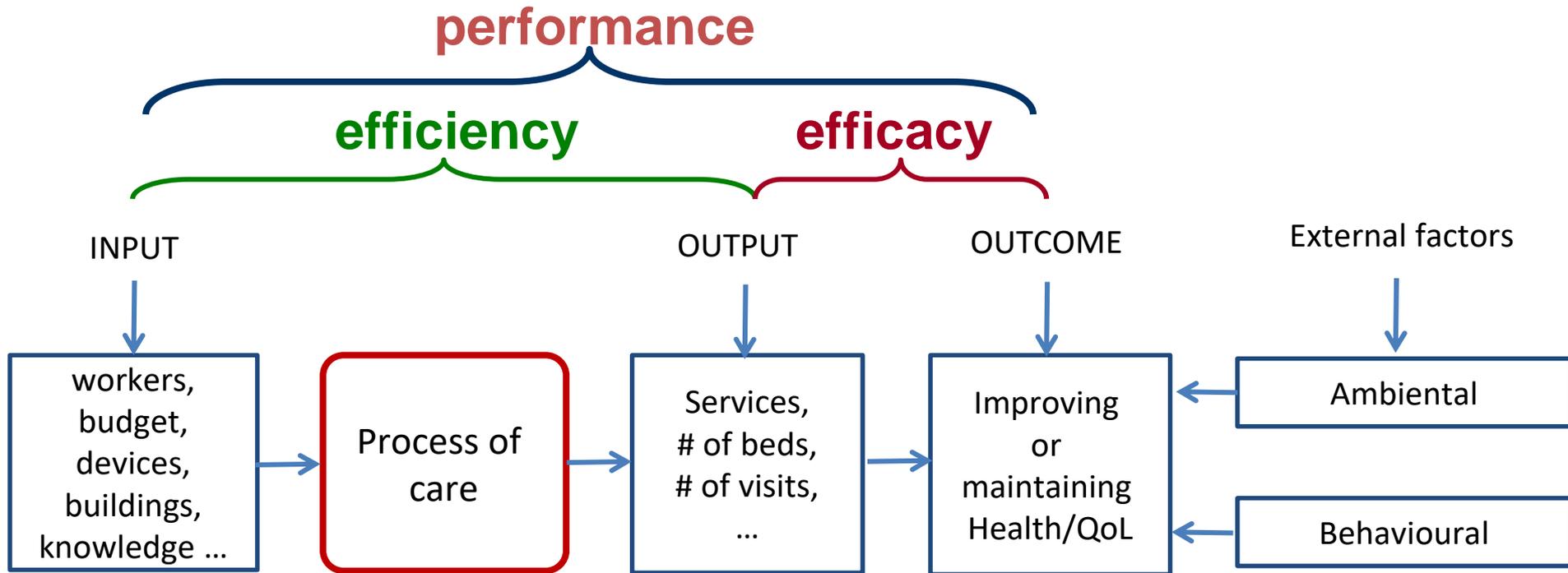
- Perfect market information
- No participant with market power to set prices
- Non intervention by governments
- No barriers to entry or exit
- Equal access to factors of production
- Profit maximization
- No externalities (other benefits/costs for non choosing a product/service)

According to the general equilibrium theory, on the assumption of Perfect Competition, and some technical assumptions about the shapes of supply and demand curves, *it is possible to prove that a market will reach an equilibrium* (Pareto optimum), in which sellers and consumers are at the best possible level of utility.

- **Market structure:**
  - number and size of firms
  - Access to market for firms
  - Product differentiation
- **Demand derivation**
  - Not “satisfaction” but “health preservation”
  - The final achievement (health) is not marketable (cannot be passed to other)
  - Low market force (demand does not affect the prices or quantity)

- **Information asymmetry:**
  - Medical Doctors:
    - Have a deep knowledge of the medical problem, but not of all the patients and not of all the technologies
    - Cannot be 100% sure of results
    - Are the suppliers, but they also act on behalf of the patient...  
... demand and supply are jointly determined
  - The patients
    - they lack necessary information about their illness
    - they lack necessary information about the effective healthcare technologies
    - Not completely free of choosing
    - Are not consistent, non stationary, not fully transitive ( $A > B$ ,  $B > C$ ,  $A ? C$ )
    - Final users of the healthcare technology, but not those that directly pay for it
  - Suppliers
    - Not all are profit-oriented (e.g. hospitals)

