The importance of observational studies and the position of medical Societies

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Conflict of interest

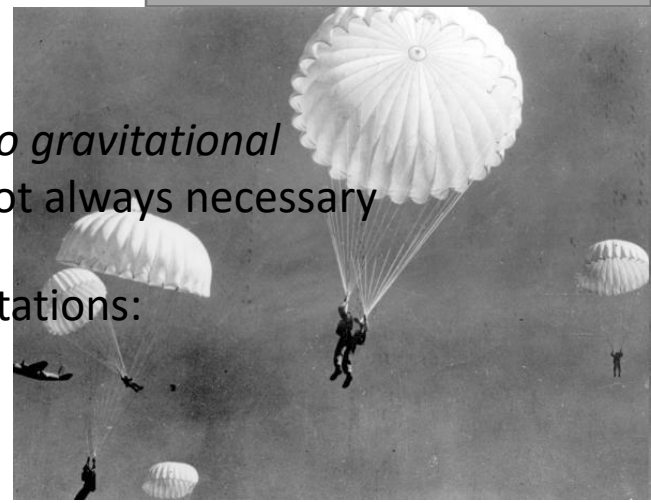
EORTC Executive Officer
EORTC *Surcare* Chairman
Past President of the French Society of Surgical Oncology
ESSO Board Member and Past Scientific Director

Honorary lecture for Sanofi and Roche

Apologies: I am only a surgeon, not a radiologist
IR is a surgical affair: it shares the same pattern, concerns and limitations
And requires the same methodological approach.

Prof. Evrard

Do we need randomised controlled trials to test the effect on parachutes on major trauma and death?



Smith & Pell's famous article, *Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials (*2013) argue that RCTs are not always necessary

High-quality observational studies could meet the demands for data in IR, but has its limitations:

- Selection bias
- Cofounding
- Overestimation of effect
- Underreporting of adverse effects

Scientific societies could be well-equipped to address these limitations

Smith GC, Pell JP. Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. *BMJ*. 2003;327(7429):1459-1461.

Prof. Evrard

RCTs are the gold standard for clinical research, but are they feasible for surgical procedures and IR?

RCTs	Observational studies
Patient recruitment – IR trials fail because of low patient recruitment. Hyperselected populations are rare and non representative of the true life people	Can recruit large numbers of patients Retrospective **but also prospective**
Randomisation and blinding is challenging (Psychological bias for MD and patients, Equipoise)	Observes routine medical practice (non-interventional or interventional)
Costly to conduct – especially when observing long-term outcomes (only 5% of money go to surgical research)	Can generate large amount of data in a cost-effective manner
Major concern with the quality control of the procedures	Idem but can include multiple outcomes of interests that can be observed in clinical practice
Great internal validation but low external validation	Low internal and great external validation: **the true life !**

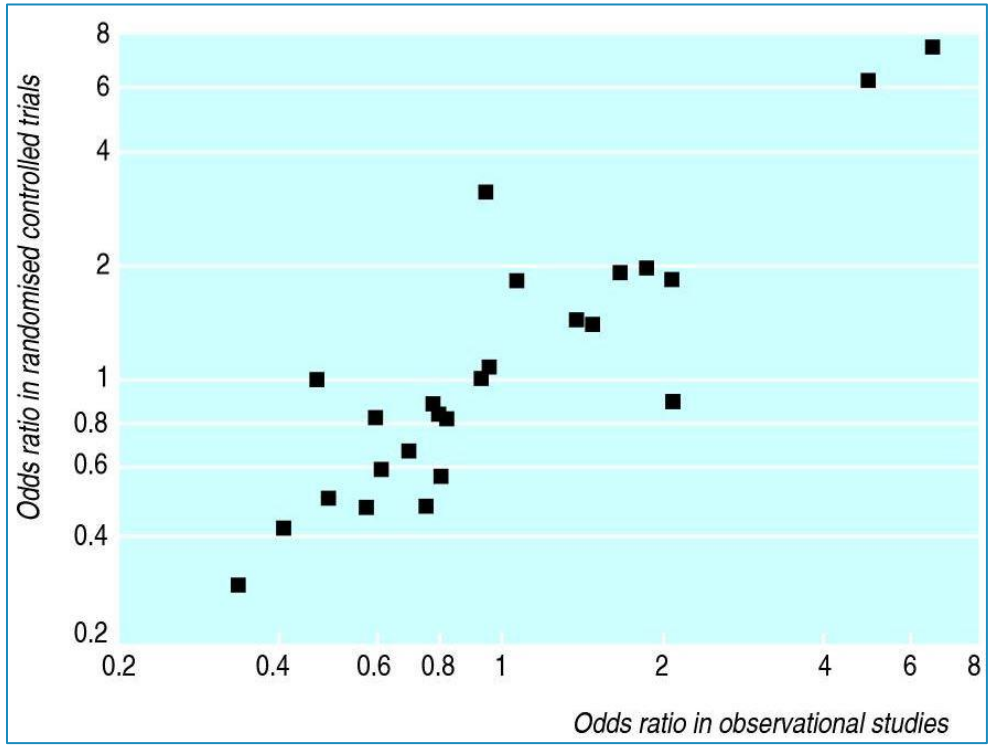
Methodology of observational studies?

