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

B. FRAYSSE

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

Improving access to new devices
Ensures safety and affordability
**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

**REIMBURSEMENT DECISION**

- Private insurance
  - AXA
- National Social Security
  - (Each country)
DEVELOPMENT OF AUDITORY IMPLANT

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

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

Clinical Experience with the Vibrant Soundbridge Implant Device

*Ugo Fisch, †Cee W. R. J. Cremer, ‡Thomas Lemer, †Benno Weber, †Gregorie Rabaylian, ‡Alan S. Urist, §David W. Proops,
**Alex Fitzgerald O’Conner, ††Robert Charach, ‡‡Ian Helms, and §§Bernard Pruysre

1998 : CE Mark

644 articles

2010

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

James R. Tyson, Sam Moore, Andrew Lee, Dan Jiang, and Alex Fitzgerald O’Conner

2015

SA suffisant

17 met
Criteria of outcomes measures
Compare with HA
Level 2b

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

HAS
Low level of evidence from the literature due to:

- Eligible population not well defined
- No pertinent main criteria of judgement
- No cost comparison assessment 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
- Committee members *(HAS, NICE)*
  - Pertinence of the main criteria
  - Size of effects vs standard of care
  - Bonus for rupture in innovation

Eminence based medicine vs evidence based medicine
Double blind, randomized controlled trial is the «Gold Standard»

1. **Randomization**: avoid confounding bias
2. **Double blind**: improves quality of the measures (especially for subjective outcomes)
3. **Control**: a new device *versus* a standard of care

But there are methodological difficulties with medical devices

→ Alternative to randomization
There are numerous articles showing how well designed observational studies and exhaustive registry may have better value than impractically randomized study.
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
There are generic methods 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 $\times$ relative weight

\[
T = 50 + \frac{10 \sum (W_i X_i)}{\sqrt{(1 - \rho) \sum W_i^2 + \rho(\sum W_i^2)}}
\]

<table>
<thead>
<tr>
<th>Goal</th>
<th>Reducing pain</th>
<th>Ease to dress</th>
<th>Able to drive</th>
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<tbody>
<tr>
<td>Baseline score</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Weight</td>
<td>6</td>
<td>4</td>
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<tr>
<td>Outcomes Score</td>
<td>+2</td>
<td>+2</td>
<td>+2</td>
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Why do we need registries?

1. Respect of medical indications and guidelines → Decision making
2. Efficacy in real life that reflects different types of practice → large cohort
3. Safety and complications comparison between centers → adverse events

Independent, representative and exhaustive
5583 CI PATIENTS INCLUDED → 2015

<table>
<thead>
<tr>
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<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
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<tbody>
<tr>
<td>Exhaustivity</td>
<td>97%</td>
<td>94%</td>
<td>93%</td>
<td>87%</td>
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<tr>
<td>Off label in adult</td>
<td>4.7%</td>
<td>13.6%</td>
<td>21.2%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Off label in children</td>
<td>2%</td>
<td>3.4%</td>
<td>5.3%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Complication rate</td>
<td>8.3%</td>
<td>4%</td>
<td>2%</td>
<td>1.6%</td>
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</table>
VARIABILITY OF AGENCIES RECOMMENDATIONS

- **NICE** and **HAS** 2007 on the same data give different recommendations 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
April 2016 – April 2017 – Chris RAINE

UK CI Adults – N= 919
18 - 2%
2 - 0%
899 - 98%

UK CI Children – N= 485
39 - 8%
86 - 18%
360 - 74%

New CI recipients in FRANCE = 1 394

FRANCE CI Adults – N= 870
30 - 4%
177 - 20%
663 - 76%

FRANCE CI Children – N= 524
37 - 7%
155 - 30%
332 - 63%

Bilateral Simultaneous
Bilateral Sequential
Unilateral
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 =

\[
\text{Cost of intervention CI} - \text{Cost of intervention HA}
\]

\[
\frac{\text{No. of QALYs produced by CI} - \text{No. of QALYs produced by HA}}{\text{No. of QALYs produced by CI} - \text{No. of QALYs produced by HA}}
\]
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

<table>
<thead>
<tr>
<th></th>
<th>Amélioration majeure</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Amélioration importante</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Amélioration modérée</td>
<td></td>
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<tr>
<td>IV</td>
<td>Amélioration mineure</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Absence d’amélioration</td>
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</table>
EVALUATION SYNTHESIS

- We can use 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

Cl with positioner

Meningitis risk of cochlear implant with positioner
SUBSTANTIAL INNOVATION
EXTENDING INDICATION

A
More cost
Less effective

B
Less cost
Less effective

C
More cost
More effective

D
Less cost
More effective
## SIZE EFFECT IN MYOCARDIAL INFARCTION

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Survival</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest (1970)</td>
<td>85%</td>
<td>$0</td>
</tr>
<tr>
<td>Streptokinase (1980)</td>
<td>93%</td>
<td>$320</td>
</tr>
<tr>
<td>STENT (1990)</td>
<td>94%</td>
<td>$2,750</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>CI</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Conduction</td>
<td>Mean 0.55</td>
</tr>
<tr>
<td>CROS</td>
<td>Mean 0.27</td>
</tr>
</tbody>
</table>

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
MULTI CENTRIC MEDICO ECONOMIC STUDY

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

Observation
CROS: N : 63
Bone cond.: N : 12
Observation: N : 9

Randomization
CI: N : 42

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

2. New rehabilitation model
When a radical innovative device or new rehabilitation model is developed it is difficult to estimate at the early phase:

- The long term efficacy
- The cost utility

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 consortium 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
  - AB
  - Cochlear
  - Oticon
  - MED-EL

• Agencies
  - HAS
  - afmps
  - NICE
  - IQWiG

• Multidisciplinary scientific board
• Patient association
DEVELOPMENT OF A EUROPEAN REGISTRY
CALL H2020

- Standardization of outcomes
- Measures near real-time adverse event information
- Stratification and outcomes prediction
- Benchmark of medical, surgical and rehabilitation procedure
- Evaluation of socio-economic differences and geographic inequalities
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)
Thank you for your attention