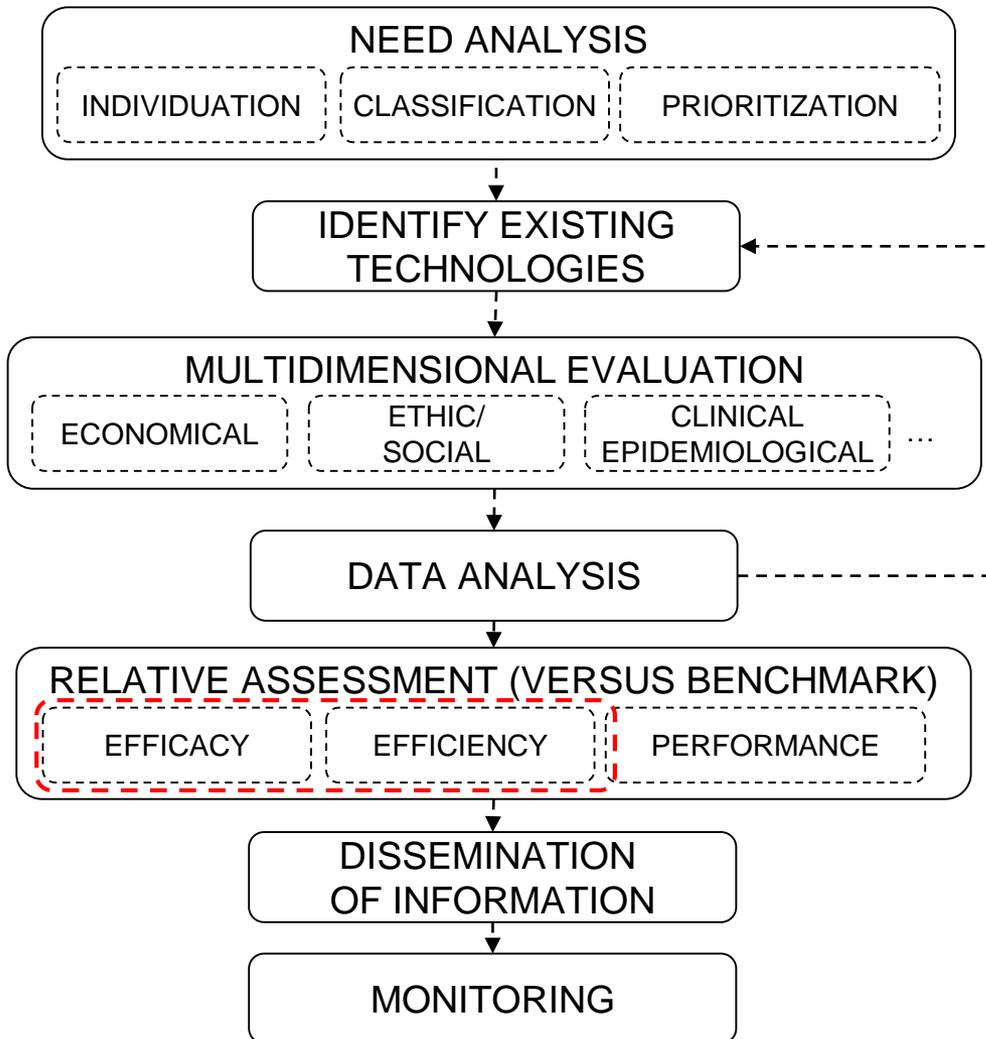
## Performance, efficiency, efficacy



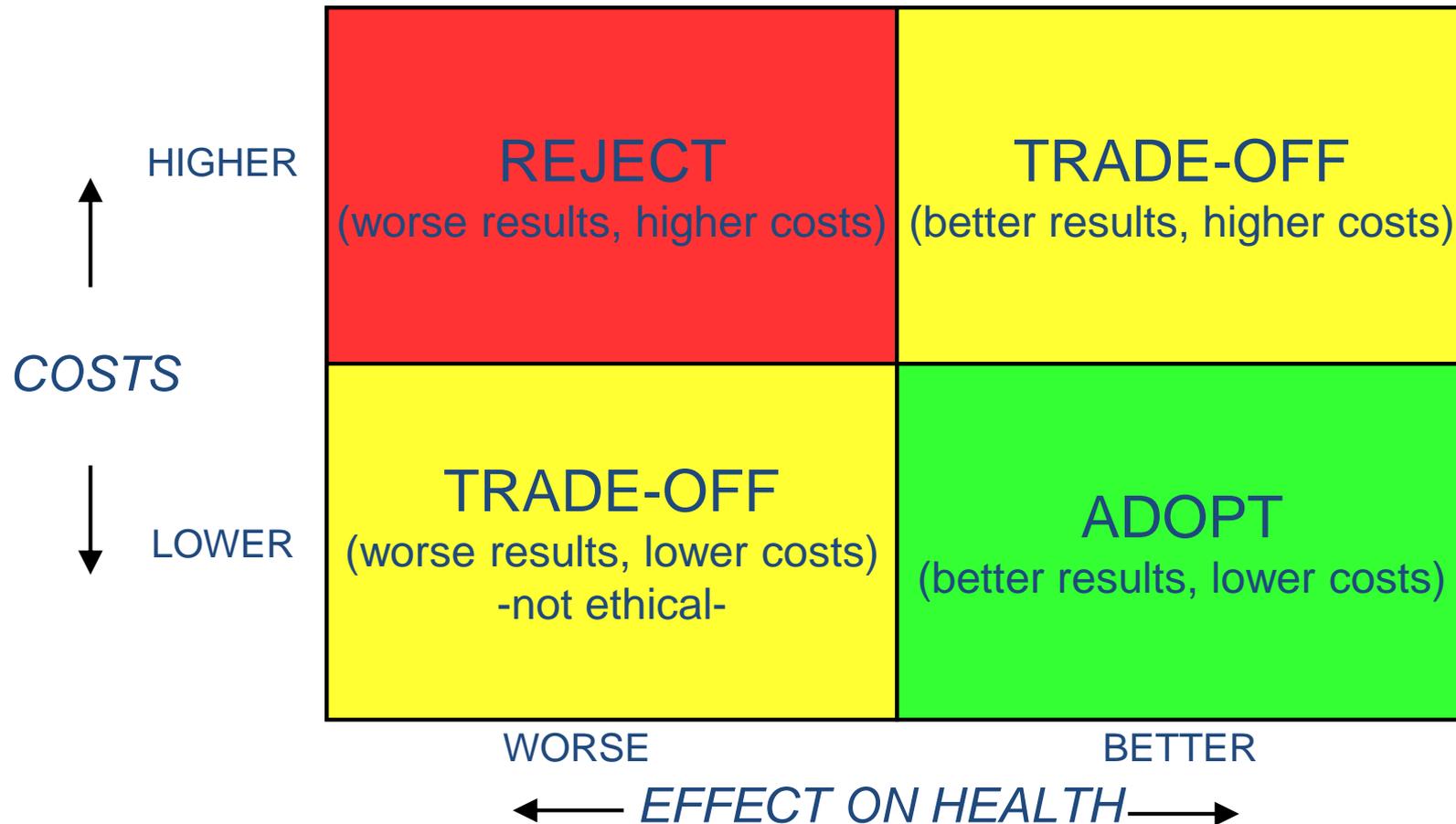
$$\text{Efficiency} = \frac{\text{output}}{\text{input}}$$

$$\text{Efficacy} = \frac{\text{outcome}}{\text{output}}$$

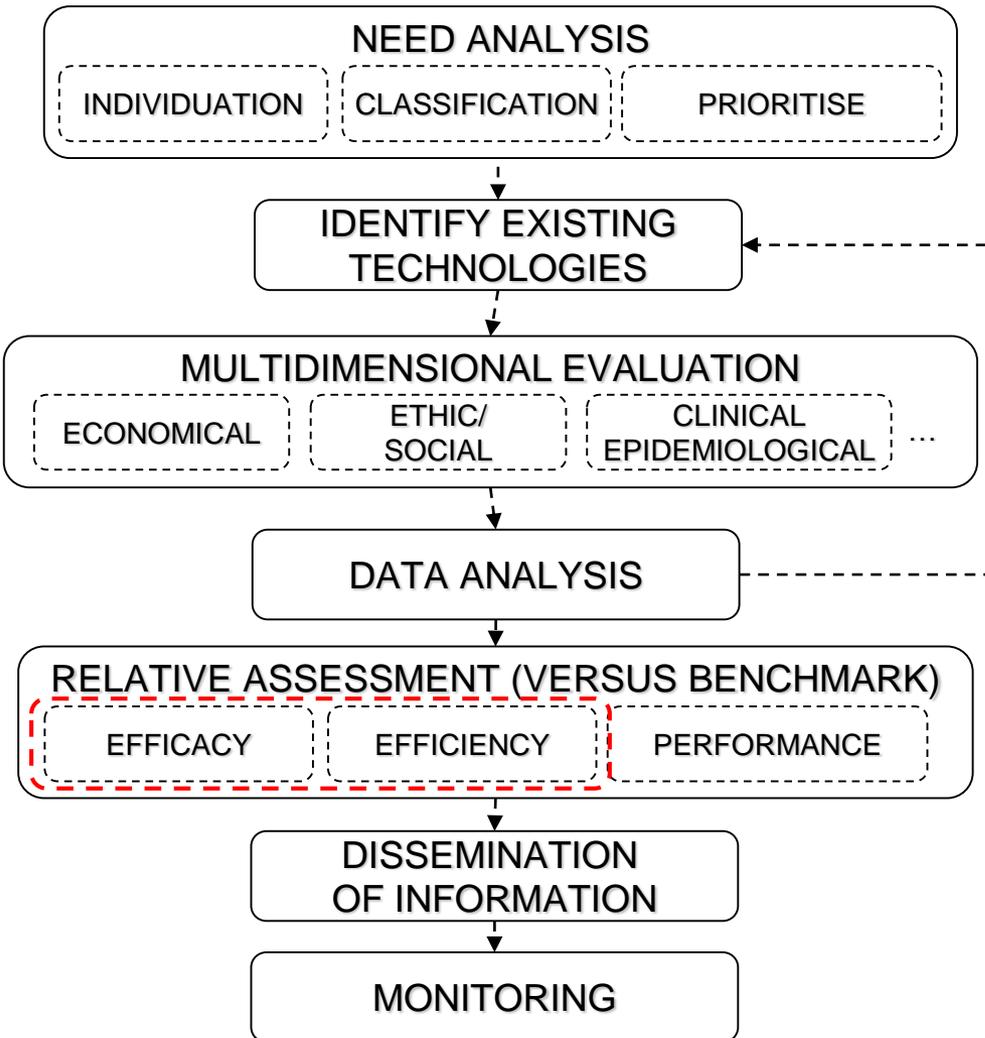
$$\text{Performance} = \frac{\text{outcome}}{\text{input}}$$



