Healthcare Technology Engineering

WARWICK

Early HTA

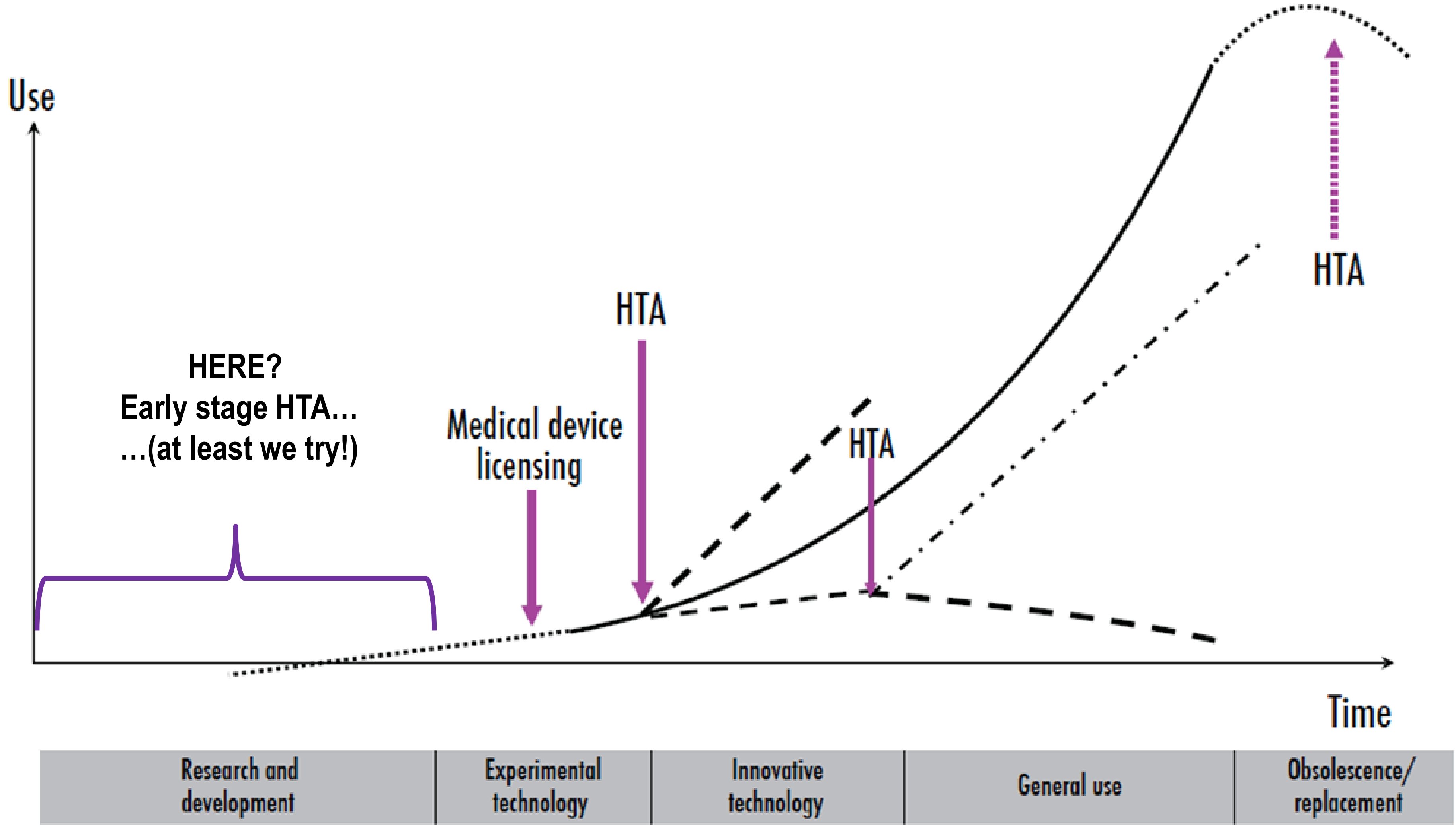
Dr Leandro Pecchia

…BME peculiar contribution?

- It is important to start thinking new inventions from the "HTA-prospective" **during the R&D** (early stage HTA, premarket evaluation…), when **a small change may have a big impact**…
- The HTA is perceived as a barrier to the introduction of new technologies in the health care systems (80% r SME in EU)
- A reason is that: *"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*)
- Research question: ***may we support R&D of new MDs with early stage HTA methods?***

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

HTA
Limits of standard methods



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

GOALS OF THIS LECTURE

- **“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?
    - **Predictive statistical methods to** designing a new home monitoring telemedicine interventions basing on the best available evidence
        - How often to collect data?
        - Which data?
        - Which target population?
    - **Analytic Hierarchy Process (AHP)** :
        - Are there more important user needs to be satisfied? (users: patients, nurses, MD…)
        - May we quantify their relative importance?
        - May we measure the fitting of our solution with these needs?

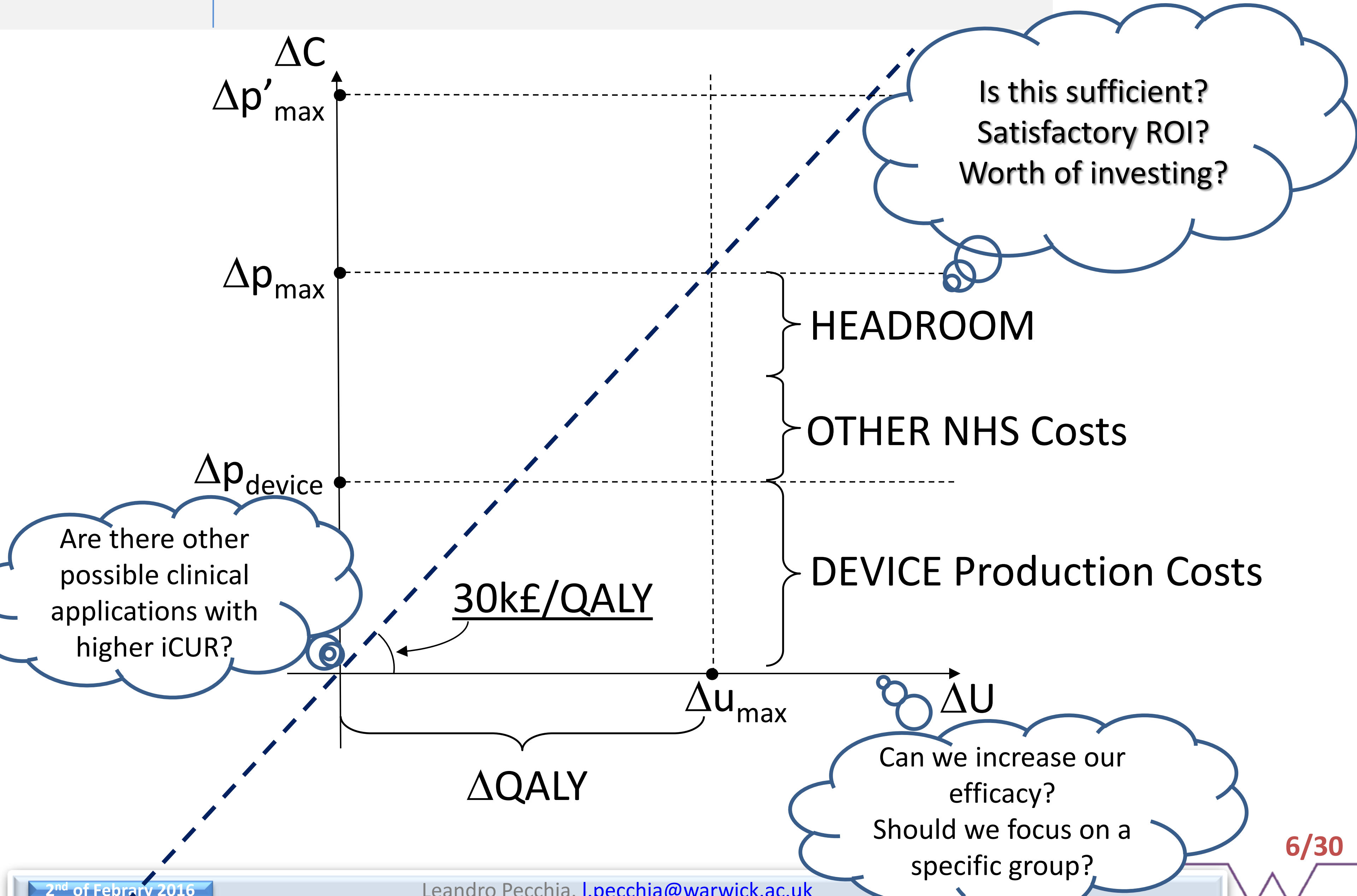
HTA

Limits of standard methods

Devices VS	Drug
Principal action	
Other than principally drugs	Pharmaco./Immunologic/Metabolic
Mechanical/Electromagnetic/Materials	Chemical based
Product life cycle	
Short life cycle	Long life cycle
Constantly evolving components/parts	Unchanging compound
Clinical evaluation	
Difficult to blind (no placebo)	Easy to blind
Multiple end users	Usually one end users
Long learning curve	Short learning curve
Strongly dependent by settings/users	Less dependent by settings/users
Complex to standardize for RCT	Easy to standardize for RCT
Use issues	
User-dependent efficacy	Efficacy is less user-dependent
Often require intensive training	Usually do not require training
Complication decrease with use	Complication increase with use
Diversity	
Mainly small companies/few large co.	Mainly large multinationals
Diagnostic or therapeutic	Therapeutic
Costs	
Varying overheads/slow return	High overheads with quicker return
Higher distribution costs	Lower distribution costs
Higher maintenance/installation costs	No maintenance/installation