- Outcomes studies, pragmatic studies , quasiexperimental studies
- Retrospective Big Data: Artificial Intelligence
- Prospective design
  - •Quasi-experimental: criteria of inclusion and exclusion, power calculation (α and β)
  - •Design and recording *a priori*

    Contre-ex: LiverMetSurvey
- Modern reporting
  - •Dindo and Clavien
  - •COMET (Core Outcome Measures for Effectiveness Trials)
  - •eCRF
- Quality control and improvement

Systematic reviews have shown that observational studies often provide results very similar to RCTs

In a comparison of 235 observational studies and RCTs over 25 topics, Ionnidis et al (2001) found that the **concordance correlation coefficient** (measuring the agreement between two variables) between the odds ratio of randomised trials and the odds ratio of observational designs is **0.84** (P<0.001).



Ioannidis JP, Haidich AB, Lau J. Any casualties in the clash of randomised and observational evidence?. *BMJ*. 2001;322(7291):879-880. doi:10.1136/bmj.322.7291.879

Observational studies – value of information

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up	Case-series, case-control dies, or historically ntrolled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or servational study with dramatic ect	Individual randomized trial or (exceptionally) observational study with dramatic effect		se-series, case-control, historically controlled dies**	Mechanism-based reasoning
	stematic review of randomized ls or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
worthwhile? (Screening)	stematic review of randomized ls	Randomized trial		Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

* Level may be graded down on the basis of study quality, imprecision, indirectn), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded u if there is a large or very large effect size.

** As always, a systematic review is generally better than an individual study.

Randomised trial or observational study with dramatic effect

… or observational study with dramatic effect

Randomised trial or (exceptionally) observational study with dramatic effect

Why should scientific societies involve themselves in observational research?

Scientific societies:

- Foster synergies between KOLs, industry, and a potential of 1000s of members available for research projects
- Benefit from being on top of the latest developments in IR technology
- Have access to good channels for the dissemination of the results of the study
- Can operate as an independent entity
- Can effectively address the scientific limitations of observational studies **and try to convince the Journals of the importance to publish them (major challenge)**

How can CIRSE do it?

Research principles:

1. Produce high-quality clinical data
2. Conduct independent research
3. Conduct research in an efficient and cost-effective manner
4. Provide a valuable service to our members and the medical community

Research infrastructure:

1. Scientific multidisciplinary Steering Committees comprised of experts in the field
2. Dedicated Clinical Research Department
3. High-quality, easy to use Electronic Data Capturing system
4. CIRSE quality manual for data monitoring and data management

Summary

1. Observational research can fill the gap between the challenges for RCTs in IR and the need for data on IR procedures

2. The observational designs are well-suited for the dynamic field of IR

3. Scientific societies are in the perfect position to drive and conduct high-quality observational research due to existing synergies between KOLs, industry, and members

4. Societies are well-positioned to address the limitations of observational research

5. CIRSE studies can offer proof of concept for clinically valuable society-conducted observational data

CIRT CIRSE Registry for SIR-Spheres Therapy
CIREL CIRSE Registry for LifePearl Microspheres
CIRT-FR CIRSE Registry for SIR-Spheres Therapy in France
CIEMAR CIRSE Emprint Microwave Ablation Registry

Thank you for your attention