

## EVALUATING MEDICAL DEVICES: HOW DOES RANDOMISED CLINICAL TRIAL DATA AND REAL-WORLD DATA FIT TOGETHER?

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### Disclosures

- ⇒ Advisory board and honoraria from: MSD, Abbvie, Sanofi, Medtronic, BMS, Janssen, Amgen, Impulse dynamics, Pfizer

## Scope of the problem

### Devices and drugs are different, because:

Devices may change over time

Their result may be operator dependent

They often require an invasive procedure

May use the same surrogate endpoints as drugs, but

➔ You assess a different device each time

➔ You assess the learning curve AND you need trained professionals

➔ You select the population willing to have the procedure

➔ Are the mechanisms of action and therefore the final endpoints identical?

(eg: renal denervation)

## How does this affect the HTA

➔ EUNEHTA has developed a core model

➔ Evidence generation for devices is more complex because of:

- Study design
- Nature of the device
- Assessment of both device and procedure

## Proposed solution: : 'Tracker studies

(<https://www.bmj.com/content/320/7226/43.long>)

Published in 2000

### Summary points

Evaluating treatments is difficult when developments or variants arise frequently

In these circumstances randomised controlled trials should not await stability, but should track progress over time, providing unbiased comparisons at each stage

These "tracker trials" should be guided by flexible protocols, without prefixed sample size (or duration), and will require sophisticated interim analyses

Following clinical practice flexibly will enable tracker trials to be comprehensive—collecting maximum amounts of randomised data and ensuring standardised outcome measures across centres

Starting trials while technology is changing will ensure maximum use of information after it has stabilised

Tracker trials would also be able to monitor treatments and centres to detect poor performance quickly and to provide an effective early warning system

## Other designs

- ⇒ Models
- ⇒ Propensity score matching/ weighing
- ⇒ Cohort nested trials
- ⇒ Preference trials
- ⇒ Trial with RWD follow up
- ⇒ External validity checked with RWD

# IDEAL framework for surgical innovation 2: observational studies in the exploration and assessment stages

Cite this as: *BMJ* 2013;346:f3011

## Box 1 | Recommendations for observational studies at stages 2b (exploration) and 3 (assessment)

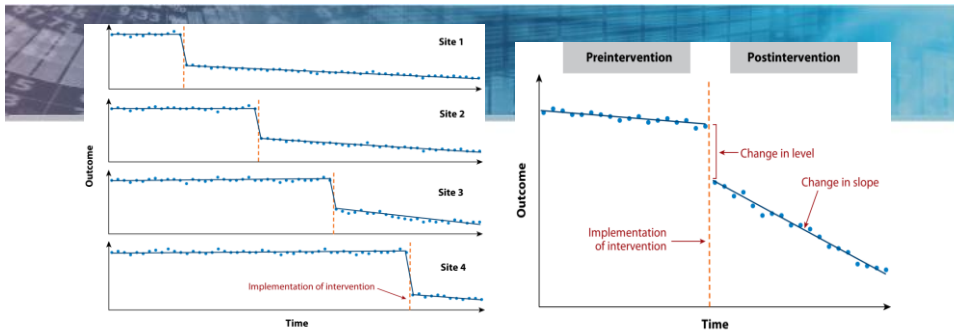
### Exploration

Observational studies should generally be prospective and have a protocol  
 A range of outcomes should be collected using standardised definitions  
 Observational studies that are uncontrolled (for example, those based on registry and routine data collection) should be diagnosis based rather than procedure based whenever possible  
 Important patient risk factors and variations in the interventions should be explored  
 Studies should record and report surgeon experience (including any specific training received). Where possible, the effect of skill differences and learning should be assessed using appropriate data analysis  
 Prospective, collaborative observational studies should be designed with a definite evaluation in mind (preferably a randomised controlled trial)

### Assessment

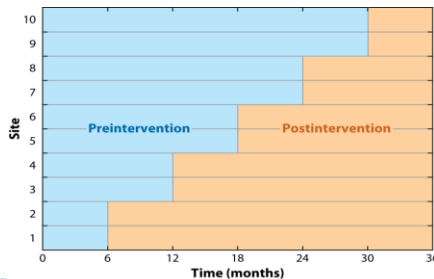
Definitive observational studies should use a quasi-experimental study design; protocol driven controlled studies with standardised eligibility and prospective data collection  
 Possible designs include non-randomised controlled trials and interrupted time series  
 Key patient and centre characteristics likely to confound analysis should be considered before conducting study and collecting appropriate data, which would facilitate assessment and adjustment of the case mix, and help matching to control for potential confounding