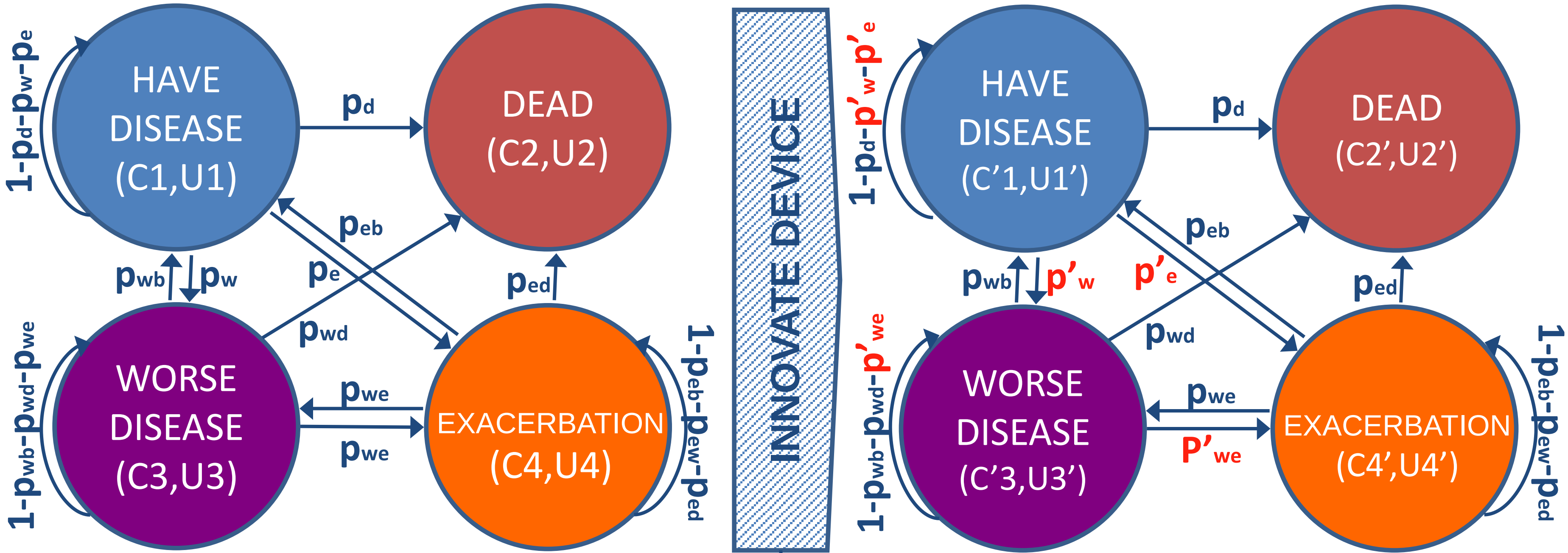
L Pecchia, MP Craven, "*Early stage Health Technology Assessment (HTA) of biomedical devices. The MATCH experience*". World Congress on Medical Physics and Biomedical 2012, 26-31 May 2012, Beijing, China.

Headroom Analysis



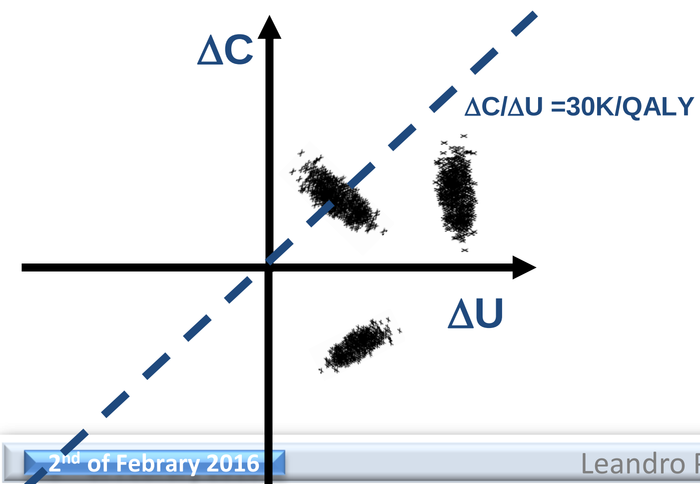
4 states Markov Models

disease/worsening/exacerbation/dead



↓ worsening ($p'_w < p_w$)

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



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Designing a new home monitoring telemedicine interventions for CHF basing on the best available evidence

- How often to collect data?
- Which data?
- Which target population?

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METHODS 1/2

1. A meta-analysis Home Monitoring (HM) vs Usual Care (UC)

2. Only well designed RCT were included

3. Outcome considered:
   - mortality for CHF,
   - mortality for all causes,
   - bed days for CHF,
   - bed days for all causes,
   - readmissions for CHF and
   - readmissions for all causes

4. RCT were classified according to: **patients' severity** and **HM complexity**

5. Correlation between the 6 outcomes and **patients' severity/HM complexity** were studied

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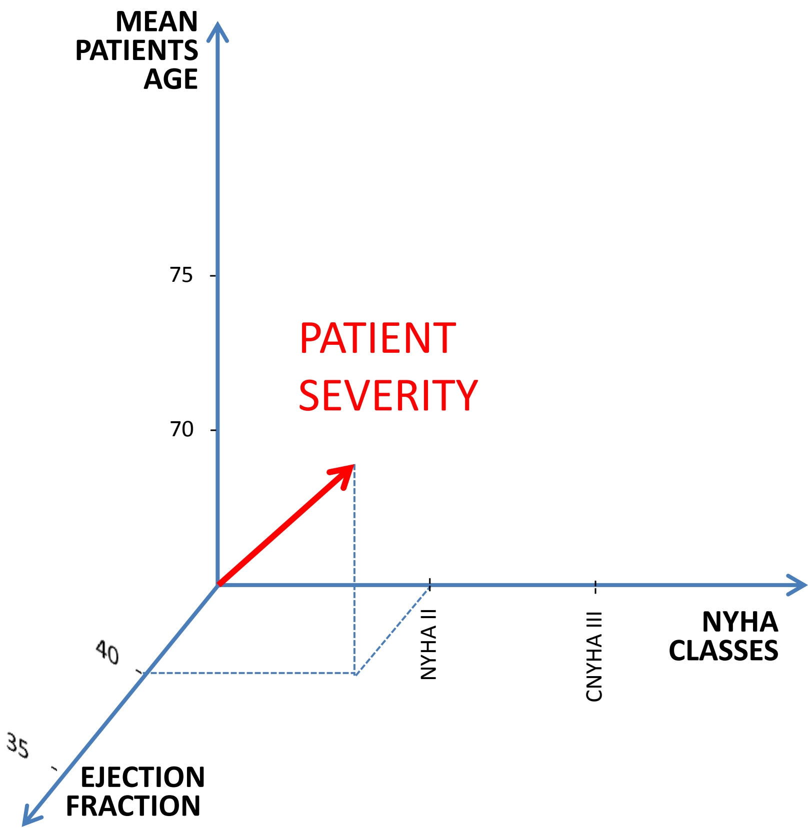
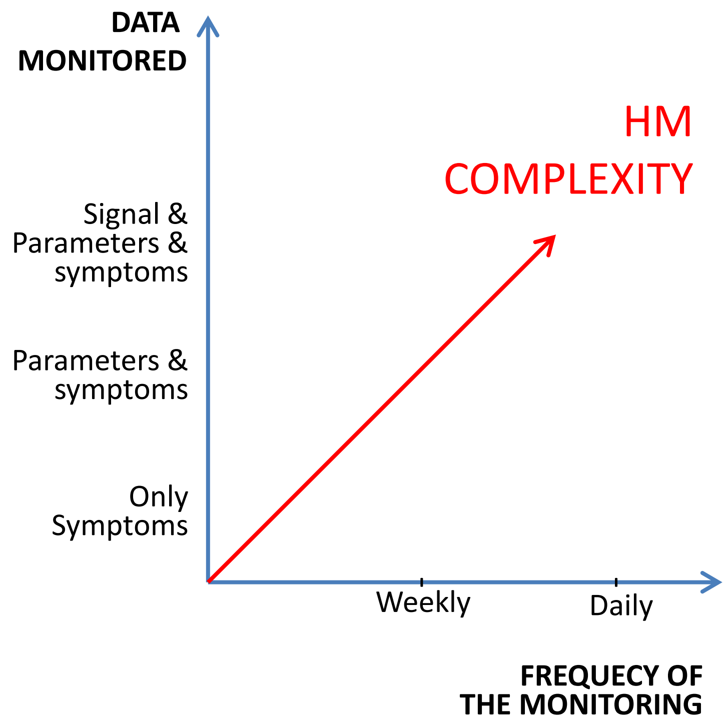
METHODS 2/2