## Possible results of complete analyses



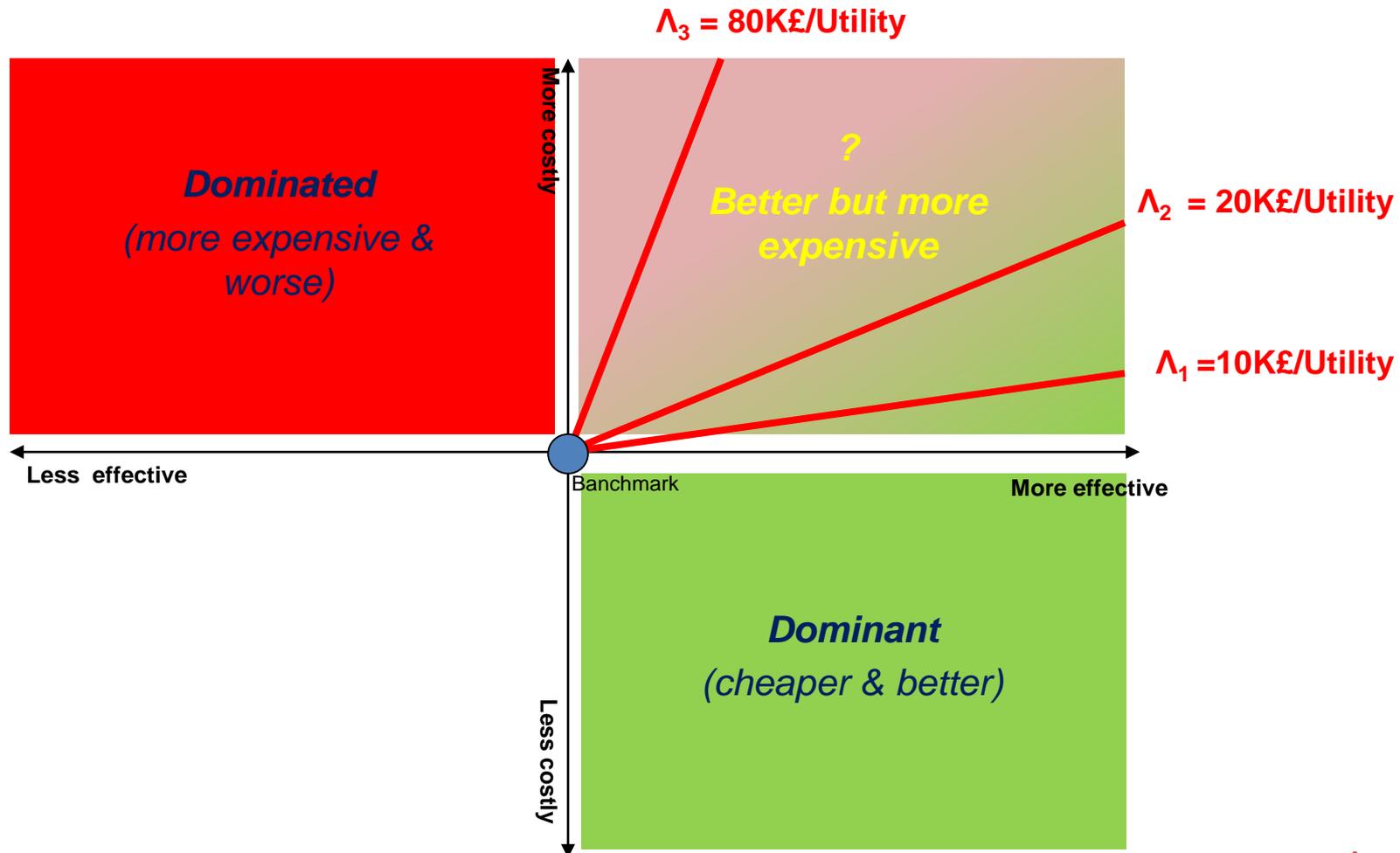
\*

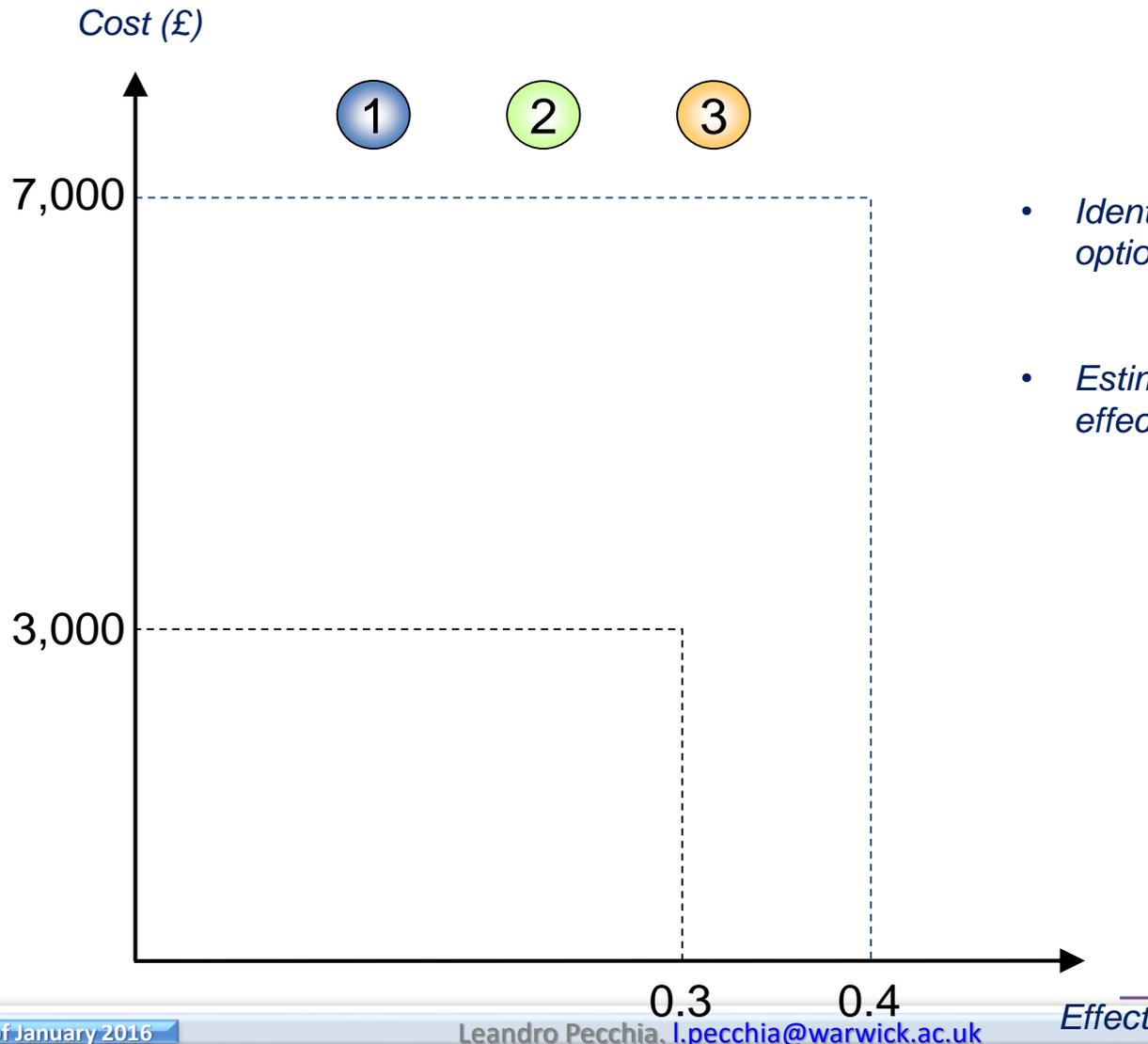


\* NHS NICE willingness-to-pay 'threshold' range of £20,000-£30,000 per QALY.

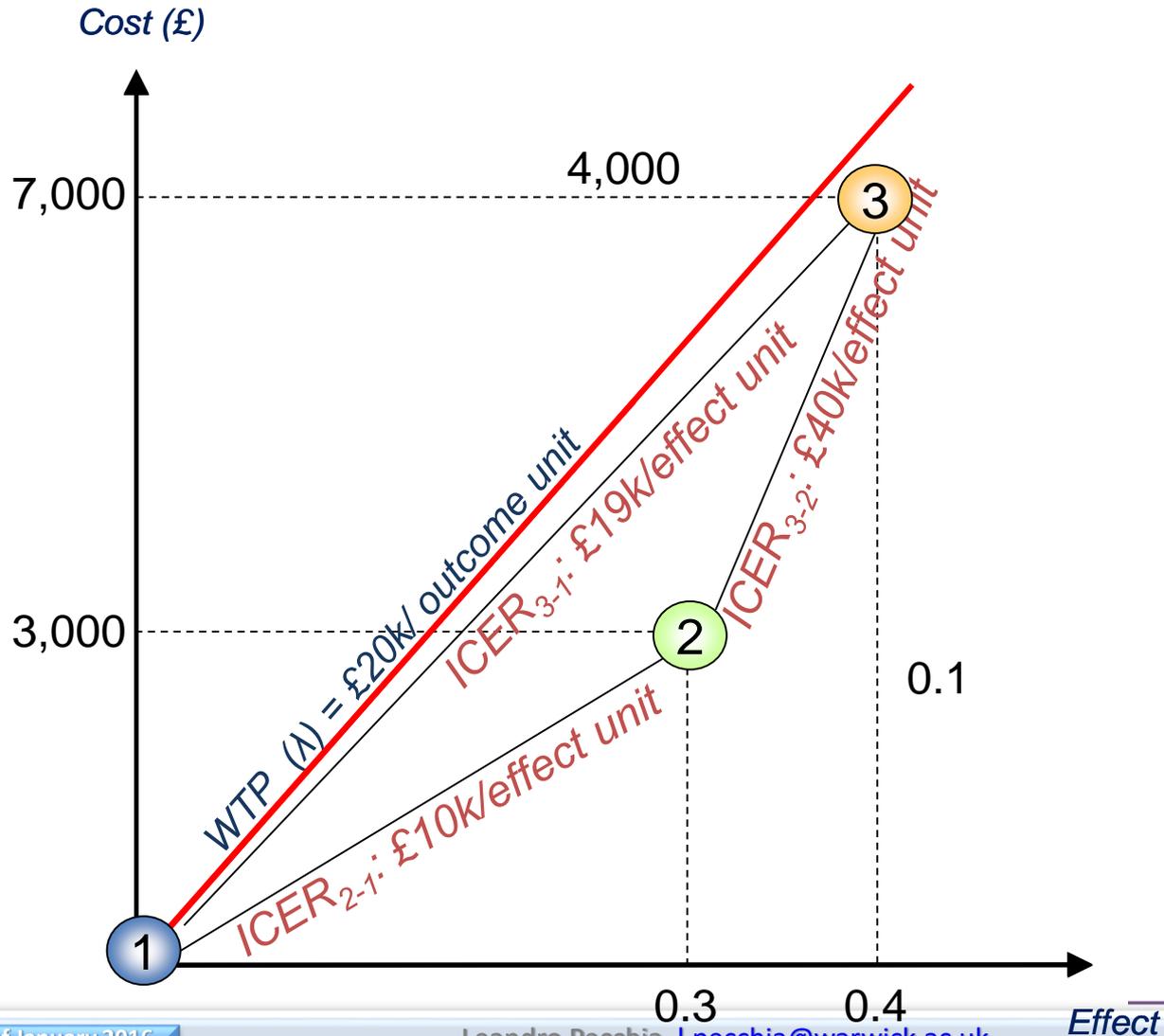
Example Example of high efficiency requirements

## Willingness to pay





- *Identify all feasible treatment options for a given patient group*
- *Estimate the costs and health effects of each and plot on graph*



		<b>COSTS &amp; CONSEQUENCES?</b>		
		<b>NO</b>		<b>YES</b>
<b>2 OR MORE ALTERNATIVES?</b>	<b>NO</b>	<u>PARTIAL ASSESSMENT (ONLY CONSEQUENCES)</u>  <b>DESCRIBE RESULTS</b>  (outcome)	<u>PARTIAL ASSESSMENT (ONLY COSTS)</u>  <b>DESCRIBE THE COSTS OF THE PROBLEM</b>  (input)	<u>PARTIAL ASSESSMENT (NO BENCHMARK)</u>  <b>ANALYSIS COST-CONSEQUENCES</b>  (input-outcomes)
	<b>YES</b>	<u>PARTIAL ASSESSMENT (ONLY CONSEQUENCES)</u>  <b>CLINICAL TRIAL</b>  (outcomes of 2 or more technologies)	<u>PARTIAL ASSESSMENT (ONLY COSTS)</u>  <b>COST ANALYSIS ABC (Activity Based Costing)</b>  (input of 2 or more technologies)	<u>VALUTAZIONE COMPLETA</u>  <b>COST-EFFICACY COST MINIMIZATION COST-UTILITY COST-BENEFIT</b>  ( $\Delta$ outcomes/ $\Delta$ input of 2 or more technologies)

