1066

HOW TO EVALUATE ? HOW TO FINANCE ? INNOVATION IN AUDITORY IMPLANT

- B. FRAYSSE

IFOS WORLD MASTER COURSE ON HEARING REHABILITATION

DUBAI

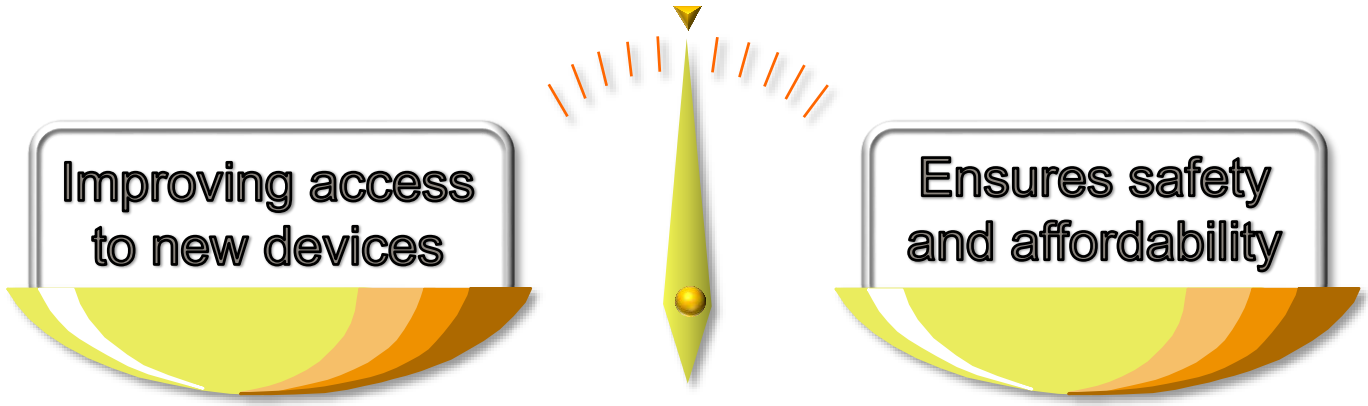
March 2019, 28-29-30

MEDICAL DEVICE / DRUGS

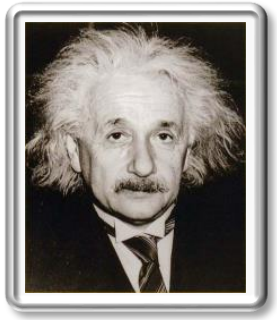
Different from drug « *Device is not drug* »

- Rapid changes in technology
- Small target population

→ Methodological difficulties in evaluation



CONCEPTION



Competent authorities
Act as advisory board

INVESTIGATIONAL PHASE

Regulated by institutional board

Potential indication
Expected effectiveness
Safety

LICENCING DECISION

FDA

- PMA
- 510(K)

NOTIFIED BODY

CE

REIMBURSEMENT DECISION

- Private insurance
- National Social Security
  (Each country)

HAS

NICE

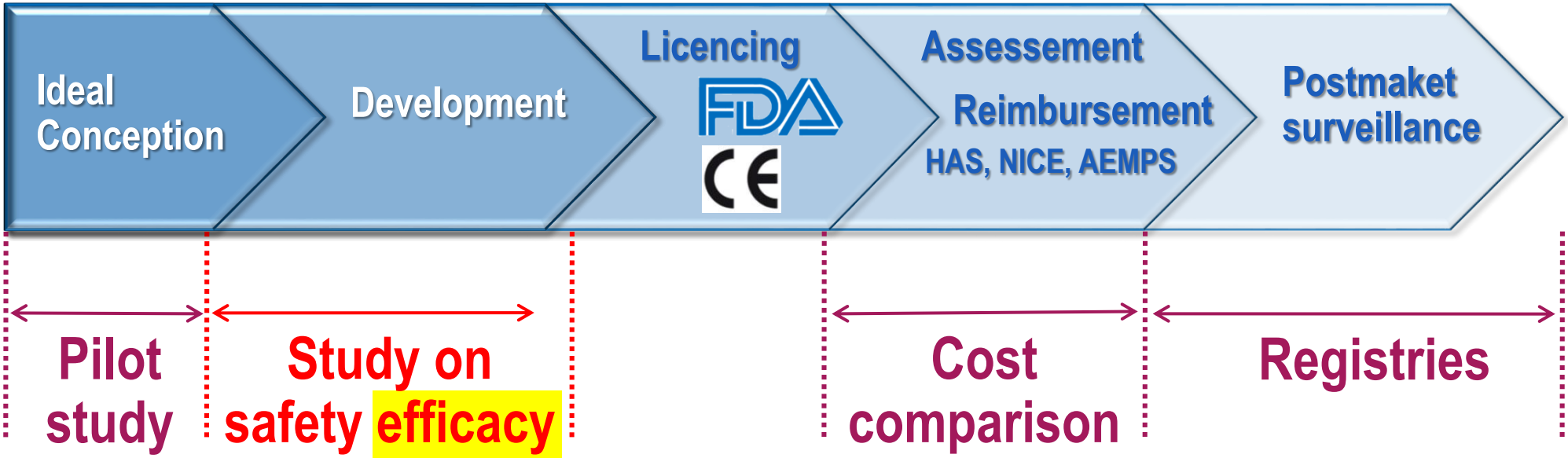
(EUROPE)