ASSISTANCE  
PUBLIQUE



Sanson-Fisher RW, et al. 2014. *Annu. Rev. Public Health.* 35:9–27

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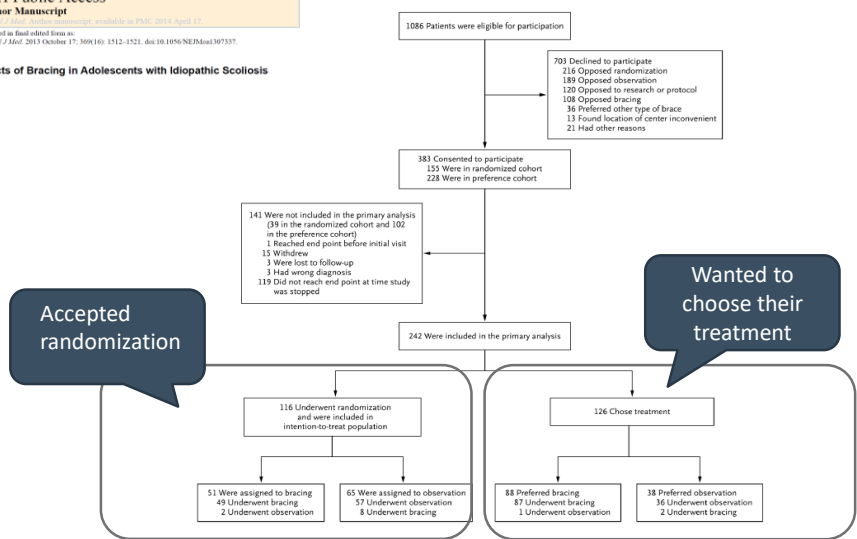
Sanson-Fisher RW, et al. 2014. *Annu. Rev. Public Health.* 35:9–27

Alternative study designs

ASSI  
PUE

che clinique en économie de la santé d'Ile-de-France

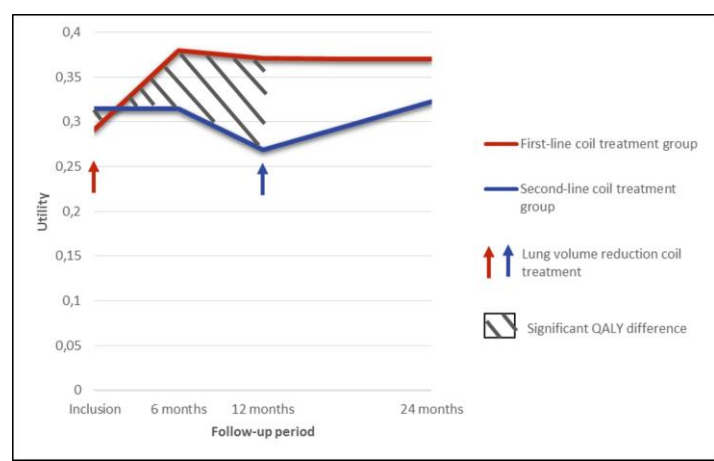




**Figure 1. Study Enrollment and Treatment of the Patients.** Between March 2007 and February 2011, a total of 1086 patients underwent screening. Of the 242 patients included in the primary analysis, 116 patients underwent randomization and were included in the intention-to-treat population. A total of 126 patients declined randomization and chose their preferred treatment. Patients were permitted to change treatment groups on request.

