



Early health economic modeling to inform medical product development and market access



Maarten J. IJzerman, PhD

Health Technology & Services Research (HTSR) and the Luxemburg Initiative for Translational Health Economics (LITHE)

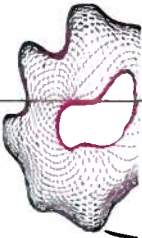
4th Annual Knowledge to Policy Day
THETA, Toronto, Canada
May, 29 2013



Some thoughts...

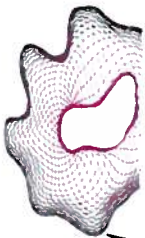
- Early models are not useful if not properly explained. Align with target audience before you start and make clear which decision has to be made, and by whom
- Commercial, R&D and health economic models are typically used in isolation from each other and most people only refer to one specific type of models if asked about early modeling
- Too often, early models are referred to as models that precede the decision they inform. Yet, they are not necessarily started early.
- It may be useful to use health economic evidence in earlier stages of R&D





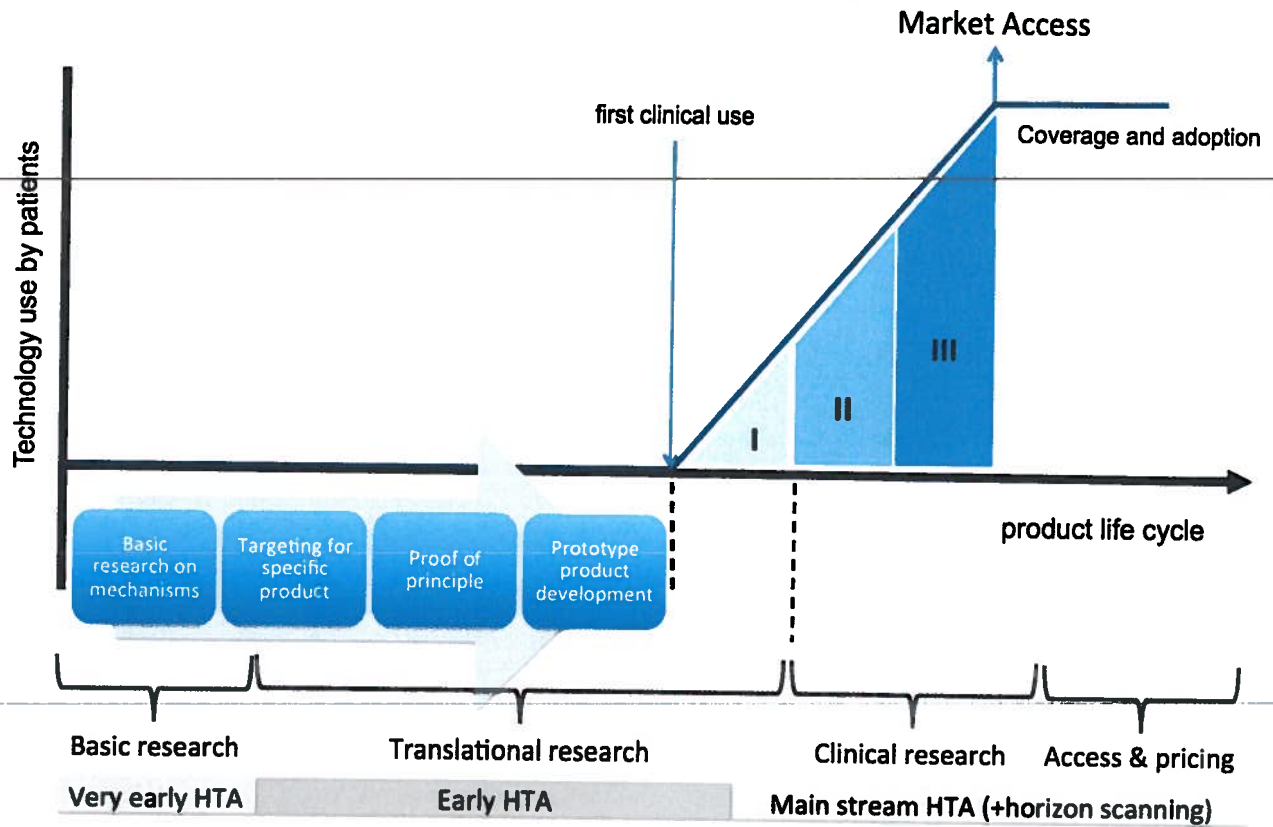
What is early modeling?

- **Emphasis on efficient use of resources in medical product development and market access**
 - Determine health economic value early on to either continue or discontinue further development (in particular SME's)
- **Different initiatives**
 - Inno-HTA, MaRS Excite, MATCH, OncoTyrol, CTMM, LITHE
 - Taskforce initiative ISPOR
- **But also different meanings:**
 - ~~Early modeling/horizon scanning for (research) priority setting~~
 - From a societal perspective – i.e. allocative efficiency
 - Early stage modeling for R&D and commercial decisions
 - From an industry perspective – i.e. business opportunities



