The importance of observational studies and the position of medical Societies

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Conflict of interest

EORTC Executive Officer
EORTC Surcare Chairman
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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.
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

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

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

- Outcomes studies, pragmatic studies, quasi-experimental studies
- Retrospective Big Data: Artificial Intelligence
- Prospective design
  - Quasi-experimental: criteria of inclusion and exclusion, power calculation ($\alpha$ and $\beta$)
  - 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, Ioannidis 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).

Observational studies – value of information

<table>
<thead>
<tr>
<th>Question</th>
<th>Step 1 (Level 1*)</th>
<th>Step 2 (Level 2*)</th>
<th>Step 3 (Level 3*)</th>
<th>Step 4 (Level 4*)</th>
<th>Step 5 (Level 5*)</th>
</tr>
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<tbody>
<tr>
<td>How common is the problem?</td>
<td>Local and current random sample surveys (or case-control)</td>
<td>Systematic review of surveys that allow matching to local circumstances**</td>
<td>Local non-random sample**</td>
<td>Case-series**</td>
<td>N/A</td>
</tr>
<tr>
<td>Is this diagnostic or monitoring tool accurate? (Diagnosis)</td>
<td>Systematic review of cross sectional studies with consistently applied reference standard and blinding</td>
<td>Individual cross sectional studies with consistently applied reference standard and blinding</td>
<td>Non-consecutive studies, or studies without consistently applied reference standard**</td>
<td>Case-control studies, or poor or non-independent reference standard**</td>
<td>Mechanism-based reasoning</td>
</tr>
<tr>
<td>What will happen if we do not add a therapy? (Prognosis)</td>
<td>Systematic review of inception cohort studies</td>
<td>Inception cohort studies</td>
<td>Cohort study or arm of randomized trial*</td>
<td>Case-series or case-control studies, or poor quality prognostic cohort study**</td>
<td>N/A</td>
</tr>
<tr>
<td>Does this intervention help? (Treatment Benefits)</td>
<td>Systematic review of randomized trials or RCTs</td>
<td>Randomized trial or observational study with dramatic effect</td>
<td>Non-randomized controlled cohort/follow-up</td>
<td>Case-series, case-control studies, or historically controlled studies**</td>
<td>Mechanism-based reasoning</td>
</tr>
<tr>
<td>What are the COMMON harms? (Treatment Harms)</td>
<td>Systematic review of randomized trials or RCTs</td>
<td>Individual randomized trial (exceptionally) observational study with dramatic effect</td>
<td>Case-series, case-control, historically controlled trials**</td>
<td>Mechanism-based reasoning</td>
<td></td>
</tr>
</tbody>
</table>

* Level may be graded down on the basis of study quality, imprecision, indirectness studies, or because the absolute effect size is very small. Level may be graded up 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

Observational studies – value of information... 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
Thank you for your attention