## Typologies of complete analyses

<i>Analysis</i>	<i>Resources (Input)</i>	<i>Consequences (outcome)</i>	<i>How we measure the outcome?</i>	<i>Advantages</i>	<i>Limits</i>
<b>Cost Minim.</b>	£	<ul style="list-style-type: none"> <li>• 1 result</li> <li>• assumed equally for each alternative</li> </ul>	Not needed  - $\Delta C$ -	<ul style="list-style-type: none"> <li>• Univocal result</li> <li>• First step for the other analyses</li> </ul>	<ul style="list-style-type: none"> <li>• No effect measured</li> </ul>
<b>Cost Eff.</b>	£	<ul style="list-style-type: none"> <li>• 1 result</li> <li>• 1 technology perform better</li> </ul>	Physical units (ages gained, pain)  -iCER-	<ul style="list-style-type: none"> <li>• Can measure univocally clinical results as far as are it is the same for all the technologies</li> </ul>	<ul style="list-style-type: none"> <li>• non heterogeneous effects</li> <li>• efficacy <math>\neq</math> effectiveness;</li> <li>• no universal scales can measure the iCER</li> </ul>
<b>Cost Util.</b>	£	<ul style="list-style-type: none"> <li>• &gt;1 results</li> <li>• 1 technology perform better</li> </ul>	QALY  -iCUR-	<ul style="list-style-type: none"> <li>• Measure heterogeneous clinical results, by introducing an objective function (i.e. QALY)</li> </ul>	<ul style="list-style-type: none"> <li>• only clinical results</li> <li>• no universal scales to measure the iCUR</li> </ul>
<b>Cost Ben.</b>	£	<ul style="list-style-type: none"> <li>• &gt;1 results not only medical</li> <li>• 1 technology perform better</li> </ul>	£  -iCBR-	<ul style="list-style-type: none"> <li>• Measure heterogeneous results (not only clinical), by converting their impact in £</li> </ul>	<ul style="list-style-type: none"> <li>• difficult to quantify the value of results in £</li> <li>• less than the 4% of studies</li> </ul>

# Typologies of complete analyses

	<b>COST-MINIMIZATION</b>	<b>COST-EFFECTIVENESS</b>	<b>COST-UTILITY</b>	<b>COST-BENEFITS</b>
<b>Costs</b>	•monetary units	•monetary units	•monetary units	•monetary units
<b>Consequences</b>	•equal in both programs	•clinical outcomes	•QALY	•monetary units
<b>Measuring</b>	•differences in costs ( $\Delta C$ )	•iCER	•iCUR	•iCBR
<b>Advantage</b>	•direct measurement •necessary for the other	•direct measurement •uniform clinical outcomes	•indirect measurements •mixed clinical outcomes •multidimensional analysis	•indirect measurements •mixed outcomes •multidimensional analysis
<b>Limits</b>	•no consequences	•one-dimensional analysis •data table missing in many national health services	•indirect measurement •data table missing in many national health services	•indirect measurement •monetization of value of life •ethical limits

- **Five attributes (5 dimensions):**

- Mobility
- Self-care
- Independency
- Pain
- Anxiety depression

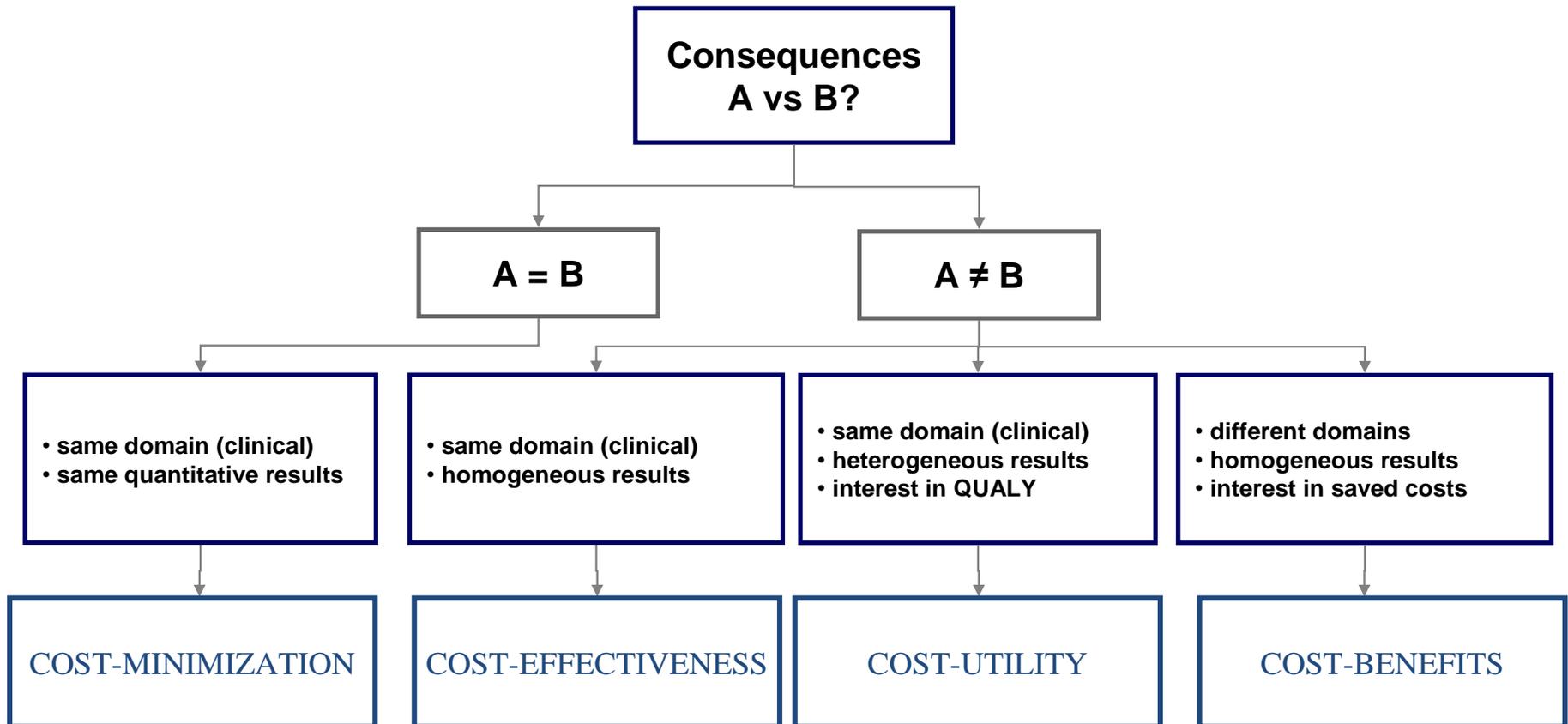
- **3 level for each attribute**

- No problem (0)
- Some problems (1)
- Significant problems (2)

243 possible states of health ( $3^5$ )  
+ 1 for unconscious  
+ 1 for death  
(total of 245 possible health statuses)

- This tool is standardise by a no-profit group: <http://www.euroqol.org/>
- Profiles of EuroQol exist for pathology, age, gender...