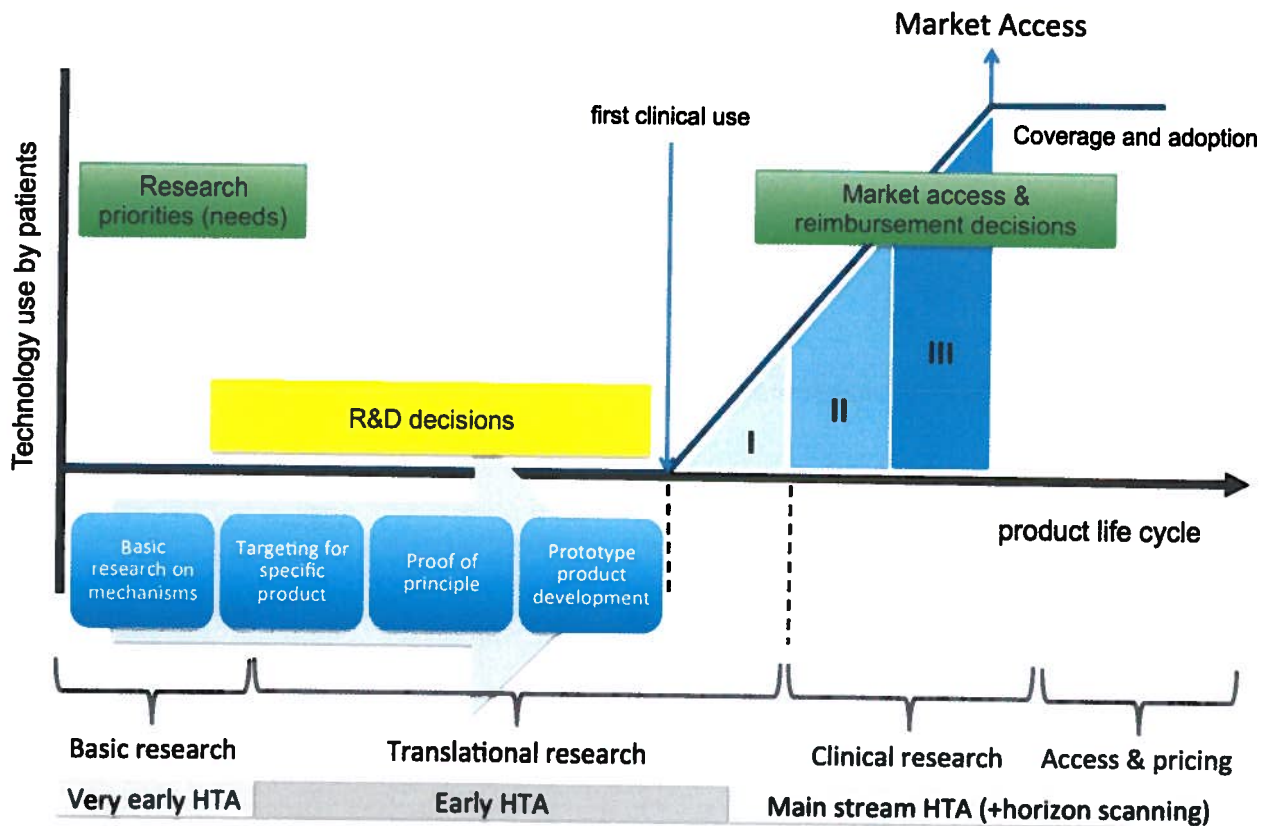
Early modeling in the view of...

- **Society**
 - Maximize health benefits given scarce resources
 - Use of early models to justify research funding (PPP)
 - Use of early models to determine health economic value
- **Engineer/scientist**
 - Ground-breaking new concepts aimed at improving health outcomes for (groups of) individuals
 - Use of models to determine development targets and competitor performance
- **Business**
 - Early identification of the commercial value of a product
 - Use of models to estimate discounted cash flow and NPV



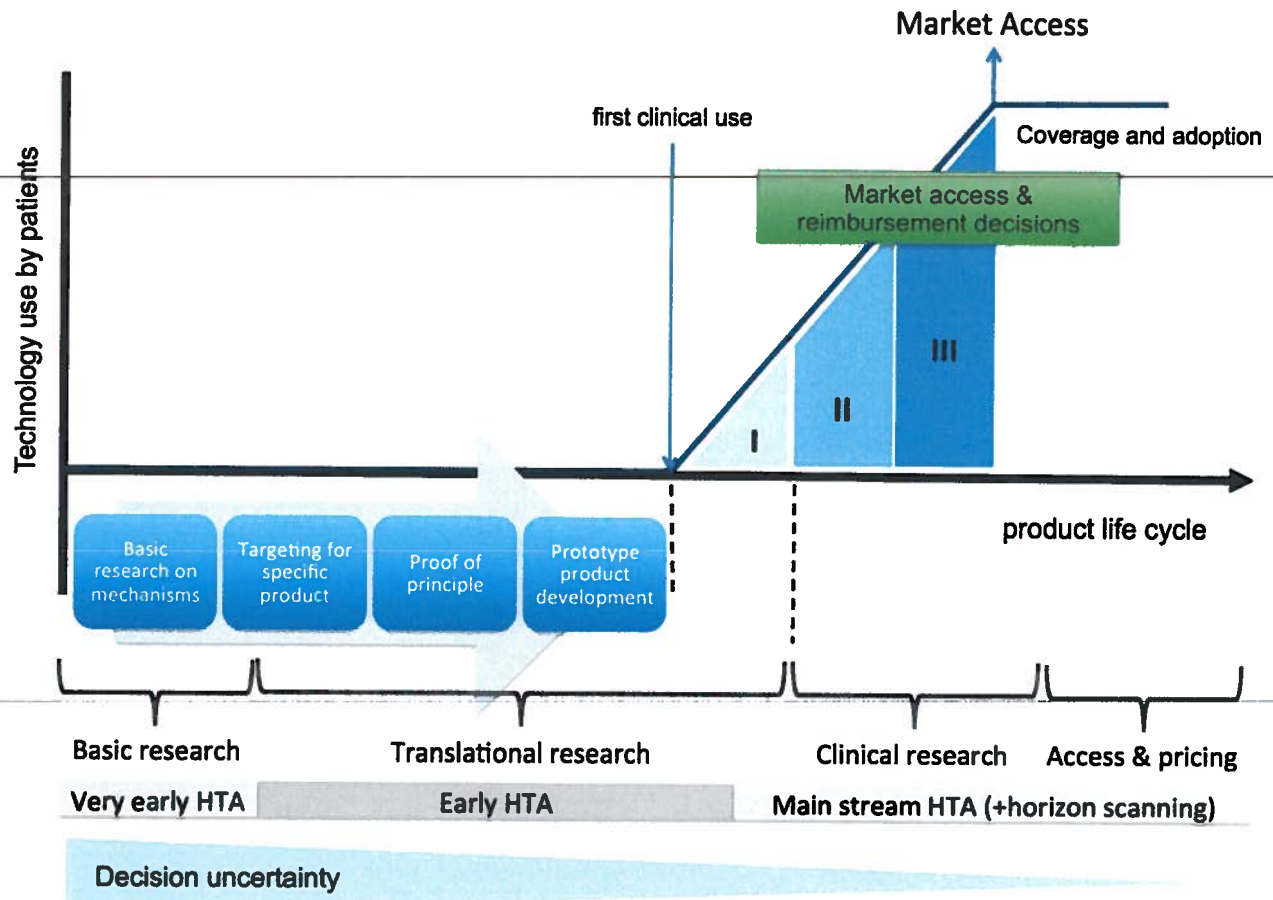
Decision uncertainty

Ijzerman & Steuten, Appl.Health Econ & Health Pol.2011



Decision uncertainty

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Ijzerman & Steuten, Appl. Health Econ & Health Pol. 2011