DEVELOPMENT OF AUDITORY IMPLANT

THE LANCET

The Lancet – September 2009 – Vol 374, 1105-12
No surgical innovation without evaluation : the IDEAL recommandations
Peter McColloch et all

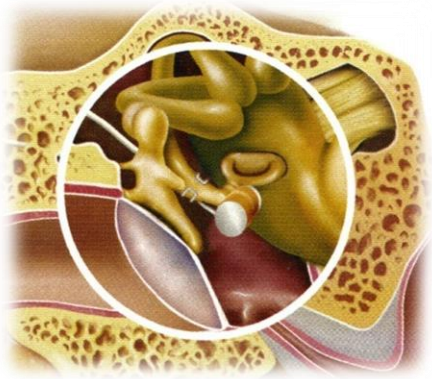
Idea **D**evelopment **E**valuation **A**ssessement **L**ong term follow up



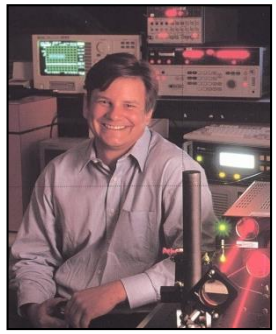
Need of coherence with the endpoint and adequate timing

TIMING IN THE DEVELOPMENT PHASE IS ESSENTIAL

- Too soon may be questionable because an early adoption of innovation may not be so effective due to a need of learning curve
- Too late « defensive strategy » emphasizes on cost containment can lead to higher price delayed technological adoption and widespread acceptance without evidence



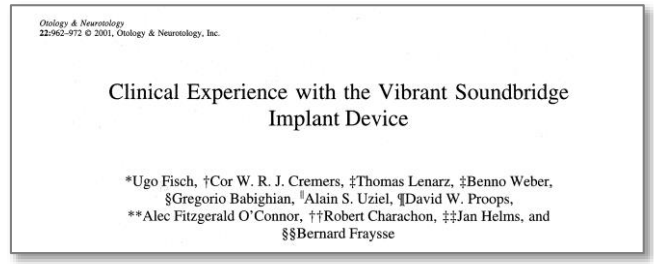
DEVELOPMENT OF MIDDLE EAR IMPLANT



G. BALL **1990**

« To set up the problem of MEI into a linear programming model »

1996 : European and US trial



Otology & Neurotology
22:962–972 © 2001, Otology & Neurotology, Inc.

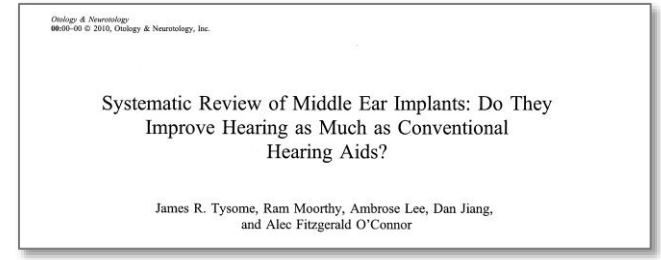
Clinical Experience with the Vibrant Soundbridge Implant Device

*Ugo Fisch, †Cor W. R. J. Cremers, ‡Thomas Lenarz, ‡Benno Weber, §Gregorio Babighian, ¶Alain S. Uziel, ¶David W. Proops, **Alec Fitzgerald O'Connor, ††Robert Charachon, ‡‡Jan Helms, and §§Bernard Fraysse

1998 : CE Mark

644 articles

2010



Otology & Neurotology
00:00–00 © 2010, Otology & Neurotology, Inc.