- HM RCT were classified according to **patients' severity** and **HM complexity**





- Correlations **effectiveness-severity** and **effectiveness-complexity** were computed

RESULTS

- Study selection:

314 papers

Title/abstract selection:
8 Not heart failure
18 Invasive hemodynamic monitoring
43 Editorial or review
70 not an RCT
41 Other heart failure intervention or research
19 Study design

115 papers

Full paper selection:
1 Not heart failure
7 Editorial or review
16 not an RCT
40 Other heart failure intervention or research
10 Study design
4 Other languages
5Short Follow-up

32 papers

23 DMP vs UC
8 HM vs UC
1DMP & HM vs UC

RESULTS

MORTALITY

	DMP vs UC RR (95% CI;p)	HM vs UC RR (95% CI;p)
All-causes	**0.826 (0.691 ; 0.987; 0.043)**	0.723 (0.402; 1.302; 0.223)
HF-related	0.848 (0.518; 1.389; 0.322)	0.602 (0.362; 1.001; 0.059)

RR < 1 <=> DMP/HM better than UC; p < 0.05 <=> resalt statistically significant (**bold**)

READMISSION

	DMP vs UC RR (95% CI;p)	HM vs UC RR (95% CI;p)
All-causes	**0.835 (0.710; 0.982; 0.037)**	0.970 (0.811; 1.159; 0.377)
HF-related	**0.797 (0.689; 0.923; 0.004)**	0.816 (0.559; 1.192; 0.230)

RR < 1 <=> DMP/HM better than UC; p < 0.05 <=> resalt statistically significant (**bold**)

BED DAYS

	DMP vs UC MD (95% CI;p)	HM vs UC MD (95% CI;p)
All-causes	0.094 (-2.680; 2.868; 0.112)	1.109 (-1.100; 3.317; 0.311)
HF-related	0.637 (-2.236; 3.510; 0.000)	1.937 (-0.792; 4.666; 0.124)

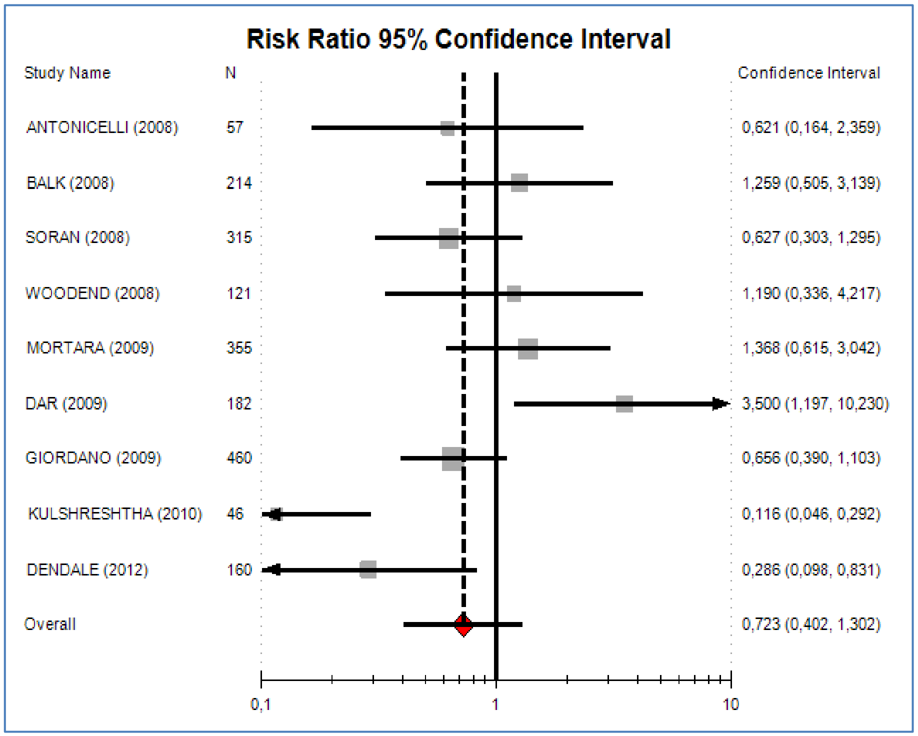
MD <0 <=> DMP/HM better than UC; p < 0.05 <=> resalt statistically significant (**bold**)

- **There is evidence that DMP are more effective that UC**
  - Reducing All-causes mortality
  - Reducing readmission (All-causes and HF-related)
- **It seems, but there is not evidence that DMPs reduce bed-days**