## How to choose the analysis?



## When the incremental analysis is needed?

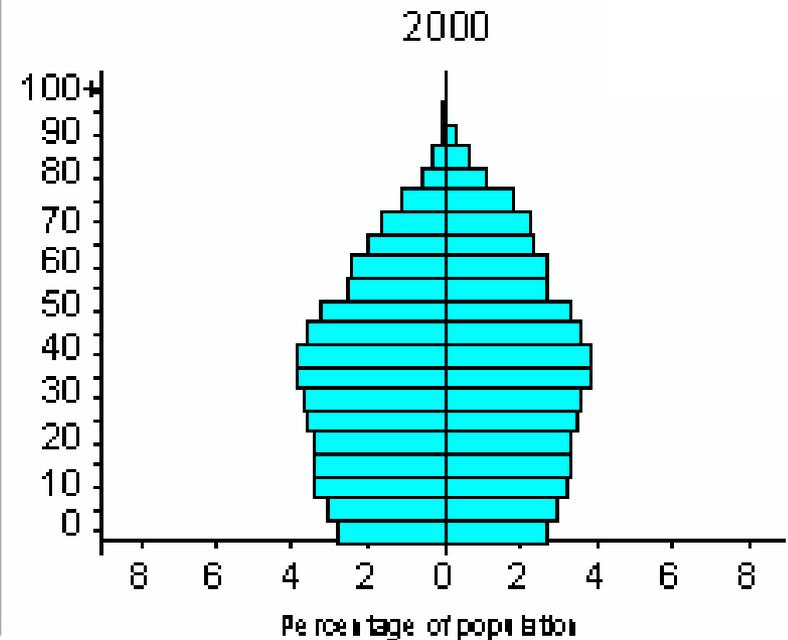
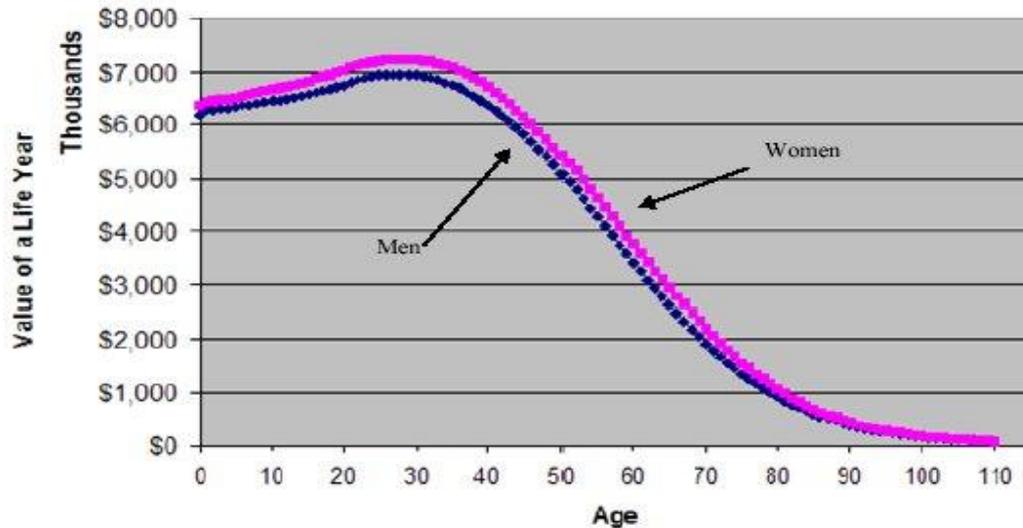
Costs	Consequences	Result
$C_A \geq C_B$	$X_A < X_B$	<p>DOMINANCE.</p> <p>A is more expensive and less effective/utile than B. B continues to be the standard.</p>
$C_A \leq C_B$	$X_A > X_B$	<p>A IS COST-SAVING.</p> <p>A is less expensive and more effective/utile than B. The new technology A is introduced gradually in the NHS.</p>
$C_A \geq C_B$	$X_A > X_B$	<p>INCREMENTAL ANALYST IS REQUIRED.</p> <p>A is more expensive and more effective/utile than B. The new technology A may be introduced gradually in the NHS if the cost for unit of effectiveness/utility is less than the last one introduced into the NHS for the same problem:</p> $\text{iRCX} = \frac{C_A - C_B}{X_A - X_B} \quad X = \begin{cases} E \\ U \\ B \end{cases}$

# Incremental Ratio in £

Can we convert (quality of) life in £ ?

Value of Life (VoL)

Figure 3: Values of Remaining Life Assuming \$6.3 Million Value of a Statistical Life



Value of a QALY (VoQ) =  $\text{VoL} / \max(\text{Qaly})$

If  $(\text{RICX} > \text{VoQ}) \Rightarrow A$  is accepted

# Incremental Ratio in £

Can we convert (quality of) life in £ ?

**Table 2. Cost per QALY of healthcare interventions (adapted from references 2–4)**

Intervention	£/QALY at 1990 prices
Cholesterol testing and diet therapy (all adults aged 40–69)	220
Neurosurgical intervention for head injury	240
GP advice to stop smoking	270
Neurosurgical intervention for subarachnoid haemorrhage	490
Antihypertensive treatment to prevent stroke (ages 45–64)	940
Pacemaker implantation	1,100
Hip replacement	1,180
Valve replacement for aortic stenosis	1,410
Cholesterol testing and treatment (all adults aged 40–69)	1,480
Docetaxel (as opposed to paclitaxel) in treatment of recurrent metastatic breast cancer	1,890*
CABG (left main-vessel disease, severe angina)	2,090
Kidney transplantation	4,710
Breast cancer screening	5,780
Heart transplantation	7,840
Cholesterol testing and treatment incrementally (all adults aged 25–39)	14,150
Home haemodialysis	17,260
CABG (one-vessel disease, moderate angina)	18,830
Hospital haemodialysis	21,970
Erythropoietin treatment for anaemia in dialysis patients (assuming 10% reduction in mortality)	54,380
Addition of Interferon- $\alpha$ 2b to conventional treatment in newly diagnosed multiple myeloma	55,060 <sup>b</sup>
Neurosurgical intervention for malignant intracranial tumours	107,780
Erythropoietin treatment for anaemia in dialysis patients (assuming no increase in survival)	126,290