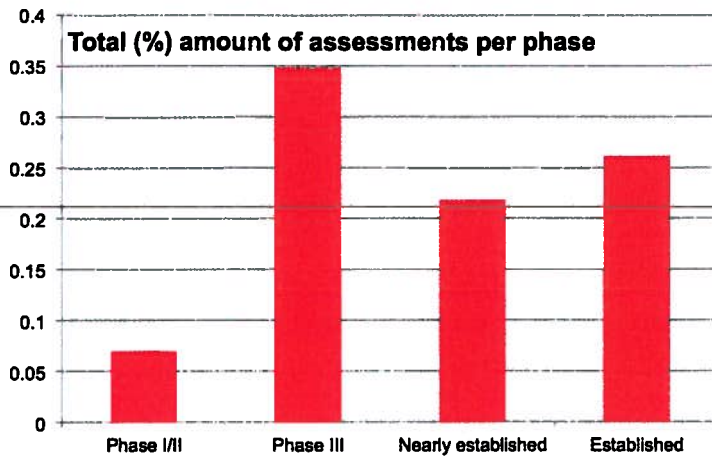
Early modeling to inform health policy

Iterative use of economic evaluation

Essay

Table Four stages of economic evaluation

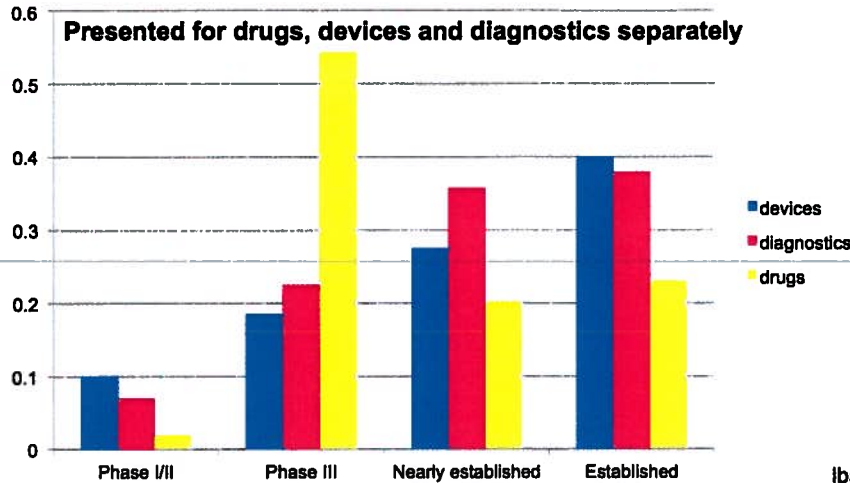
Stage	Typical level of diffusion	Dominant clinical research strategy	Types of economic analysis
I: Early developmental	Small number of innovators	Small, uncontrolled case series	Systematic review of evidence relating to cost and effectiveness of existing practice; use of informal clinical opinion to assess the potential value of the new technology
II: Maturing innovation	A few specialist centres	Case series and small RCTs	Modelling studies using data from existing clinical studies; pilot studies of economic data collection alongside controlled trials
III: Close to widespread diffusion	A larger number of centres (specialist and other)	Large RCTs	Economic data collection alongside RCTs; refined modelling studies using systematic overviews of clinical data
IV: Moving into practice	Generalised adoption	Pragmatically designed controlled trials; observational studies of the technology in normal use	Economic data collection alongside pragmatic trials; modelling studies to generalise results to other settings, or to extrapolate to the long term



Source:
Euroscan database

N=1085 cases

14 HTA agencies



Ibargoyen et al, Int. J. TA Healthcare 2009

Disability and Rehabilitation, May 2006; 28(10): 645–651



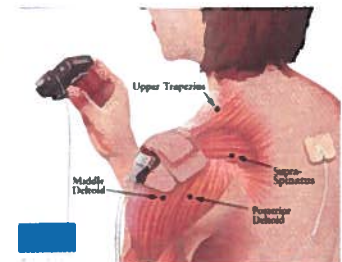
RESEARCH PAPER

A preliminary economic evaluation of percutaneous neuromuscular electrical stimulation in the treatment of hemiplegic shoulder pain

JANINE A. VAN TIL^{1,3}, GERBERT J. RENZENBRINK^{1,2}, KARIN GROOTHUIS¹ & MAARTEN J. IJZERMAN^{1,3}

¹Roessingh Research and Development, Enschede, The Netherlands, ²Rehabilitation Center 'Het Roessingh', Enschede, The Netherlands, and ³Biomedical Signals and Systems Group, University of Twente, Enschede, The Netherlands

Accepted July 2005



Abstract

Objective. The objective of this study was to compare the cost-effectiveness of various treatment modalities for hemiplegic shoulder pain.

Design. A stage II economic evaluation.

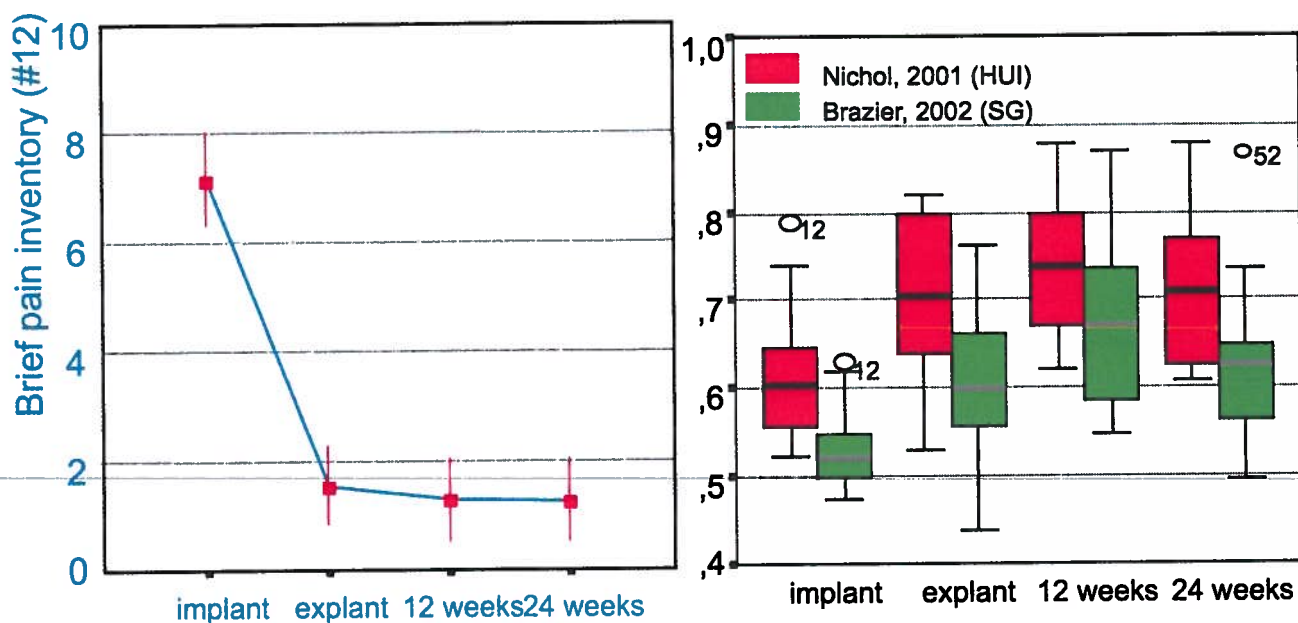
Main outcome measures. Incremental cost effectiveness ratio of P-NMES, compared to slings and anti-inflammatory injections.