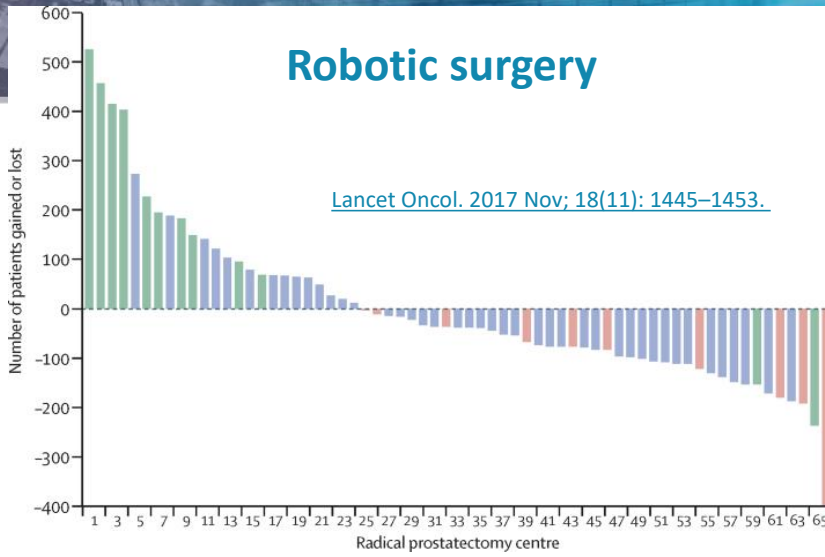
ASSIS PUBL

## The Revolens study

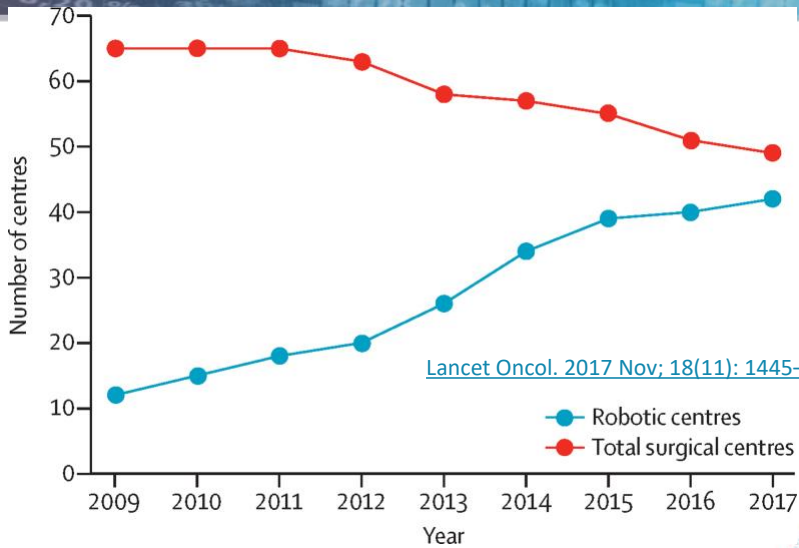


.JAMA. 2016 Jan 12;315(2):175-84  
 Respir Res. 2018 May 9;19(1):84.

# Robotic surgery



Net gains and losses of patients for each radical prostatectomy centre (n=65) during the study period



# A tool for HTA and market access in France

## 'Innovation Fund' by the MoH

### → Protocol HTA:

- Has to be approved by the HTA agency
- Limited number of centers
- MoH will pay for the device & the procedure in the centers of the trial only
- MoH will not pay for data collection & analysis

### → Current protocols:

- Argus 2 retinal implant (Second Sight)
- Ultrasound for prostate cancer (Focal One)
- Ultrasound for benign breast adenoma (Theraclion)

# Market access & price: is HTA useful?



The impact of HTA and procurement practices on the selection and prices of medical devices  
Gaudita Gallego<sup>1\*</sup>, Fabrizio Arnesi<sup>2</sup>, Marta Marsilio<sup>3,4</sup>, Claudio Jonani<sup>5,6</sup>, Rosanna Tarantini<sup>7</sup>

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Our results clearly show that regional HTA programs play a role in the selection of MDs and that within each class of devices, the costliest products are recommended. An example of this impact in the orthopedic sector is provided by ceramic femoral heads. Specifically, the share of costly ceramic femoral heads purchased by hospitals when regional HTA programs are active is 96%, compared to 52% when hospital-based HTA models are in place. One interpretation of this result is that regional-level HTA favors more innovative devices, assuming that the costliest devices are also the most innovative. In other words, regional HTA does not appear to be a barrier to innovative products. The opposite phenomenon is observed in regions with hospital-based HTA but no regional-level HTA programs; when HTA is performed at the hospital level only, costly devices are less likely to be selected and purchased, which suggests that hospital-based HTA acts as a cost-containment tool.



# Conclusion: work in progress

- ➔ What are the acceptable designs?
- ➔ Complementarity EU and national HTA bodies:
  - EUNetHTA core model and evidence generation
    - ➔ Merge registries?
  - Local evidence generation
    - ➔ Trained professionals
    - ➔ Limited number of centers
    - ➔ Price negotiation