# HTA of Medical Devices

## Medical devices vs Drugs



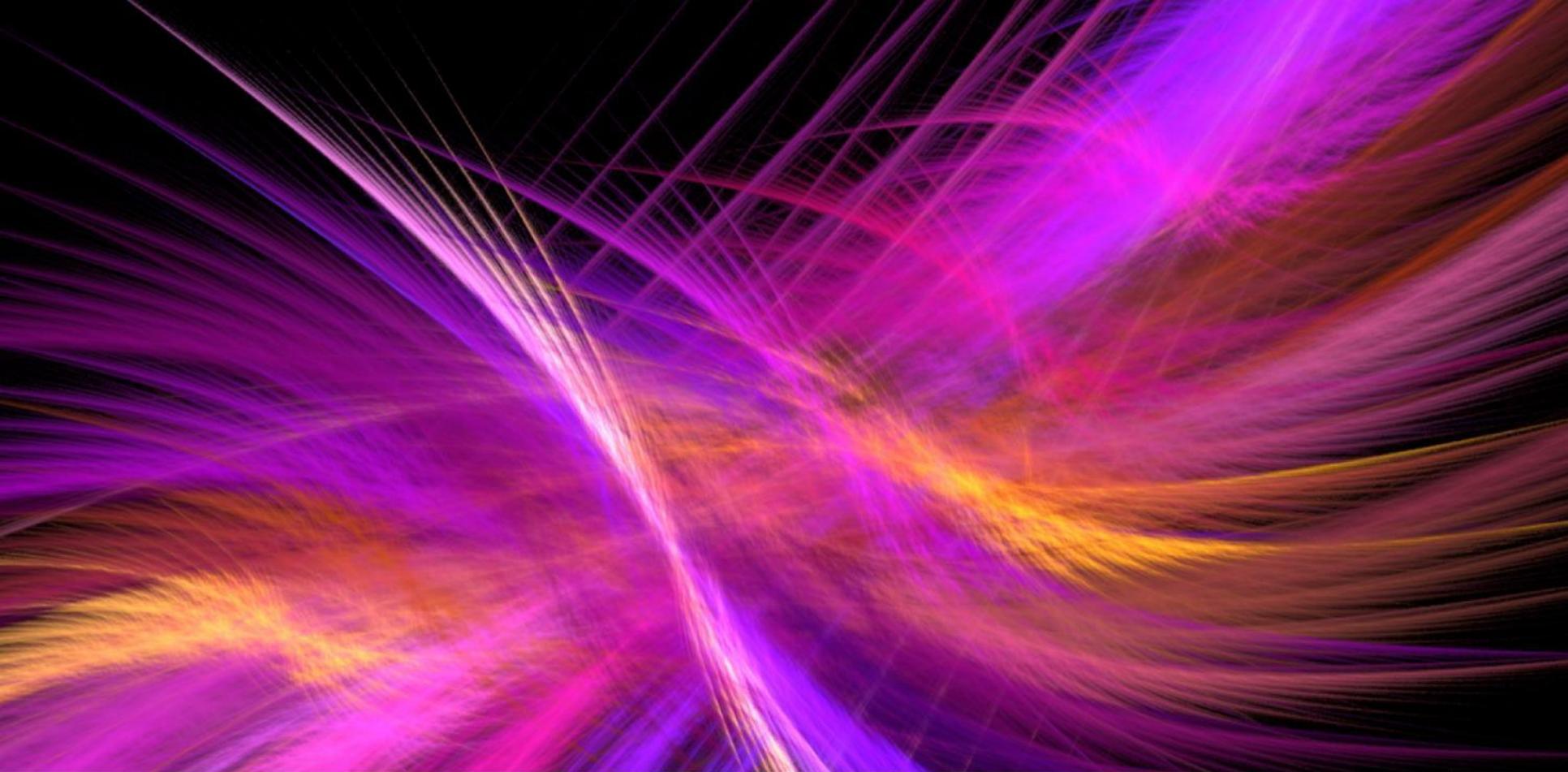
Devices

VS

Drug

*...for MD, HTA should assess the whole process, not only the procurement and many more dimensions than efficacy, safety and costs.*

*(MCDA?)*



# HTA of MD

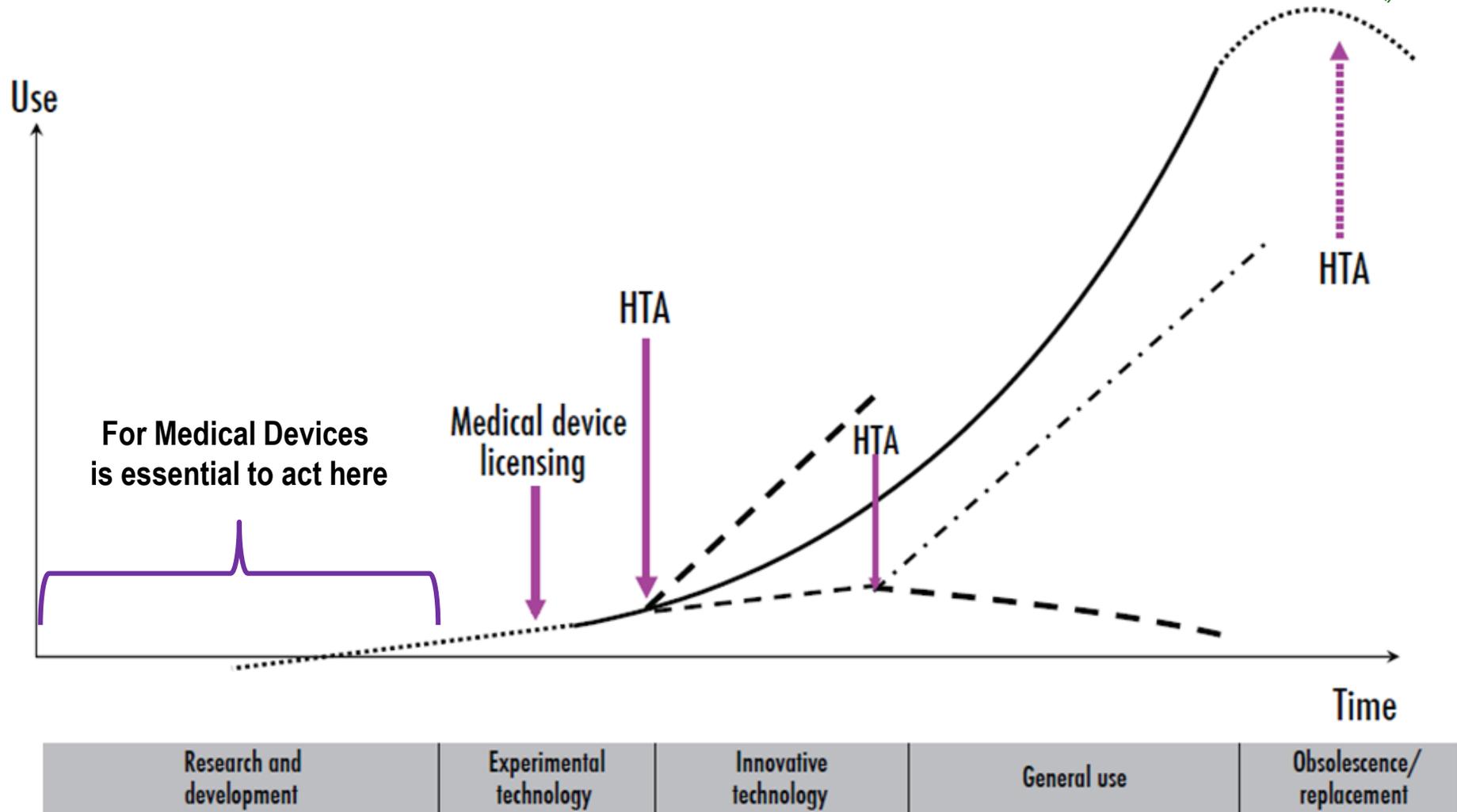
Dr Leandro Pecchia – 12/04/2017

Roma



- *Sfide ~~in Europa~~ nel Mondo:*
  - *Focus: shift dal farmaco al dispositivo medico.*
    - *Metodologie*
    - *Risorse umane (e.g. NICE, CADHT)*
    - *R&D: barriera o guida?*
    - *Training*
    - *Contenimento spesa*
    - *Up-take*

# HTA during design



\*WHO web site (last access 15.09.2012): [http://www.who.int/medical\\_devices/assessment/en/](http://www.who.int/medical_devices/assessment/en/)

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

**THE CHANGING FACE OF CLINICAL TRIALS**

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D.,  
and Janet Woodcock, M.D., *Editors*

# An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials

Owen Faris, Ph.D., and Jeffrey Shuren, M.D., J.D.