Results. The incremental cost effectiveness ratio (ICER) of p-NMES, compared to anti-inflammatory injections is €6,061 (± 3,285). The incremental cost of the first quality-adjusted life year after implantation of the P-NMES device compared to anti-inflammatory injections is €33,007 (± 5,434). This decreases to ≈ €7,000 after 5 years, and to ≈ €5,000 after 10 survival years.

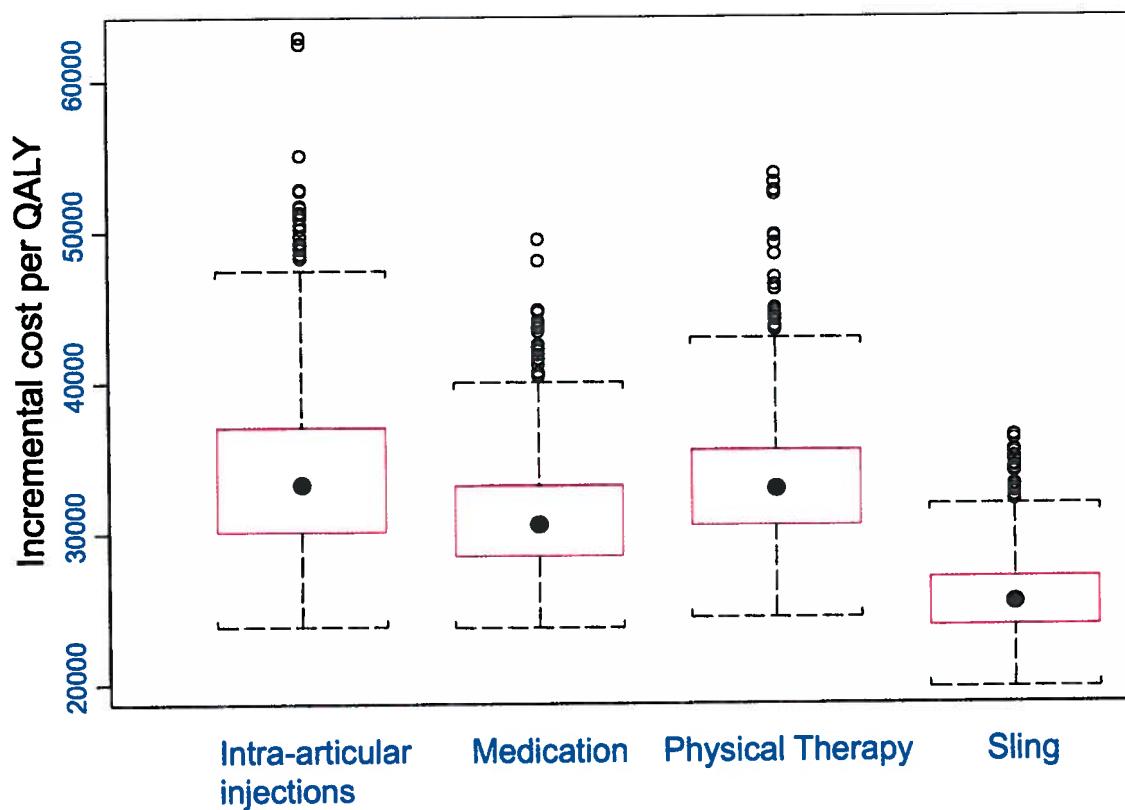
Conclusion. In this early evaluation, P-NMES seems to be cost-effective according to known guidelines. Treatment with P-NMES is recommended for patients with chronic HSP.

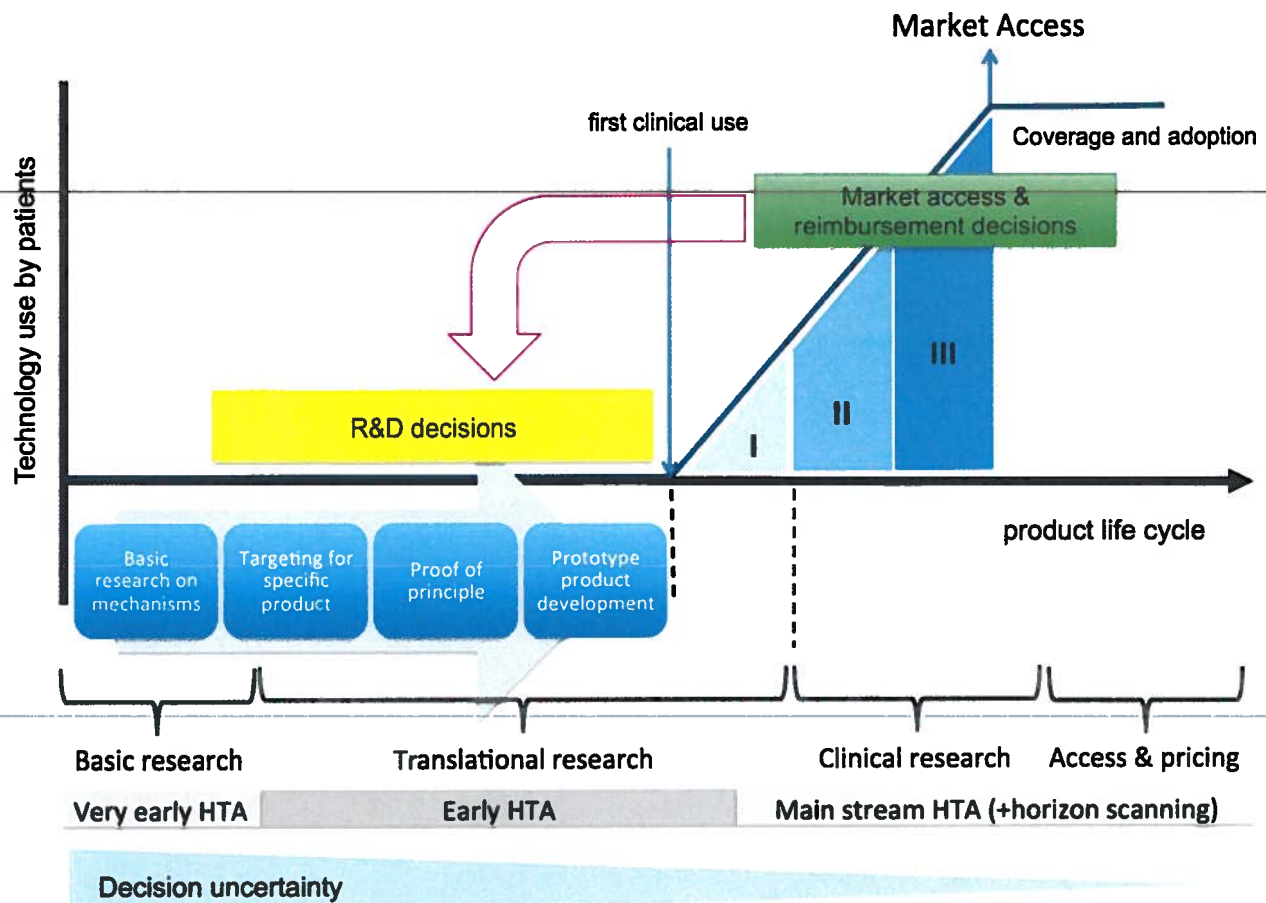
Keywords: Electrical stimulation, hemiplegic shoulder pain, stroke, economic evaluation