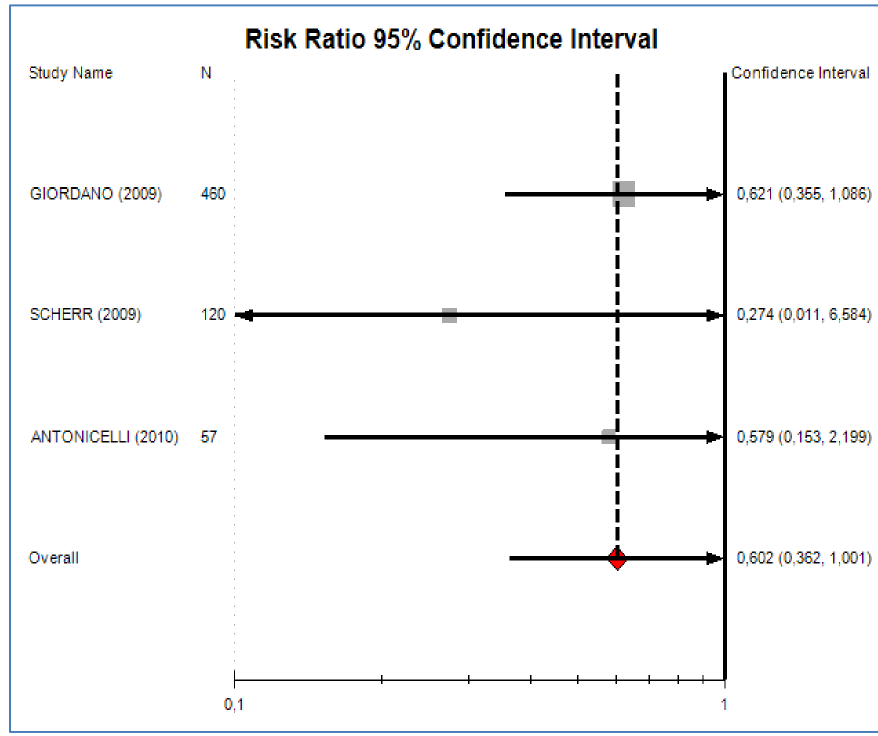
RESULTS

- **Mortality**: HM vs UC

All causes



HF mortality

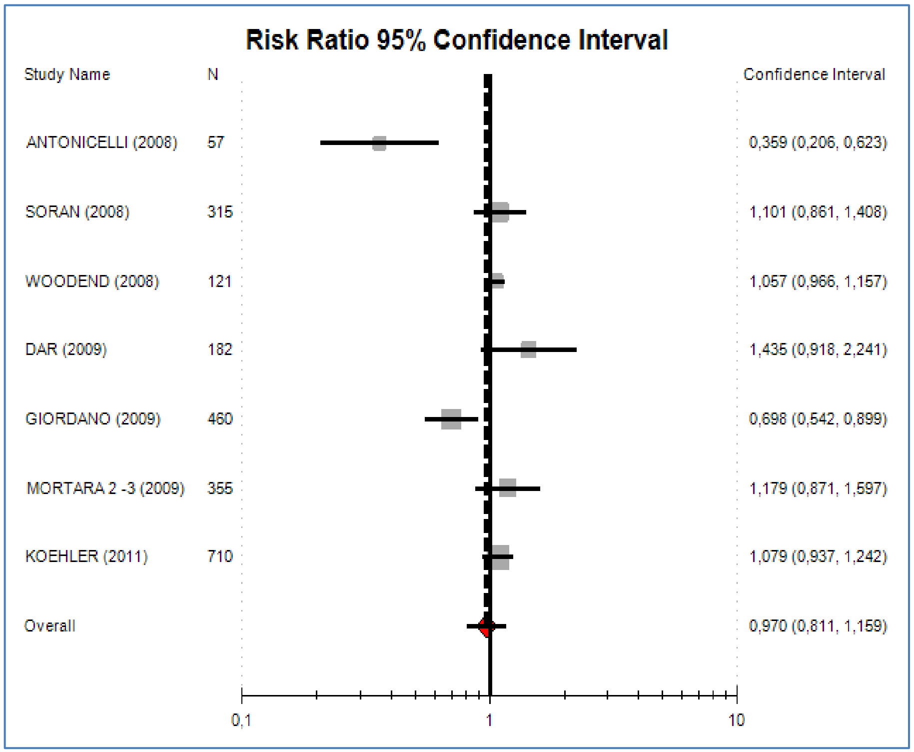


The HM RCT seems (no statistically significant result) more effective than UC

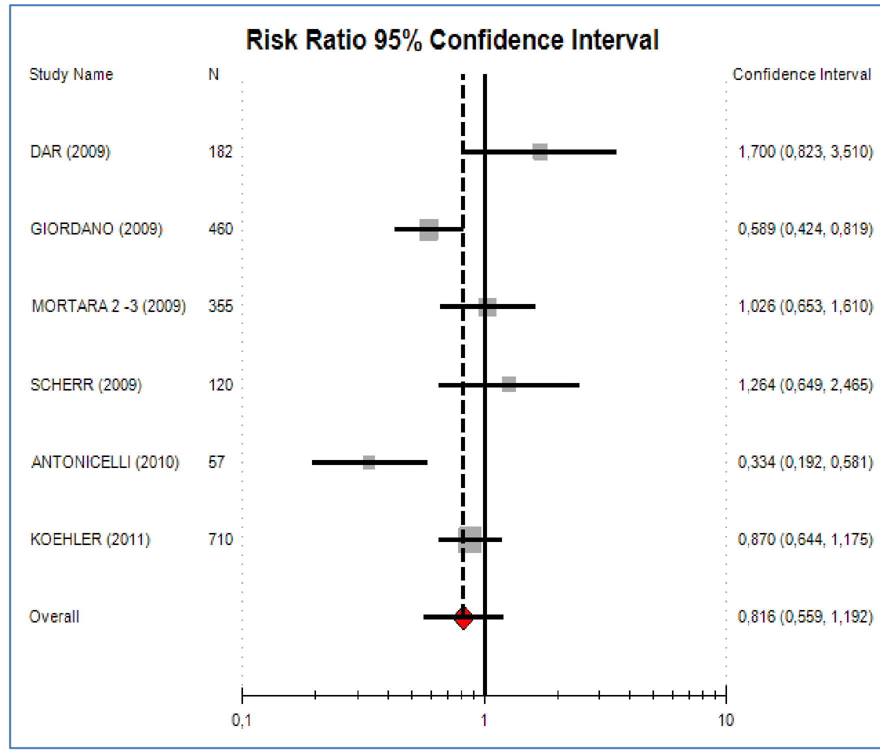
RESULTS

- **<u>Readmission</u>**: HM vs UC

All causes



HF mortality

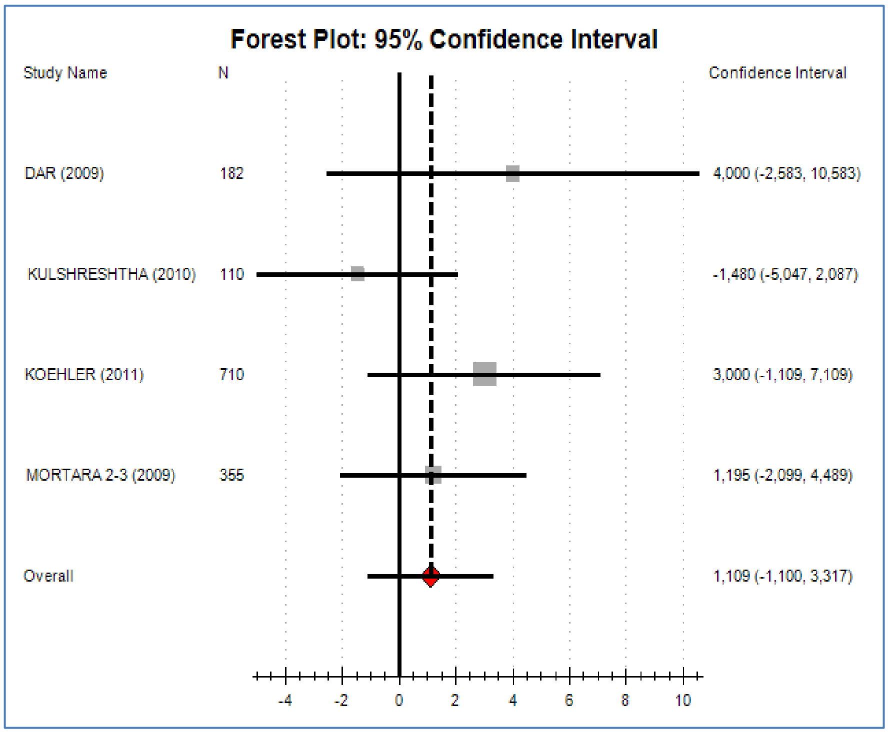


The HM RCT seems (<u>no statistically significant result</u>) more effective than UC

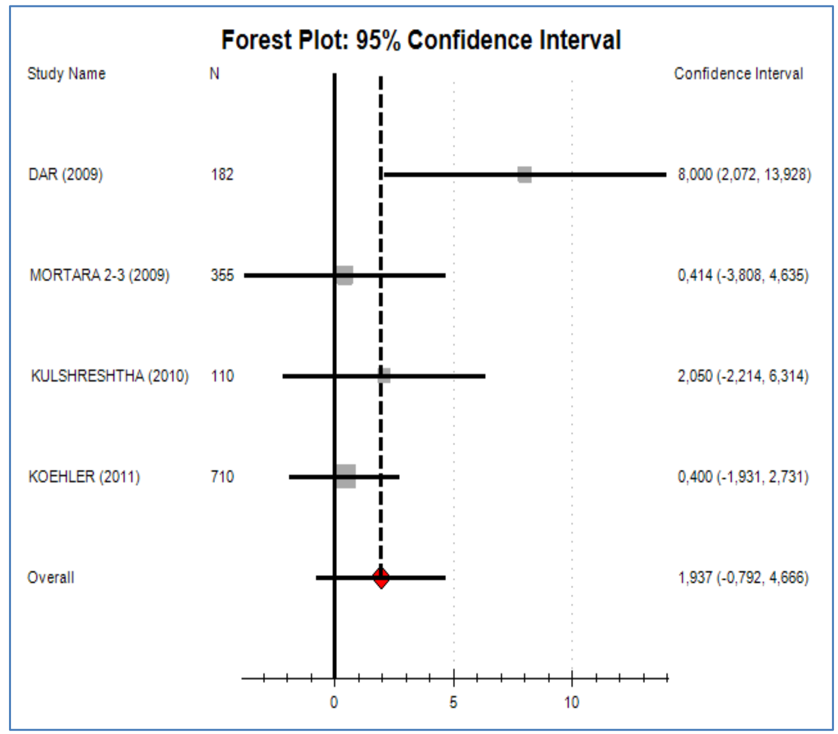
RESULTS

- **<u>Bad days</u>**: HM vs UC

All causes



HF mortality



The HM RCT seems (<u>no statistically significant result</u>) more effective than UC

RESULTS

- HM RCT classification: **Patients' severity**

	NYHA	Ejection Fraction	Mean Age	Patient Severity
Sherr 2008	3	<40	73	8
Dendale, 2011	3	<40	76	7
Dar, 2009	3	>40	72	6
Koehler,2011	2&3	<35	67	5
Antonicelli, 2010	2&3	<40	78	4
Soran, 2008	2&3	<40	76	4
Kulshreshtha, 2010	2&3	<40	68	3
Giordano, 2010	2	<40	70	2
Mortara, 2009	2	<40	60	1