Systematic Review of Middle Ear Implants: Do They Improve Hearing as Much as Conventional Hearing Aids?

James R. Tysome, Ram Moorthy, Ambrose Lee, Dan Jiang, and Alec Fitzgerald O'Connor

17 met

Criteria of outcomes measures

Compare with HA

Level 2b

2015

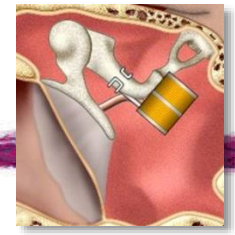
HAS

SA suffisant

CEPS

- Target population 170
- Size effect vs HA ASA IV vs BAHA

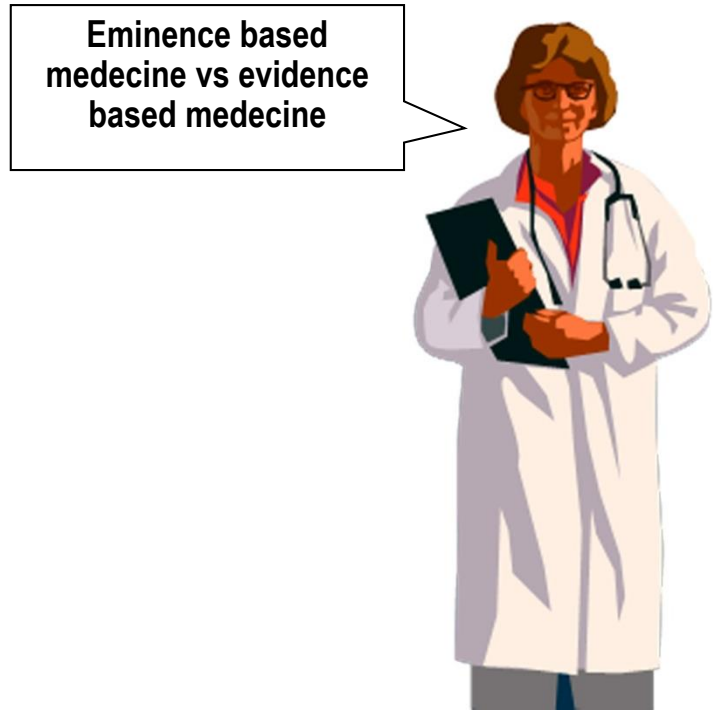
COMMENTS ON MEI



- Low level of evidence from the literature due to :
  - Eligible population not well defined
  - No pertinent main criteria of judgement
  - No cost comparison assessement with the standard of care *(hearing aid)*
  - No long term study by registry

HOW AGENCIES GIVES ADVICE FOR REIMBURSEMENT

- Level of evidence from the literature
- Multidisciplinary expert advice
- Companies data
- Commitee members *(HAS, NICE)*
  - Pertinence of the main criteria
  - Size of effects vs standard of care
  - Bonus for rupture in innovation



GOLD STANDARD IN THE EVALUATION

RCT

Double blind, randomized controlled trial is the «Gold Standard»

❶ **Randomization :** avoid confounding bias

❷ **Double blind :** improves quality of the measures (especially for subjective outcomes)

❸ **Control :** a new device *versus* a standard of care

But there are methodological difficulties with medical devices

➔ Alternative to randomization

ALTERNATIVE TO RANDOMIZATION

THE LANCET

Volume 353 · April 1999 www.thelancet.com

There are numerous articles showing how well designed observational studies and exhaustive registry may have better value than impratically randomized study

N Engl J Med 2000;342:1998

RANDOMIZED, CONTROLLED TRIALS, OBSERVATIONAL STUDIES, AND THE HIERARCHY OF RESEARCH DESIGNS

JOHN CONCATO, M.D., M.P.H., NIRAV SHAH, M.D., M.P.H., AND RALPH I. HORWITZ, M.D.