1350

N ENGL J MED 376;14 NEJM.ORG APRIL 6, 2017

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

### I. GENERAL INFORMATION

Device Generic Name:	Implantable Pacemaker System
System Trade Name:	Revo MRI™ SureScan™ Pacing System
Applicant's Name and Address:	Medtronic, Inc. Cardiac Rhythm Disease Management 8200 Coral Sea Street Mounds View, MN 55112
Date of Panel Recommendation:	March 19, 2010
Premarket Approval Application (PMA) Number:	P090013
Date of FDA notice of approval:	February 8, 2011

**Medtronic Revo** MRI pacemaker system: approved in 2011 as the first pacemaker indicated to allow patients implanted with the device to undergo magnetic resonance imaging (MRI)  
(75% of implanted patients can expect to have a clinical indication for MRI over the lifetime of their device)

\*FDI report: [https://www.accessdata.fda.gov/cdrh\\_docs/pdf9/P090013b.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf9/P090013b.pdf)



MR safe		The device or implant is completely nonmagnetic, nonelectrically conductive, and nonradiofrequency reactive, therefore eliminating all the primary potential risks during MRI scanning
MR conditional		The device or implant may contain magnetic, electrically conductive, or radiofrequency-reactive components that are safe for operation in proximity to the MRI, provided the conditions for safe operation are defined and observed (both for the MR scanner and the device itself)
MR unsafe		Objects that are significantly ferromagnetic and pose a clear and direct threat to persons and equipment within the magnet room

## Re-engineered regulation of medical devices. What role for *in silico* trials?

C. Federici<sup>1</sup>, O. Ciani<sup>1,2</sup>, L. Pecchia<sup>3</sup> and R. Tarricone<sup>1</sup>

<sup>1</sup>Centre for Research on Health and Social Care Management (CERGAS) – Bocconi University

<sup>2</sup>Institute of Health Research, University of Exeter Medical School

<sup>3</sup>University of Warwick

- *Round table @WHO III Global Forum on Medical Devices, Ginevra (May 2017)*
- *Invite Talck @AfricaHealth2017, Johannesburg, S. Africa (June 2017)*
- *Invited Session @EMBEC2017, Tampere, Finlandia (June 2017)*
- *Pannel Session @HTAi2017, Roma (June 2017)*

# Tank you for your attention!



## Applied Biomedical Signal Processing and Intelligent eHealth (ABSPIE) Lab PhD Students



**Rossana Castaldo**  
Signal processing/  
Machine learning  
(2014)



**Luiss Montesinos**  
Balance/falls  
(2015)



**Tim Siu Wang**  
Behavioural modelling  
(2016)



**Michaela Porumb**  
Signal processing/  
data analytics  
(2017)



**Marina Gilic**  
HTA in LMIC  
(2017)



**Carlo Federici**  
eHTA  
(2017)

## 2015/2016 Visiting Students/Researchers/Academics



**Dr Paolo Melillo**  
Second University of Naples



**Dr Giovanna Sannino**  
Italian CNR



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Philips



**Tarricone**  
Bocconi



**Polisena**  
CADHT



**Clark**  
NICE



**Ciani**  
Bocconi



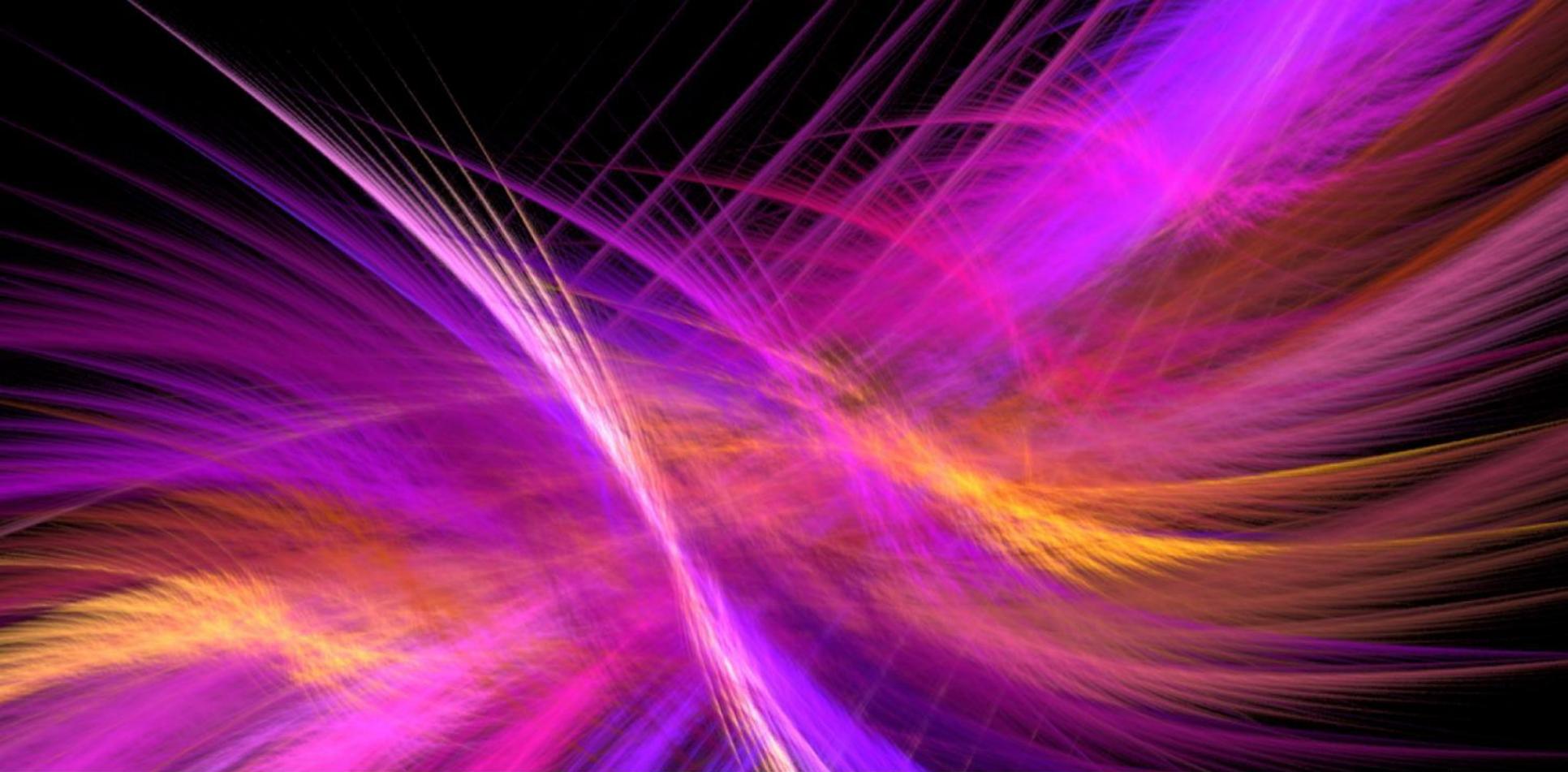
**Fico**  
Madrid



**Velazquets**  
WHO



**Böhler**  
European Commission



# IFMBE HTAD Training

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WARWICK



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# IFMBE HTAD resources on HTA



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- **IFMBE HTAD:**
  - <http://htad.ifmbe.org/>
- **IFMBE HTAD eLearning:**
  - <http://htad.ifmbe.org/elearning/>