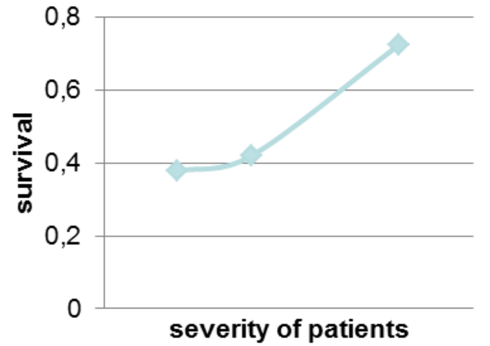
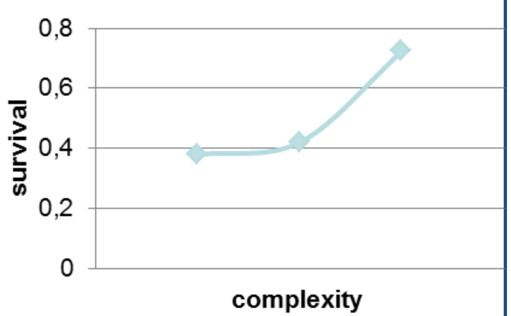
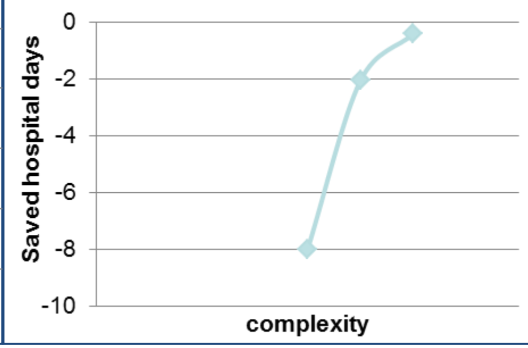
RESULTS

- HM RCT classification: **HM protocol complexity**

	Simptomps	Parameters	Signals	Frequency	Complexity
KOEHLER, 2011		x	ECG	Daily	6
KULSHRESHTHA, 2010		X		Daily	5
DAR, 2009	X	X		Daily	4
SORAN, 2008	X	X			4
GELLIS, 2012		X		Daily	4
SHERR, 2008		X		Daily	3
DENDALE, 2011		X		Daily	3
ANTONICELLI, 2010	X	X	ECG	Weekly	2
MORTARA, 2009	X	X	ECG	Weekly	2
GIORDANO, 2010		X	ECG	Each 15 days	1

RESULTS

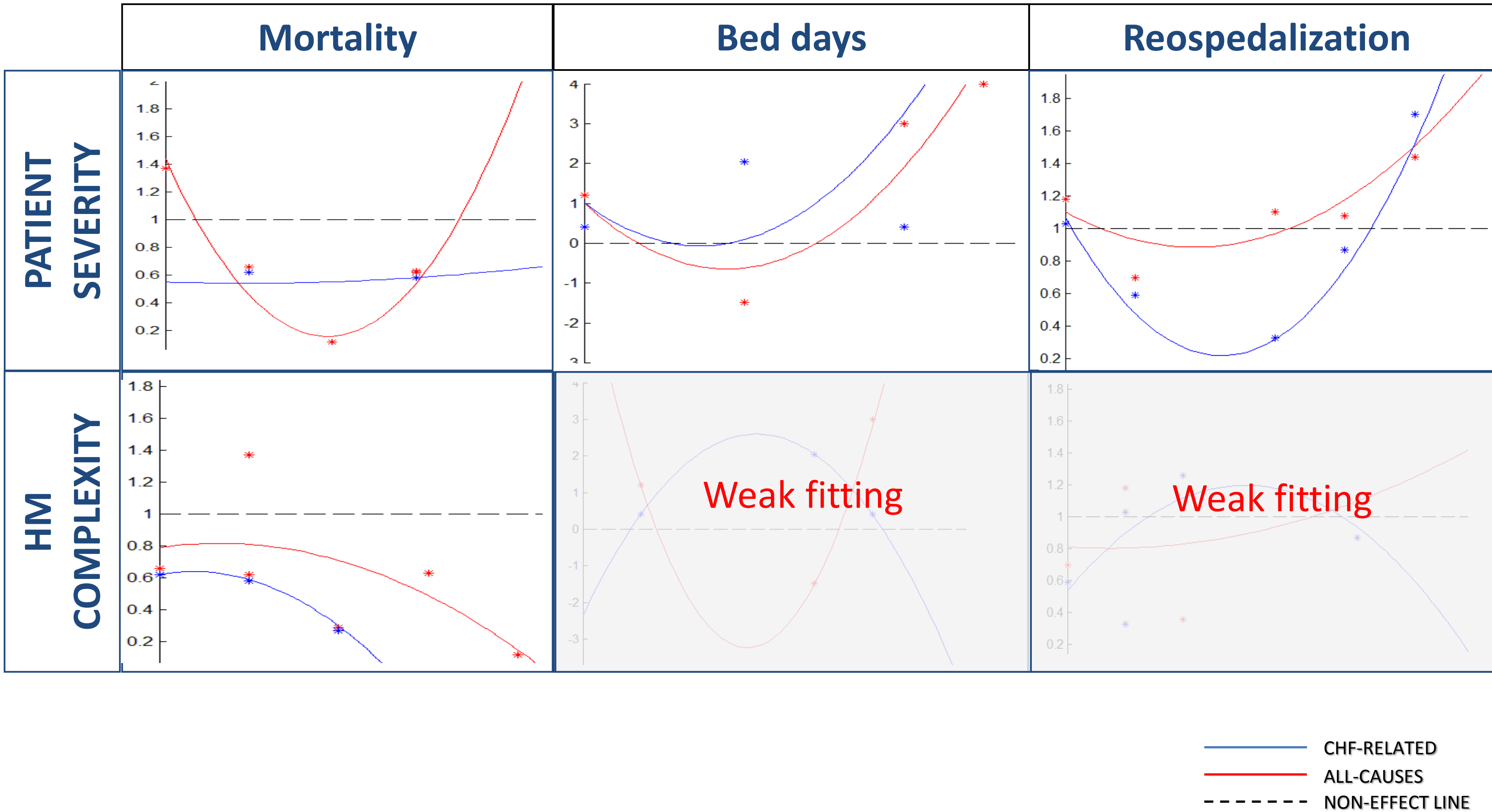
- HM outcomes vs Pz complexity and HM complexity:

<table>
<tr><th></th><th>Survival</th><th>Saved Bed days</th><th>Reospedalization</th></tr>
<tr><td>PATIENT SEVERITY</td><td>
</td><td>No significant correlation</td><td>No significant correlation</td></tr>
<tr><td>HM COMPLEXITY</td><td>
</td><td>
</td><td>No significant correlation</td></tr>
</table>

- Evidence:
  - HM is more effective for more severe patients
  - More complex HM are more effective in reducing mortality and bed-days

RESULTS

- HM outcomes vs Pz complexity and HM complexity:

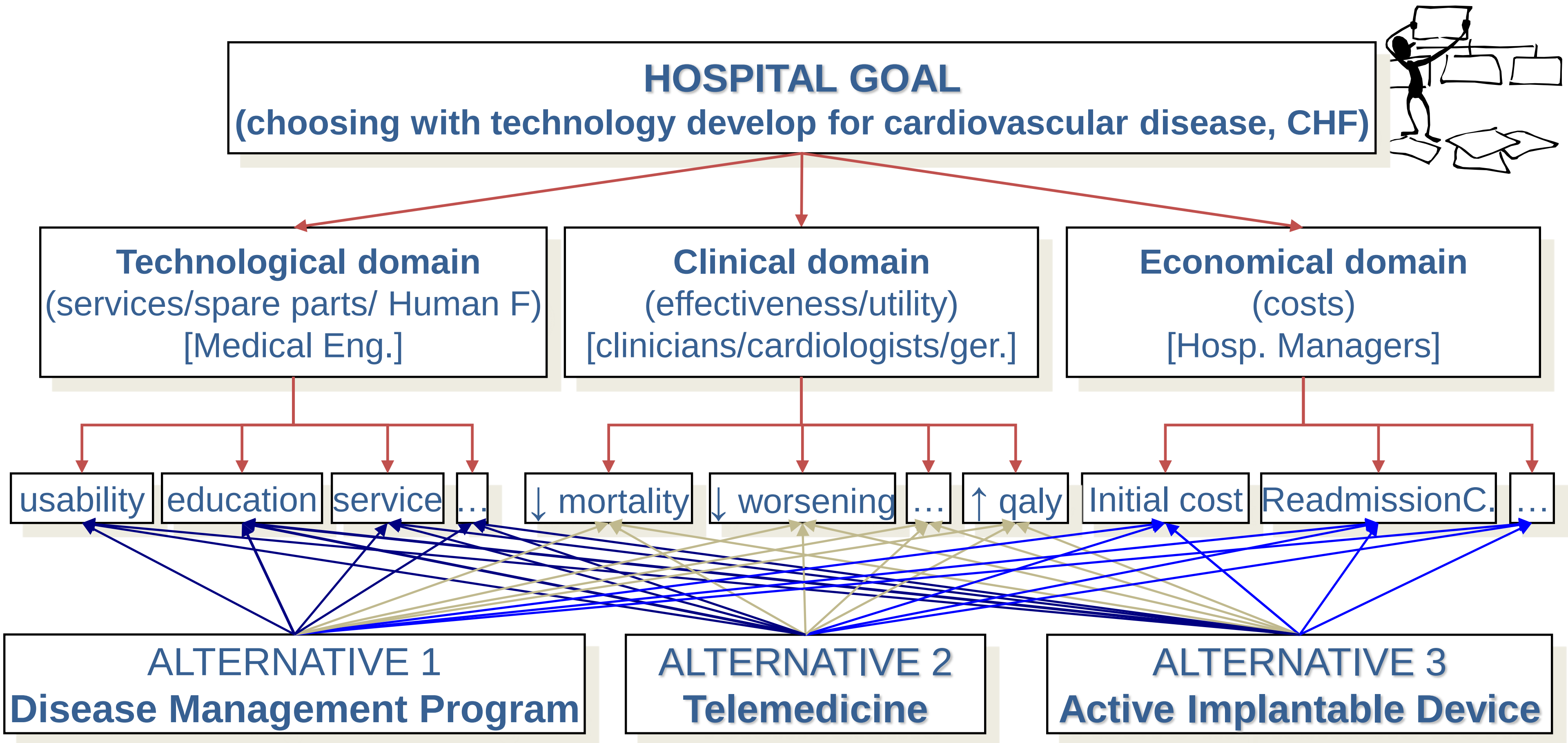


Measure user needs to design most appropriate technology

- What are the most important needs?
- How your innovative idea meet these needs?
- And the other?