THE LANCET

Reflections on randomized controlled trials in surgery

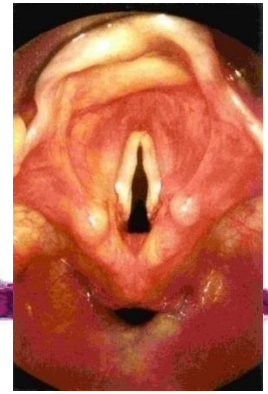
Michael Baum

- Center based randomization
- Goal Attainment Scaling *(GAS)*
- Registries

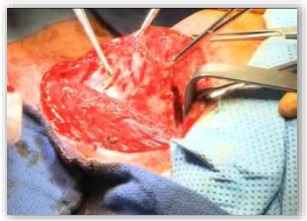
HAS

www.has-sante.fr

RANDOMIZATION BY CENTER



- Need for long term results and medico economic study



GETTEC Prospective randomized

Centers without robot
Conventional surgery

Centers with robot

- Advantage : Better acceptance
- Disadvantages : Difficulty to know if the superiority is due to the technique or the surgeon

Clinical Rehabilitation 2009; **23**: 362–370

Goal attainment scaling (GAS) in rehabilitation: a practical guide

Lynne Turner-Stokes Kings college London, School of Medicine, Regional Rehabilitation Unit, Northwick Park Hospital, Harrow, UK

Received 5th November 2008; manuscript accepted 7th November 2008.

- There are generic method taking into account the patient's goal and physician ability to predict outcomes this method gives a single numeric score
- T Score : Score of expected outcomes x relative weight

$$= 50 + \frac{10\Sigma(W_i X_i)}{\sqrt{((1-\rho)\Sigma W_i^2 + \rho(\Sigma W_i^2))}}$$

Goal	Reducing pain	Ease to dress	Able to drive
Baseline score	0	0	0
Weight	6	4	2
Outcolmes Score	+2	+2	+2

REGISTRIES

Why do we need registries ?

❶ Respect of medical indications and guidelines

→ Decision making

❷ Efficacy in real life that reflects different types of practice

→ large cohorte

❸ Safety and complications comparison between centers

→ adverse events

Independant, representative and exaustive

5 583 CI PATIENTS INCLUDED → 2015

2012 - 2015

	2012	2013	2014	2015
Exhaustivity	97%	94%	93%	87%
Off label in adult	4.7%	13.6%	21.2%	9.6%
Off label in children	2%	3.4%	5.3%	3.1%
Complication rate	8.3%	4%	2%	1.6%

VARIABILITY OF AGENCIES RECOMMENDATIONS

Example

- NICE and HAS 2007 on the same data give different recommandation on bilateral cochlear implant in children :
  1. The difficulty to identify the long term impact on education
  2. The methodological difficulties and randomization in children

  The process of decision in the different agencies :
  - HAS ▶ Purely scientific
  - NICE ▶ Based on incremental cost effectiveness : medico economic

- HAS New guideline (2011)