Utility estimates from phase I, uncontrolled trial



Simulated Incremental Cost-Effectiveness Ratio (1 year)



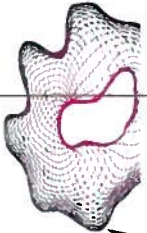


Ijzerman & Steuten, Appl. Health Econ & Health Pol. 2011

Early modeling for R&D and commercial decisions

Table 1. Similarities and Differences between Classical HTA and Early HTA

	Classical HTA	Early HTA
Aim	Assess safety, effectiveness, and cost-effectiveness profiles of a new technology	Assess (likely) safety, effectiveness, and cost-effectiveness profiles of a new technology
Decision support	Decision support for regulators, payers, and patients about <i>market clearance, payment, and usage of a technology</i>	Decision-support for manufacturers and investors about <i>design and management of a technology, as well as regulatory and reimbursement strategy</i>
Available evidence	Usually evidence from clinical studies performed with the new technology	Evidence from early bench and animal testing, early clinical experience, and from previous generations of the technology
Influence on technology performance	Limited or no influence on clinical performance of a new technology	Potentially significant influence on (future) clinical performance of a new technology

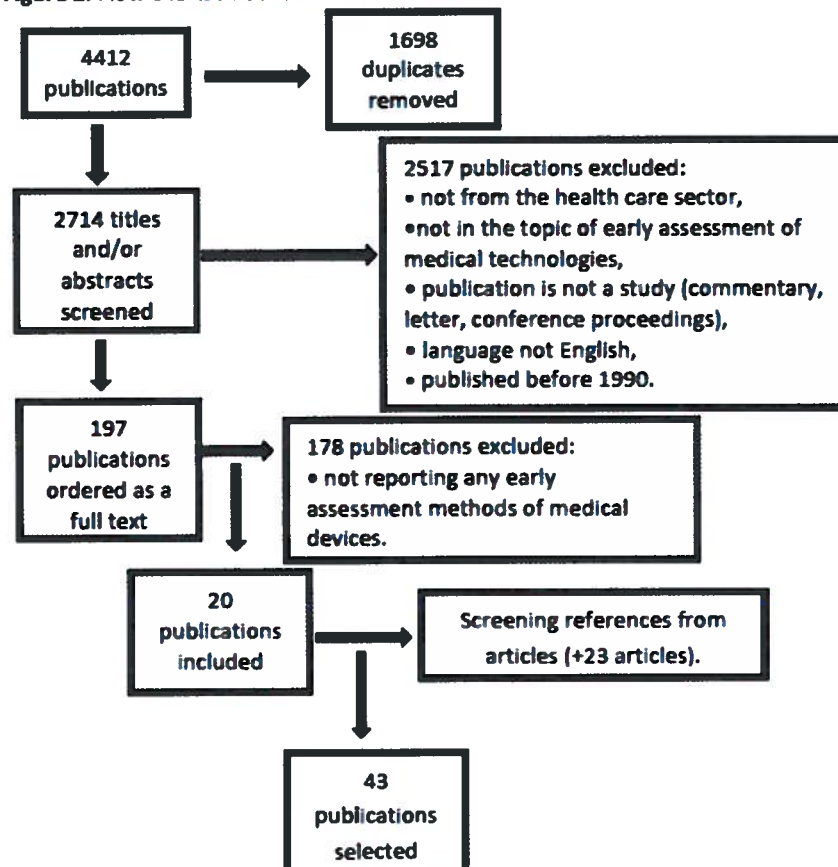


Scoping review on methods in early assessment

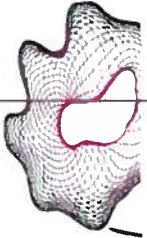
- Which methods are used to determine value in early development stages?
- Databases: Pubmed, Scopus, Science Direct and cochrane databases
- Key-words:
 - *Generic*: early HTA, device, innovation, technology assessment, decision model, industrial engineering, healthcare
 - *Methods*: horizon scanning, clinical trial simulation, conjoint analysis, multi-criteria decision analysis, health impact model

Markiewicz *et al*, 2013 submitted

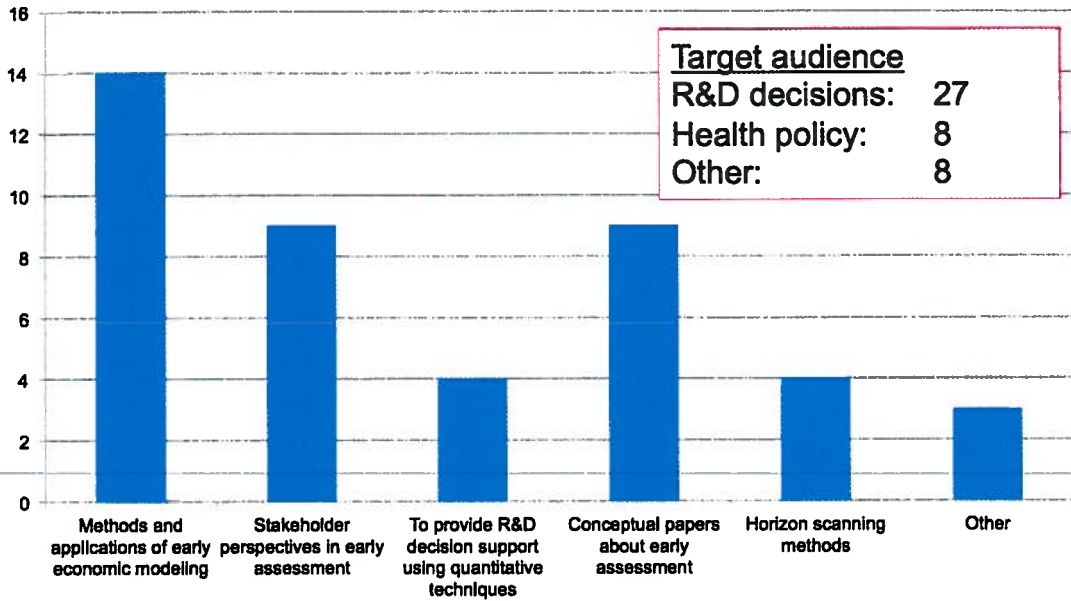
Figure 2. Flow chart: selection of the literature.