AHP for HTA

Hierarchy via an exempla

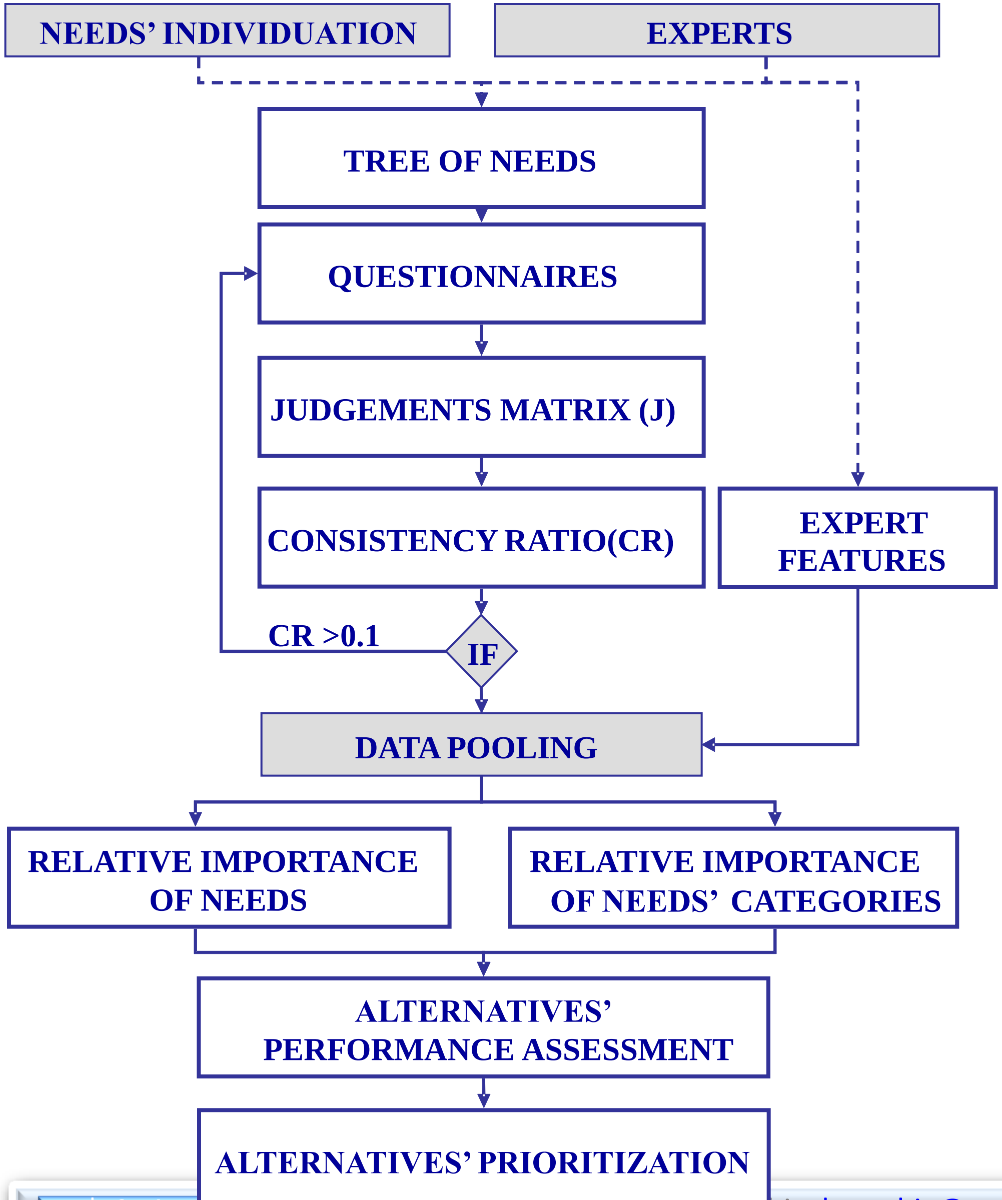


How important is each factor (outcome/output/need) for the assessment?

How each alternative satisfy each factor?

AHP method

pairwise comparisons Process



AHP method

pairwise comparisons Process

NEEDS' INDIVIDUATION

EXPERTS

TREE OF NEEDS

QUESTIONNAIRES

According to your experience, how important is each need on the left compared with each one on the right?

Need 1 (↓ mortality)	Is:	*much more*	*more*	*equally*	~~*less*~~	*much less*	important hen	***Need 2 (↓ Pz. worsening)***
Need 2 (↓ Pz. worsening)	is:	*much more*	*more*	~~*equally*~~	*less*	*much less*	important hen	***Need 3 (↑ QALY)***
Need 3 (↑ QALY)	is :	~~*much more*~~	*more*	*equally*	*less*	*much less*	important hen	***Need 1 (↓ mortality)***

RELATIVE IMPORTANCE OF NEEDS

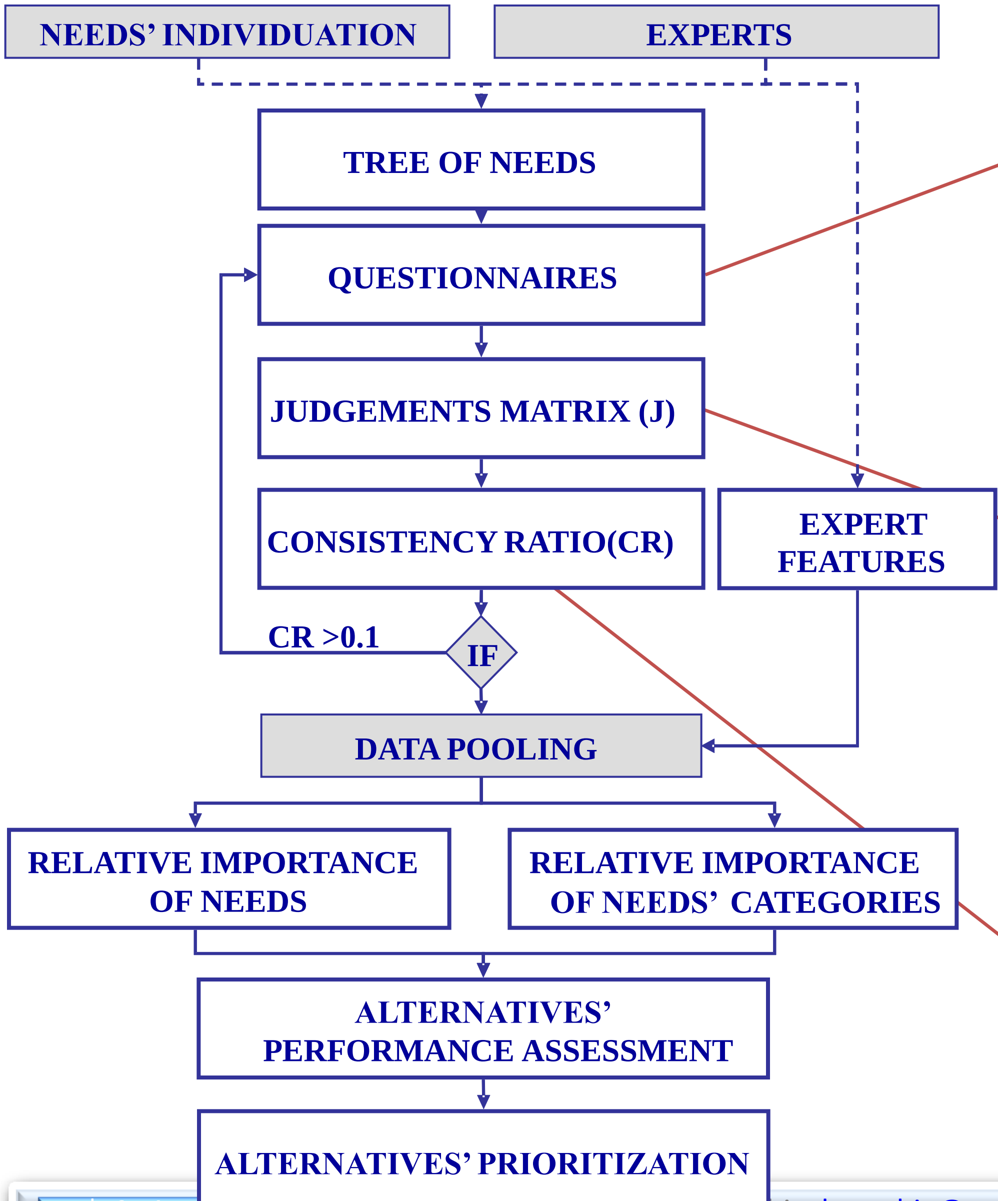
RELATIVE IMPORTANCE OF NEEDS' CATEGORIES