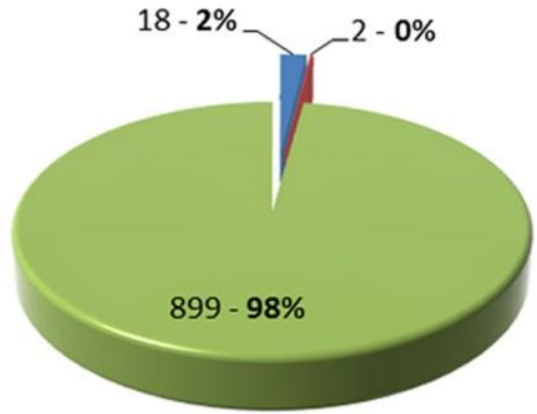
New CI recipients in UK = 1 404

New CI recipients in FRANCE = 1 394

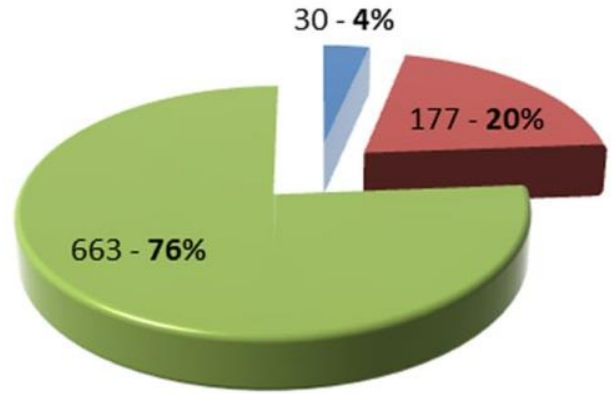
April 2016 – April 2017 – Chris RAINE

popsicube 2017

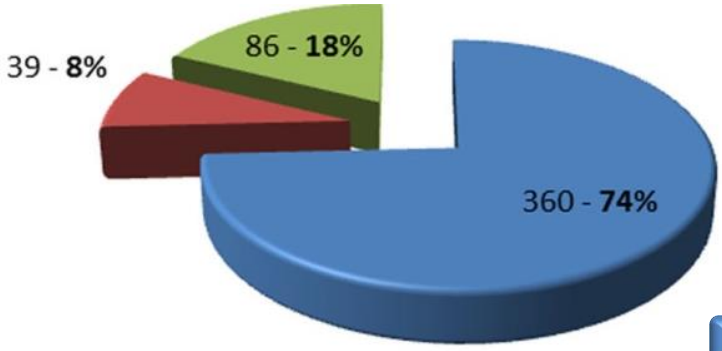
UK CI Adults – N= 919



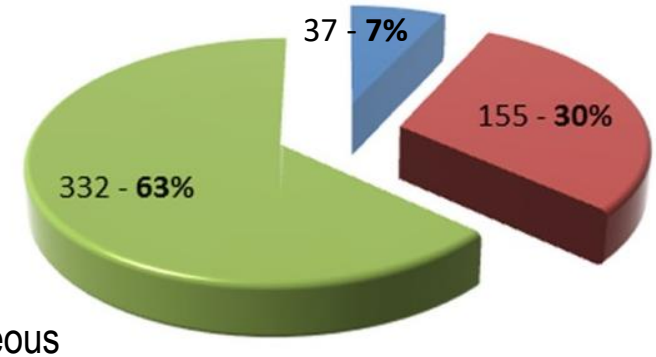
FRANCE CI Adults – N= 870



UK CI Children – N= 485



FRANCE CI Children – N= 524



Bilateral Simultaneous
Bilateral Sequential
Unilateral

NICE

National Institute for Health and Clinical Excellence

- The goal of NICE in 1999 is to provide guidance in an academic way reviewing cost effectiveness !

  Incremental cost effectiveness (ICER)

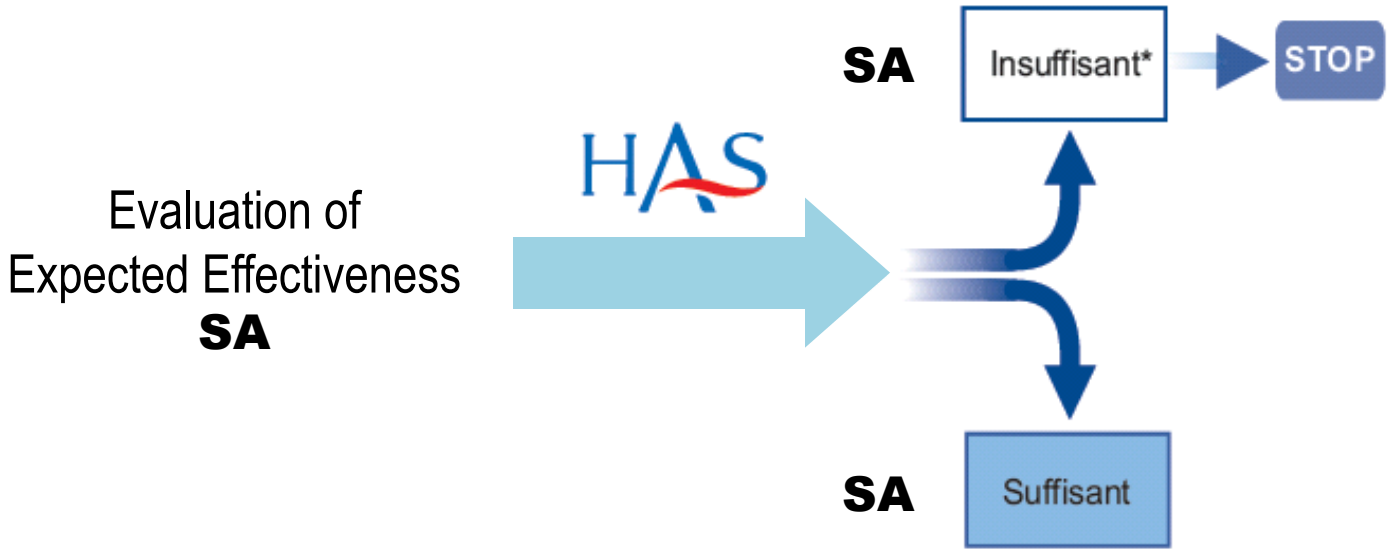
  - The **ICER** expressed as the cost per QALY gained =

$$\frac{\text{Cost of intervention CI} - \text{Cost of intervention HA}}{\text{No. of QALYs produced by CI} - \text{No. of QALYs produced by HA}}$$