Markiewicz *et al*, 2013 submitted

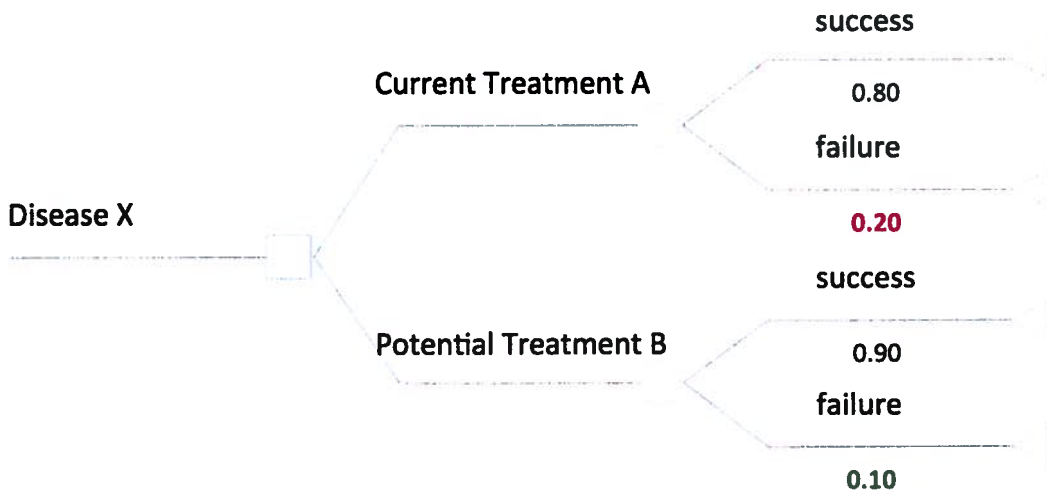


An overview of 43 papers



Markiewicz *et al*, 2013 submitted

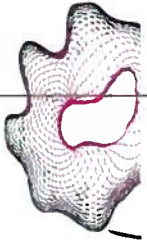
Early Health Economic Modeling: A simple starting point



Key questions in this example:

- What is the incidence (X, σ) of failure in real life?
- What is the QALY loss (X, σ) of failure/disease?
- How is failure managed in real life
- what is the cost (X, σ) of failure?

Anticipated in TPP
(target product
profile)

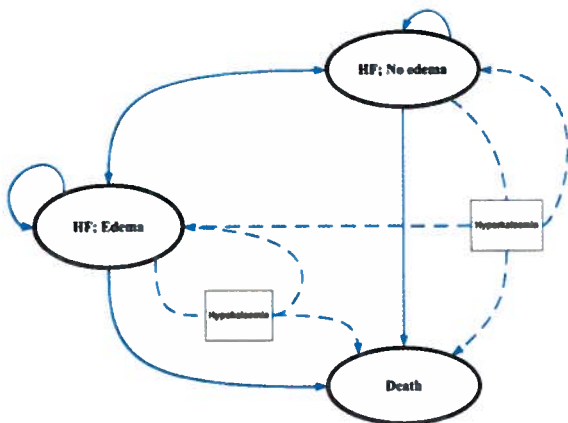


Early health economic models

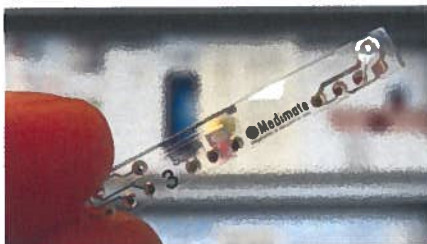
- **Deterministic sensitivity analysis**
 - What effect size would be needed to demonstrate value
 - What range of prices is acceptable
 - What model parameters drive value
 - What priorities for evidence generation
- **Uncertainty in early models**
 - Parameter uncertainty, possible to quantify using VOI
 - Decision maker uncertainty, i.e. probability of approval
 - What criteria are used for decision making ?
 - Market uncertainty: expected volume / share
- **Some uncertainty can be solved if comparator is known, yet this is difficult to determine early stage**

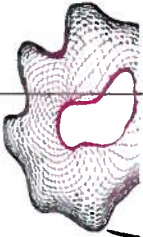
Early Health Economic Modeling

Bayesian model of Lab-on-Chip potassium monitoring



- State transition model
- Transition probabilities obtained from literature
- Costs of each health state obtained from literature
- Estimated benefit of monitoring in terms of change in transition probability
- 20,000 simulations

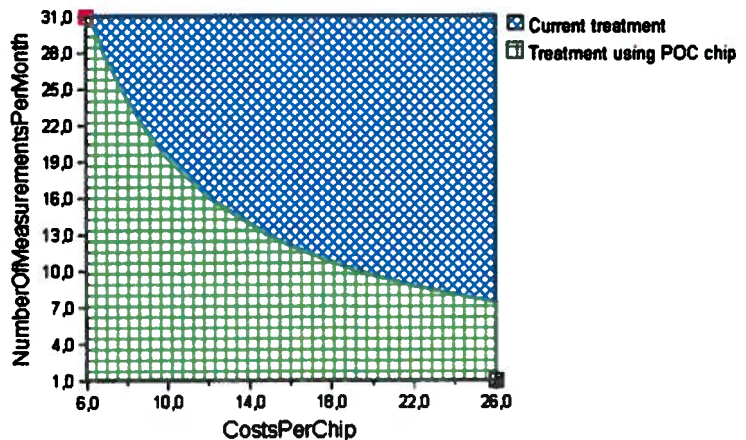
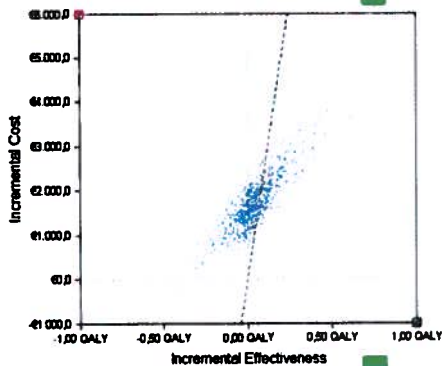