ALTERNATIVES' PERFORMANCE ASSESSMENT

ALTERNATIVES' PRIORITIZATION

AHP method

pairwise comparisons Process



Numerical values	
Much more	(5)
More important	(3)
Equally important	(1)
Less important	(1/3)
Much less important	(1/5)

$$\begin{array}{c|ccc} & N1 & N2 & N3 \\ \hline N1 & 1 & I_{21} & I_{31} \\ N2 & I_{12}=1/I_{21} & 1 & I_{32} \\ N3 & I_{13}=1/I_{31} & I_{23}=1/I_{32} & 1 \end{array}$$

Eigenvector (priorities)

Eigen value (coherence)

$$N1>N2 \ \& \ N2>N3 \Rightarrow \begin{cases} N1 \gg N3 \\ N1 > N3 \\ \cancel{N1 < N3} \end{cases}$$

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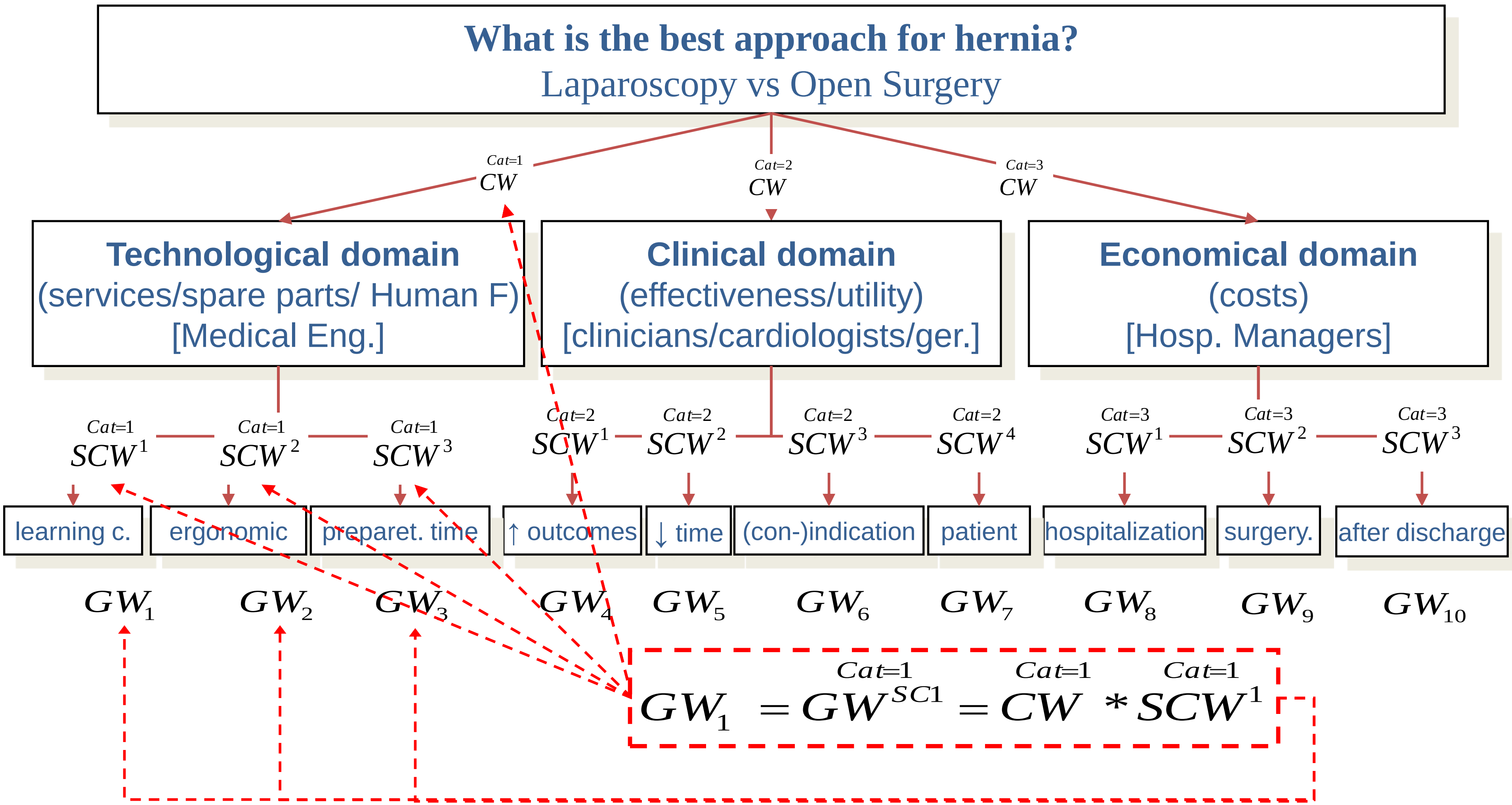
Method

AHP method

Analytic needs prioritization



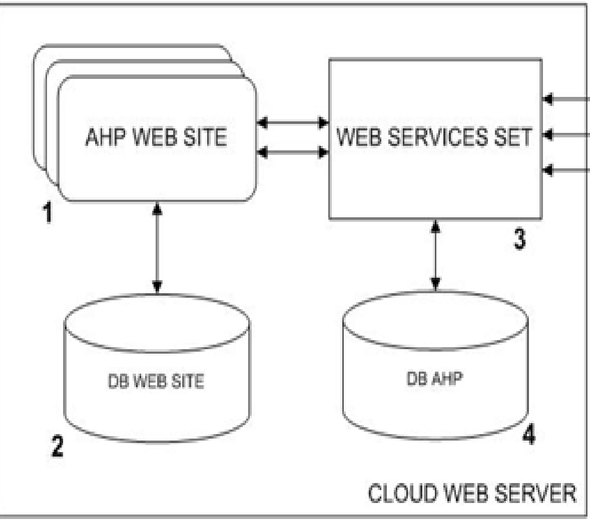
AHP for HTA

	Global importance	ALTERNATIVE 1 **DMP**	ALTERNATIVE 2 **Telemedicine**	ALTERNATIVE 3 **Active Implantable D.**
usability	GW_1	P_1^{A1}	P_1^{A2}	P_1^{A3}
education	GW_2	P_2^{A1}	P_2^{A2}	P_2^{A3}
service	GW_3	P_3^{A1}	P_3^{A2}	P_3^{A3}
↓ worsening	GW_4	P_4^{A1}	P_4^{A2}	P_4^{A3}
↓ mortality	GW_5	P_5^{A1}	P_5^{A2}	P_5^{A3}
↑ qaly	GW_6	P_6^{A1}	P_6^{A2}	P_6^{A3}
Initial cost	GW_7	P_7^{A1}	P_7^{A2}	P_7^{A3}
ReadmissionC.	GW_8	P_8^{A1}	P_8^{A2}	P_8^{A3}

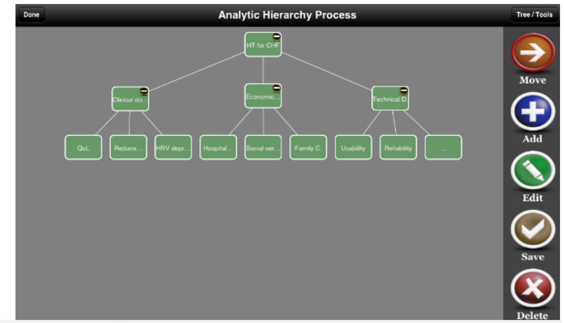
$$Global\ Perfomance\ Alternative_j = \sum_{i=1}^{8} GW_i * P_i^{Aj}$$