HAS

Haute Autorité de Santé

- The French HAUTE AUTORITE DE SANTE is an independent scientific public organization formed in January 2005. The goal is to evaluate reimbursement submissions on a scientific basis
- Evaluation committee CNEDIMTS



I	Amélioration majeure
II	Amélioration importante
III	Amélioration modérée
IV	Amélioration mineure
V	Absence d'amélioration

EVALUATION SYNTHESIS

- We can used alternative to randomization trials, **but we have to justify why**
- **Some methodological principal are always true**
  - **Select a relevant population** close to the target population
  - **Clearly define the main criteria of judgement**
  - **Have a relevant control standard of care**
  - Calculate the **appropriate sample size**

HOW TO FINANCE INNOVATION ?

Incremental innovation

- Adding a new feature to an existing product

Substantial innovation

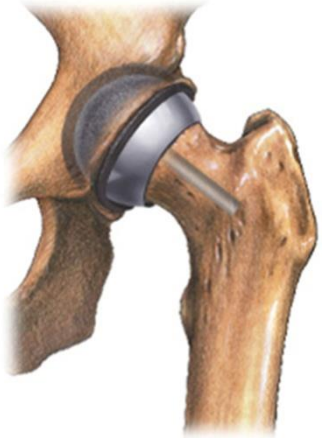
- New generation of device

Radical revolutionary concept

- Disruptive innovation

INCREMENTAL INNOVATION

▲ Due to the absence of value companies used the substantial equivalence process for reimbursement

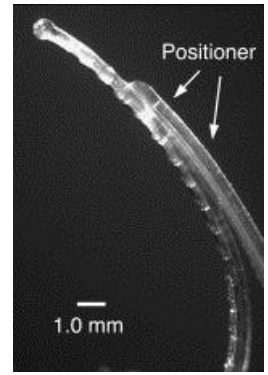


Metal-On-Metal Hip Implants

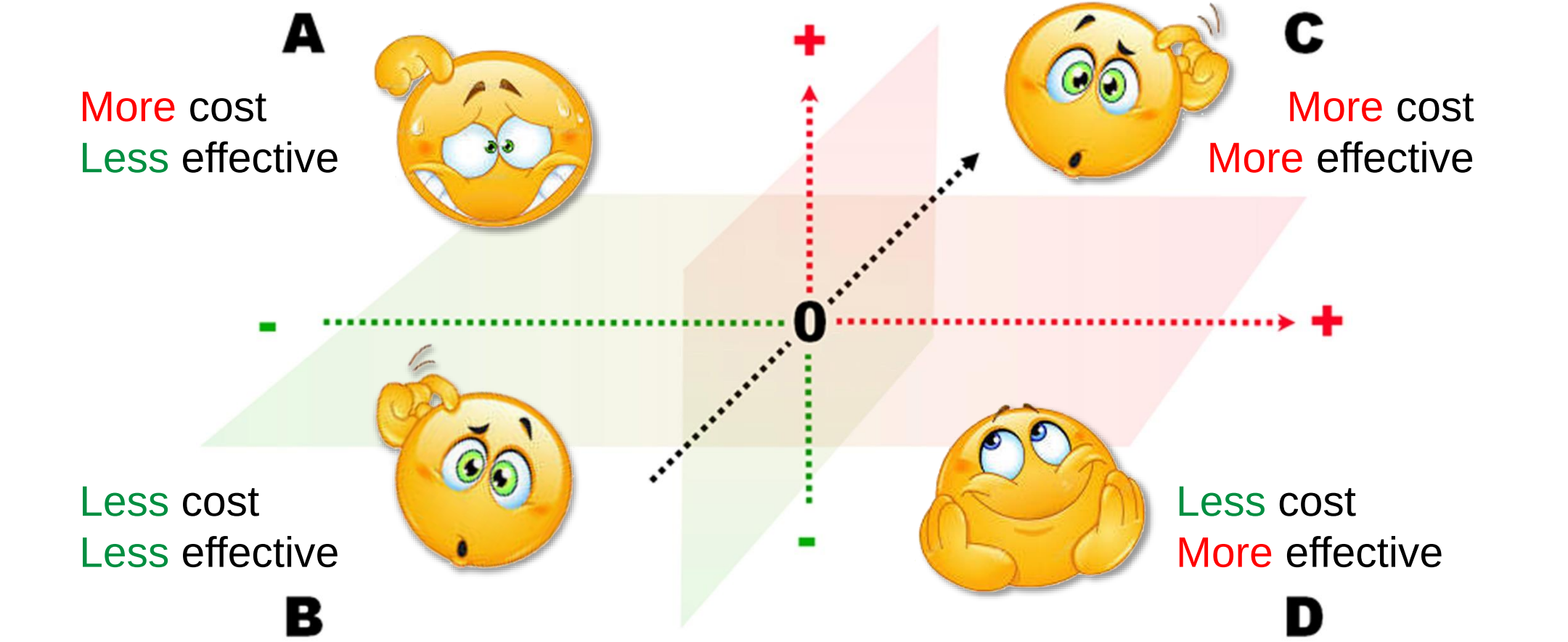
◀ Revision rate 49% at 6 years vs 12% with other devices