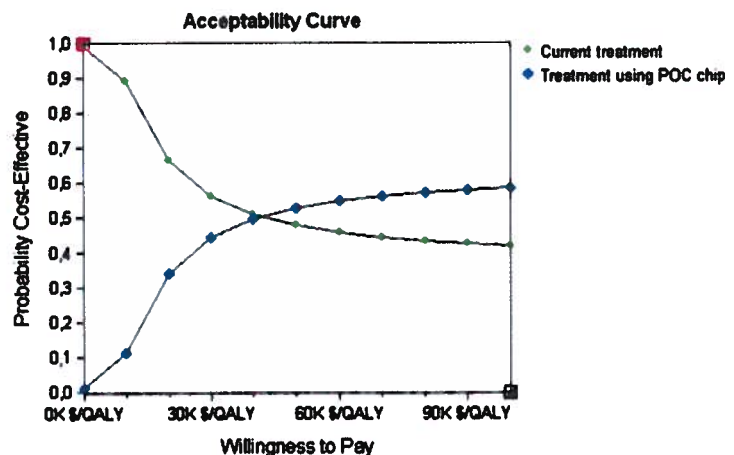
Cost-effectiveness gap analysis

- Headroom for improvement, given expected benefits
- Requires
 - Willingness to pay for a QALY (e.g. 30K€/QALY)
 - Incremental QALY gain (estimated)
 - Expected duration of the QALY gain
- If $ICER = \Delta C / \Delta U$ then, $\Delta C = ICER * \Delta U$ or $\Delta C = WTP * \Delta U$
- Case: POCT for potassium monitoring (vd Wetering, 2011)
 - Cost of severe potassium imbalance: 752 €
 - Utility decrement of potassium imbalance: 0.04/year (low probability)
 - CE-gap: $30,000 * 5 * 0.04 + 752 = 6752€$
 - Offers good prospects: unit cost of POCT not likely to exceed 6752€

Deterministic sensitivity analysis to estimate model sensitivity for uncertain priors (e.g. pricing)

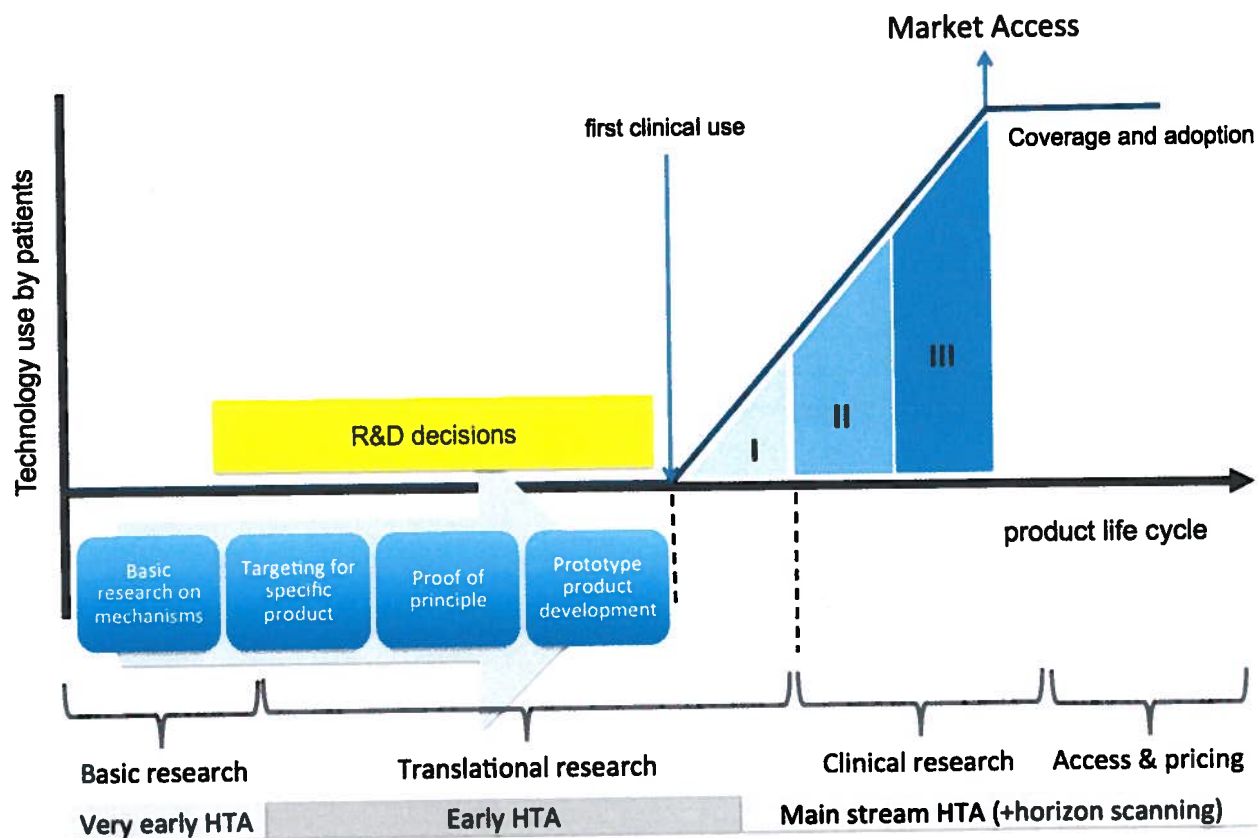


Value of information to determine value of additional research to reduce decision uncertainty
 EVPI: 432 Meuro
 (threshold 25KEuro/QALY)