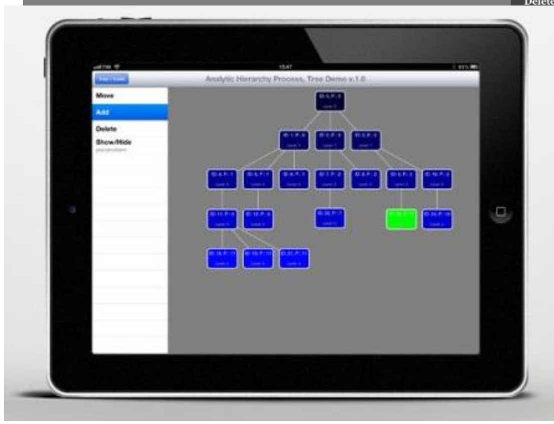
CS2 AHP

The system
a web tool with App

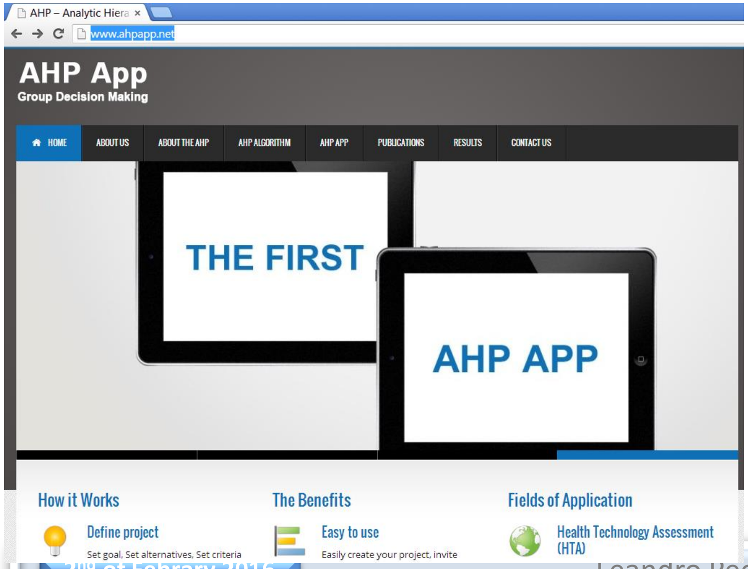


1. AHP WEB SITE: WORDPRESS BASED
2. DB WEB SITE: MYSQL BASED
3. WEB SERVICES SET: C#.NET BASED – AHP COMPUTING AND MANAGEMENT
4. DB AHP: MYSQL BASED
5: INTERNET
6: CLIENT APP ON IPAD





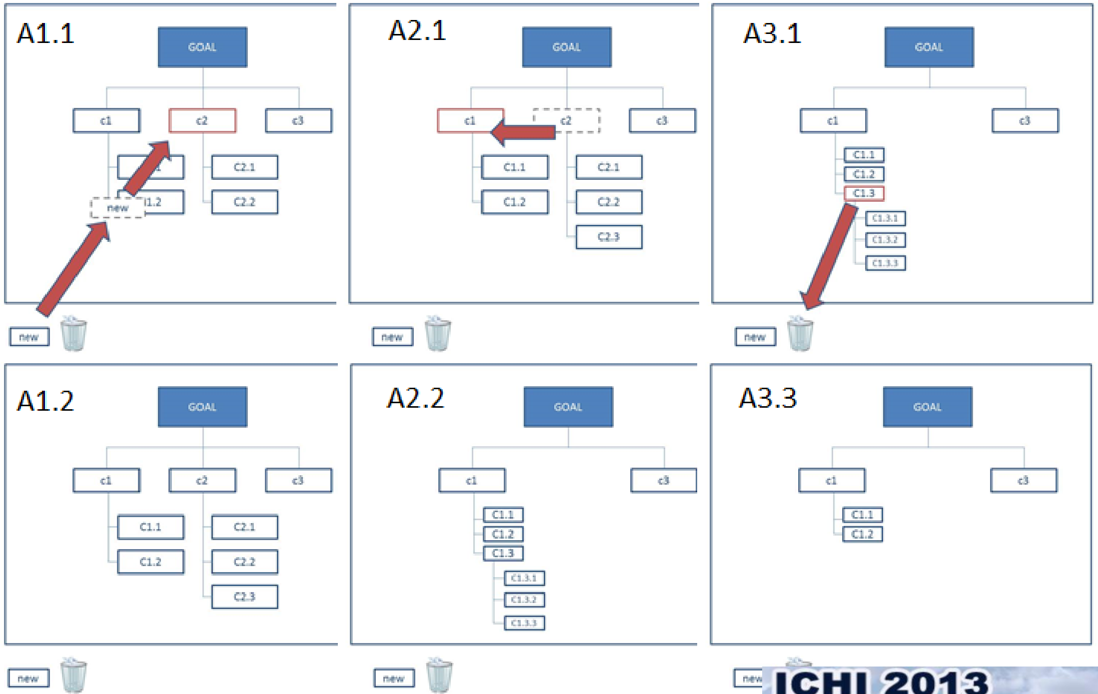
http://www.ahpapp.net/



- **Method:** AHP for HTA/User need elicitation
- **Applications:** Publication in Healthcare whit the App
- **Models:** to be downloaded and adapted in your study
- **Community:** experts willing be involved

CS2 AHP

The system
a web tool with App



A software tool to support the Health Technology Assessment (HTA) e the user need elicitation of medical devices via the Analytic Hierarchy Process (AHP)

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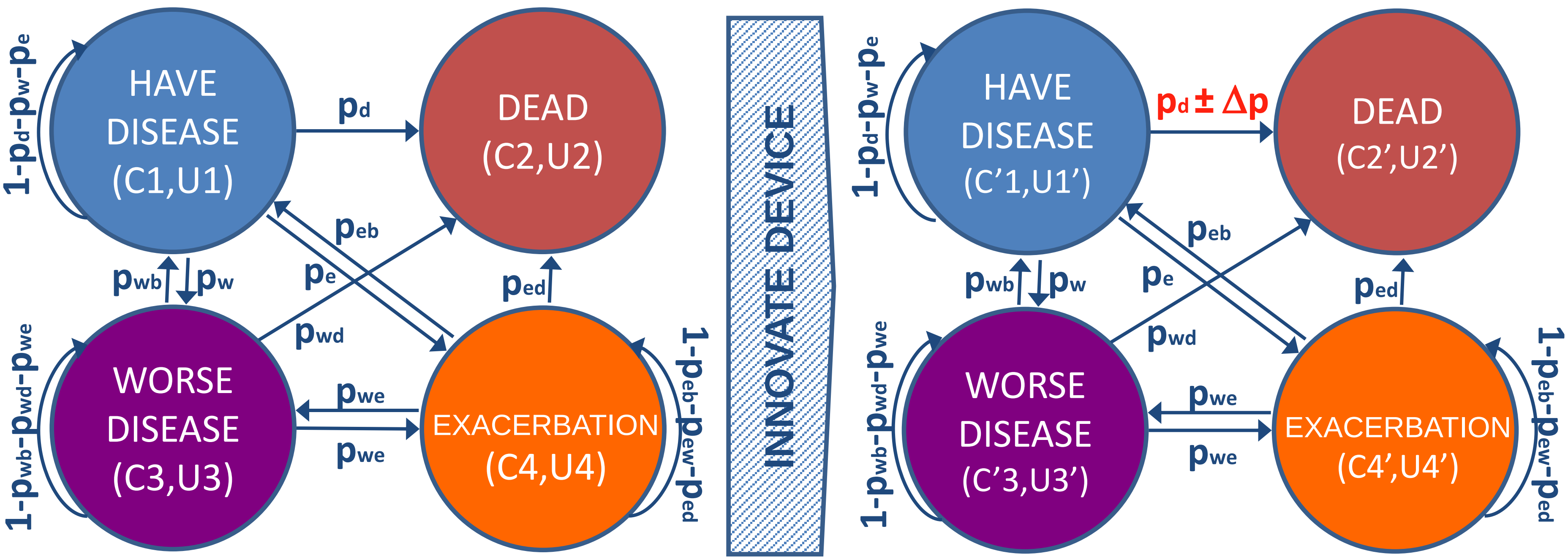
[2] Solution Engineering, Avellino, Italy
[3] Electrical Systems and Optics Research Division, University of Nottingham, Nottingham, UK

Markov Models & AHP

What if some information are missing (eHTA)?
Missing data can be estimated using AHP...



...and using sensitivity analysisto estimate worst/best cases.

CONCLUSIONS

- The assessment of a new technology should be considered as soon as possible (R&D)
- **Standard methods of HTA are not sufficient for HTA of BME devices at early stage**
- **Headroom Analysis** may be used to evaluate in the ROI/max reimbursability cost of a new health technology in the best case
- **Analytic Hierarchy Process (AHP)** may be used to priorities needs, outcomes and outputs
- **4-state Markov Models (MM)** can be used to estimate cost-effectiveness at early stage (4 state can be used for many different cases) and update the R&D process
- **MM and AHP** can be combined to estimate unknown parameters when information are missing
- **Predictive statistical methods to** designing a new home monitoring telemedicine interventions basing on the best available evidence