CI with positioner

Meningitis risk of cochlear implant with positioner ▶



SUBSTANTIAL INNOVATION EXTENDING INDICATION



SIZE EFFECT IN MYOCARDIAL INFARCTION

Treatment	Survival	Cost
Rest (1970)	85%	$0
Streptokinase (1980)	93%	$320
STENT (1990)	94%	$2,750

HOW MUCH SHOULD BE THE SIZE EFFECT TO FINANCE CI IN UNILATERAL HEARING LOSS ?

- The standard of care in unilateral hearing loss is controlateral rerouting of signal with :
  - Hearing aid
  - Bone conduction

- Pr. MARX is conducting a medicoeconomic study on 150 patients to compare standard rerouting vs CI
  - Effect size clinically relevant should be > 30% (HRQol)

Audiol Neurotol 2015;20 (suppl 1):79-86
DOI: 10.1159/000380753

Improving Health-Related Quality of Life in Single-Sided Deafness : A Systematic Review and Meta-Analysis

Pádraig T. Kitterick, Laura Lucas, Sandra N. Smith

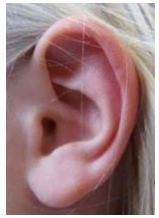
CI	Mean	0.97
Bone Conduction	Mean	0.55
CROS	Mean	0.27