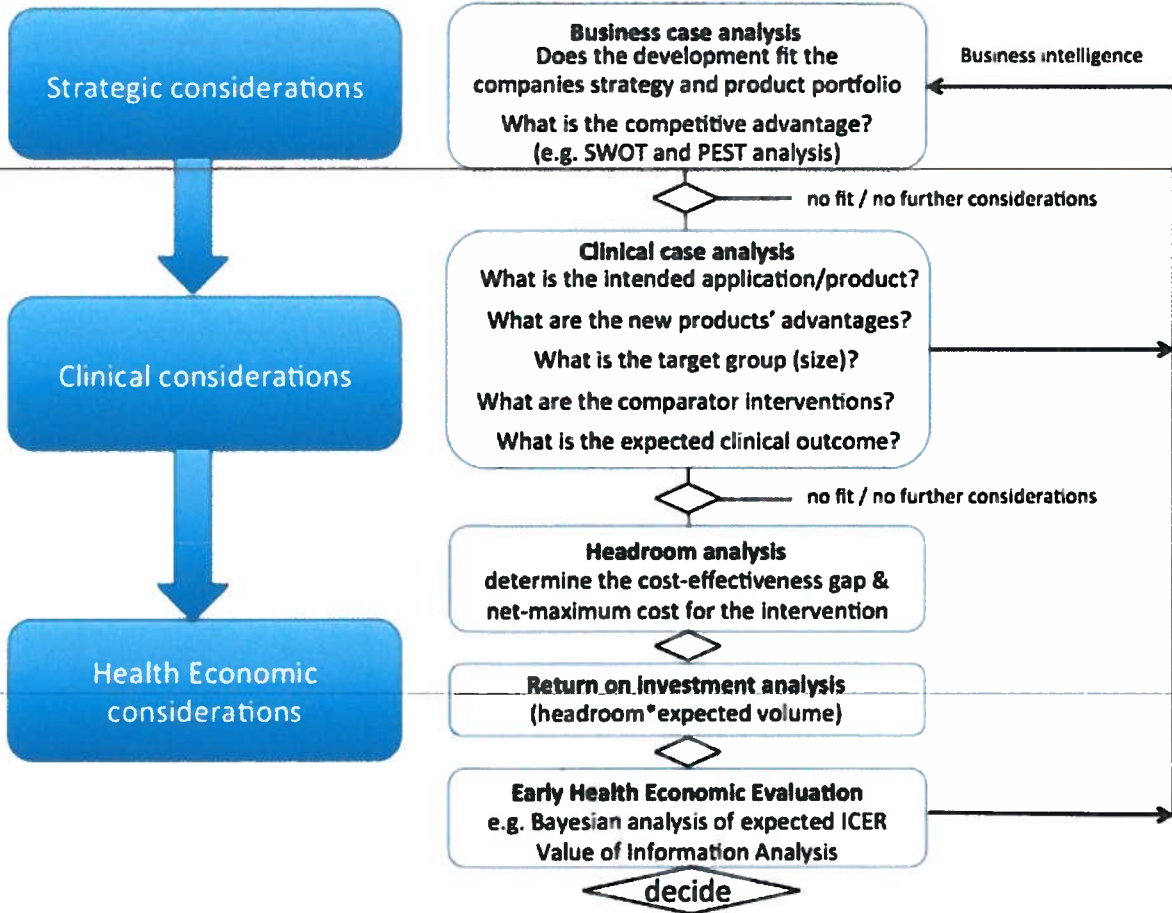


Uncertainty in (early) models

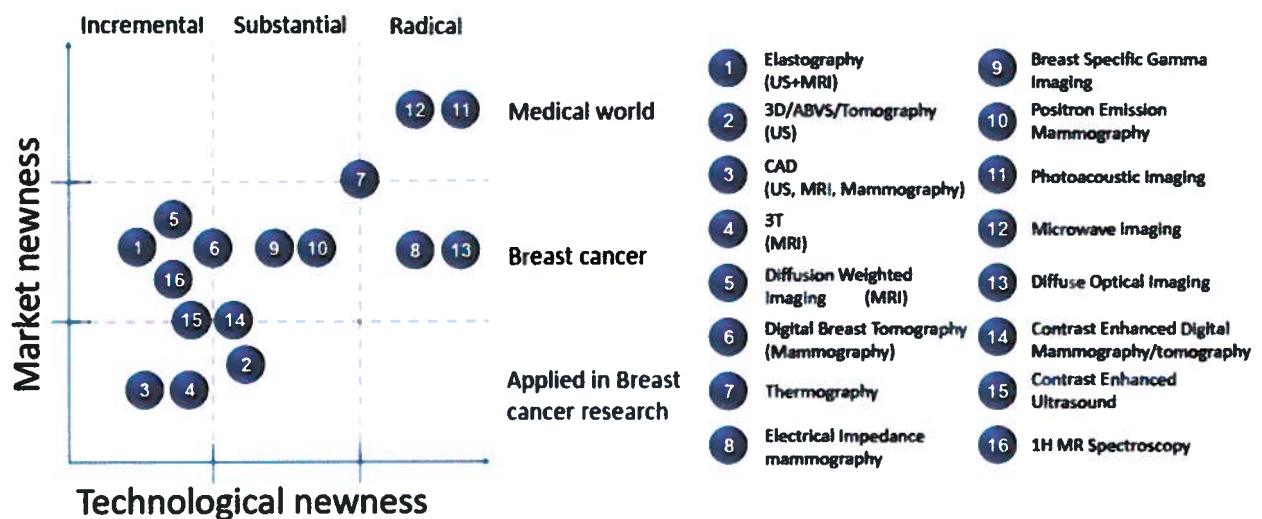
	IN THE MODEL DESIGN	IN THE MODEL ANALYSIS
Structural Uncertainty (model simplifications)	<ul style="list-style-type: none"> Scenario drafting Focus groups MCDA methods 	---
Methodological Uncertainty	Modeling guidelines (eg. Gold and Ramsey)	
Parameter uncertainty	<ul style="list-style-type: none"> Clinical trials Meta analysis Indirect treatment comparison (ITC) Expert elicitation techniques for estimating priors 	<ul style="list-style-type: none"> Deterministic Sensitivity Analysis Probabilistic Sensitivity Analysis Value of Information analysis



Decision uncertainty



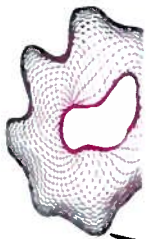
Developments in medical imaging for breast cancer



Technical requirements and uncertainty

		Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
Value:		460000	391000	139100	-175800	-295800
Uncertainties:	Estimated probability of success					
1 Very high diagnostic value	29%	1	1			
2 High diagnostic value	50%	1	1	1	1	1
3 Implementation of HBM at other positions	42%	1				
4 Detection algorithm	85%	1	1	1		
5 Acceptation among patients	82%	1	1	1	1	1
6 Technical uncertainties	98%	1	1	1	1	
Probability per scenario:		8,40%	11,40%	14,30%	6,00%	0,80%
Contribution to option value:		38640	44574	19891,3	0	0
Option value:		103105,3				

Breteleer, Roorda, van Putten, Ijzerman, 2013



Some thoughts...

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- Commercial, R&D and health economic models are typically used in isolation from each other and most people only refer to one specific type of models if asked about early modeling
- Too often, early models are referred to as models that precede the decision they inform. Yet, they are not necessarily started early.
- It may be useful to use health economic evidence in earlier stages of R&D