MULTI CENTRIC MEDICO ECONOMIC STUDY

N : 126/150

Inclusion
CROS: 3 weeks trial
Bone conduction : 3 weeks trial

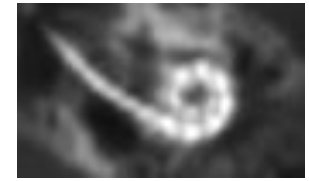
Observation **N : 9**



CROS **N : 63**

Bone cond. **N : 12**

CI **N : 42**



Randomization

Comparison

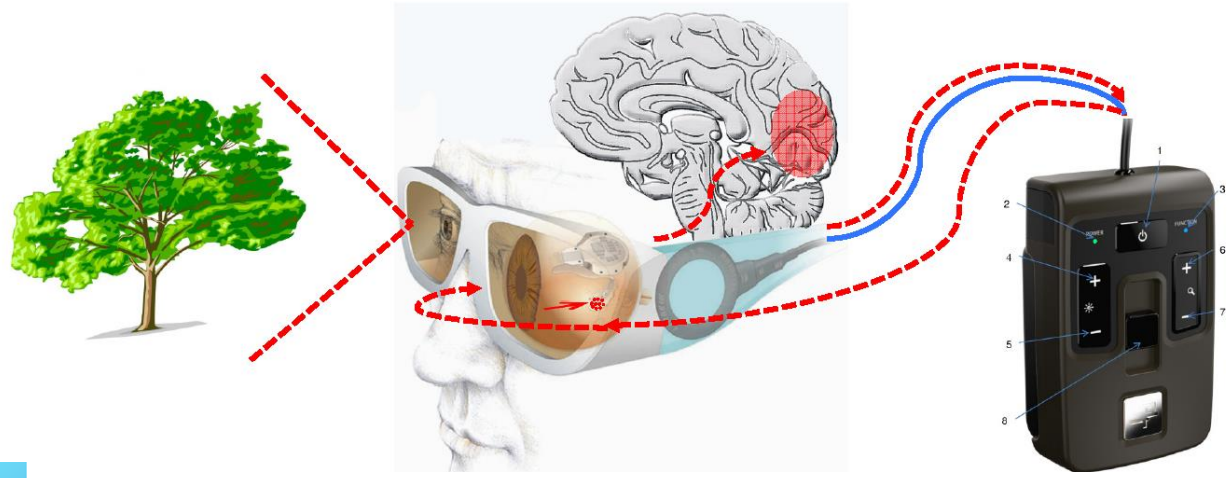
Objectives

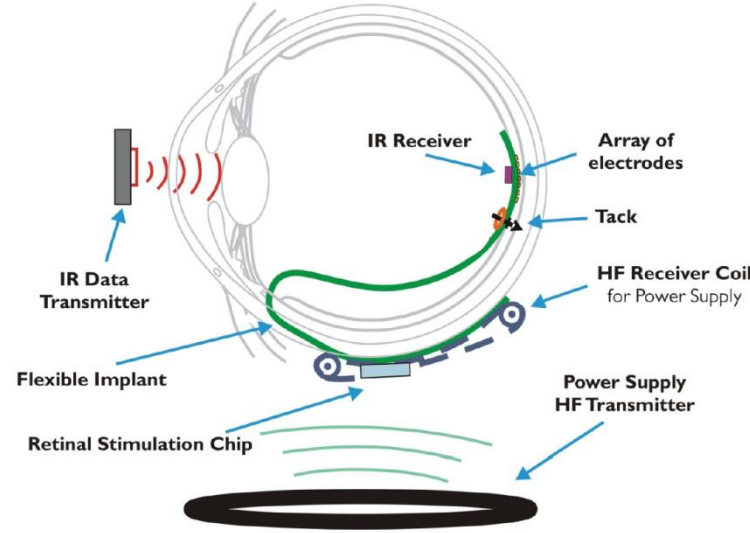
Describe the cost-utility ratio of each treatment
Compare the two randomized groups (Immediate CI vs initial observation).

HOW TO FINANCE DISRUPTIVE INNOVATION ?
NEW DEVICE OR NEW REHABILITATION ?

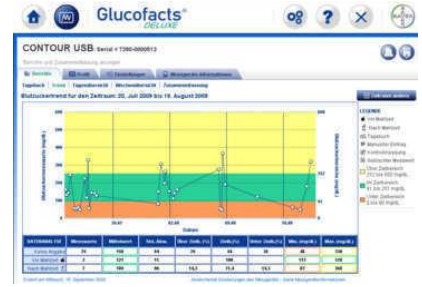
1 Retinal Implant

Pixium vision





2 New rehabilitation model



DISRUPTIVE INNOVATION / CONCEPT OF CONDITIONAL APPROVAL

- When a radical innovative device or new rehabilitation model is developped it is difficult to estimate at the early phase
  - The long term efficacy
  - The cost utility

FORFAIT INNOVATION

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Alternative funding mechanism « as coverage with evidence development » for a limited period

  - Intermediate criteria of judgement
  - Vigilant postmarket surveillance

POSSIBLE INITIATIVE / FUTURE ACTION

- Create a consertium of all stakeholders
- Develop an European Registry – **Ear-One Project**
- Promote robust scientific evidence when randomization is not possible
- Develop specific paradigms of evaluation for the new model of rehabilitation

- Companies

- Agencies

- Multidisciplinary scientific board

- Patient association

DEVELOPMENT OF A EUROPEAN REGISTRY CALL H2020

Ear-One Project

Commission européenne

Hôpitaux de Toulouse

Centre Hospitalier Régional Universitaire de Lille

UNI FREIBURG

MHH

MONTPELLIER CHU CENTRE HOSPITALIER UNIVERSITAIRE

ATHENS STATE UNIVERSITY

UCL

Universidad de Navarra

University of Antwerp

NHS Guy's and St Thomas' NHS Foundation Trust

UNIVERSIDAD DE LAS PALMAS DE GRAN CANARIA

- Standardization of outcomes
- measures near realtime adverse event information
- Stratification and outcomes prediction
- Benchmark of medical, surgical and rehabilitation procedure
- Evaluation of socio economic differencies and geographic inequalities

PROMOTE ROBUST SCIENTIFIC EVIDENCE

- Propose specific paradigms when randomization is not possible
- Standardize main common criteria of judgment
  - Adaptative procedure (discrimination in noise)
  - Quality of life questionnaire
- Develop Goal Attainment Scaling (GAS) [PORMS]
- Alternative funding mechanism in case of disruptive innovation
  - Medical device
  - e-Health rehabilitation model

« The best way to predict the future is to create it »

Peter DRUCKER *(1909-2005)*

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D'ORL ET DE CHIRURGIE
DE LA FACE ET DU COU

Thank you for your attention