Journal Watch

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A novel proposal for article discussion sections

We know that the discussion and conclusion sections of research articles are too often subjective, containing over-interpretation of data and spins (manipulation of language to mislead the reader).

To address this problem, the editors of *The British Journal of Anaesthesia* (BJA) developed an interesting publishing experiment: They invited a group of independent experts to write a *second* discussion section for a research article published in the same issue. The independent experts had not participated in the research and were only provided with the methods and results of the original paper.

As stated in a *Nature* note: "We're all biased and this gives a second pair of eyes".[1] Indeed, with similar data, authors can make inferences or tell different stories.

The BJA published several articles in connection with this experiment:

1. A randomised controlled trial with 13 American authors (anaesthetists, orthopaedists, geriatricians, statisticians);[2] patients were included in a Johns Hopkins Medical Center, Baltimore; this publication concerns a secondary endpoint of the study; the conclusion of the publication:

   This study found that in elderly patients having hip fracture surgery with spinal anaesthesia supplemented with propofol sedation, heavier intraoperative sedation was not associated with significant differences in mortality or return to pre-fracture ambulation up to 1 year after surgery.

2. The next article proposed a new discussion written by three experts: two anaesthetists, (one of whom was handling editor of the initial article), and a biostatistician.[3] This article compares the two discussions (initial authors and external experts) and comments on the comparisons. The interpretation of the main result is the same. There are interesting comments explaining that the trial did not include enough patients to reach such a conclusion:

   The major inferential difference between the Discussions is in relation to appropriateness of the sample size. In the Original Discussion the investigators opine that the study was large enough to detect a clinically meaningful reduction in mortality. In contrast, the Independent Discussant infers that the estimated mortality was too high and that the estimated decrease in mortality with the intervention was unrealistic; thus, with only 200 patients, the study was not sufficiently large to address the research question. There are also differences in emphasis in the Discussions regarding existing evidence and contextualization, and whether comorbidity should be a major issue for future research. In many other respects, there is inferential reproducibility between the Discussions.

3. Another article focuses on the reproducibility crisis in science and details the idea of including a second discussion section for articles:[4]

   Although replication of methods and results is necessary to demonstrate reproducibility, it is not sufficient. Also fundamental is consistent interpretation in the Discussion section. Current deficiencies in the Discussion sections of manuscripts might limit the inferential reproducibility of scientific research. Lack of contextualisation using systematic reviews, over-interpretation and misinterpretation of results, and insufficient acknowledgement of limitations are common problems in Discussion sections; these deficiencies can harm the translational process. Proposed solutions include eliminating or not reading Discussions, writing accompanying editorials, and post-publication review and comments; however, none of these solutions works very well. A second Discussion written by an independent author with appropriate expertise in research methodology is a new testable solution that could help probe inferential reproducibility, and address some deficiencies in primary Discussion sections.

4. The accompanying editorial discusses the feasibility of having two discussions for a paper.[5] The idea is rather interesting. Who would accept an offer to spend time writing a discussion for a study that he or she has not done? The reviewers are best positioned for writing discussions. But the question is the incentive: Will they then

become authors? Discussion sections are probably the weakest section of a paper, and they must be improved. Structuring the discussion, as proposed by the BJA, is part of the solution. Few journals have considered structuring the discussion with a standard format. The editorial notes that editorials can serve some of the function of a second discussion.

The BJA includes in its instructions to authors a list of elements that should be included in the discussion and notes the pattern it should follow: main finding, relationship of main finding to previous studies, additional (secondary) findings, relationship of additional (secondary) findings to previous studies, limitations, strengths, future directions, and conclusion.

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Journals increase their requirements for the publication of randomised controlled trials

The requirements of editors and reviewers are increasing. Editors want to be sure that the authors are telling the truth about the observations.[1]

What are these requirements? Some have become routine: Record the protocol, supplement data with all key trial data, include the completed CONSORT guideline flowchart and adhere to CONSORT guidelines, structure summaries with key points or highlights, sometimes add an abstract for the public and a sentence entitled "Conclusion and Relevance" at the end of the abstract. Other requirements appear, depending on the journal: No longer use *P* values for statistics and instead report the effect sizes with 95% confidence intervals (the 0.05 significance level represents a historical tradition rather than a rationally established cut point), report the number of secondary outcomes of the protocol and precisely how many are being reported in the manuscript, be explicit about the post hoc analysis, and provide a visual abstract (see for example https://jamanetwork.com/journals/jama/article-abstract/2752470).

These requirements, the objective of which is transparency and the fight against the crisis of reproducibility, could justify adopting the registered reports (RR) model in medicine. The RR model (Figure 1) is defined by the Center for Open Science (https://cos.io/rr/) as "Peer review before results are known to align scientific values and practice".

> *Registered Reports is a publishing format used by over 200 journals that emphasizes the importance of the research question and the quality of methodology by conducting peer review prior to data collection. High quality protocols are then provisionally accepted for publication if the authors follow through with the registered methodology.*[2]

Among the journals that develop RRs in parallel with their other reviewed articles, there are some in medicine (*BMC Medicine, BMJ Open Science, Cancer Medicine*).

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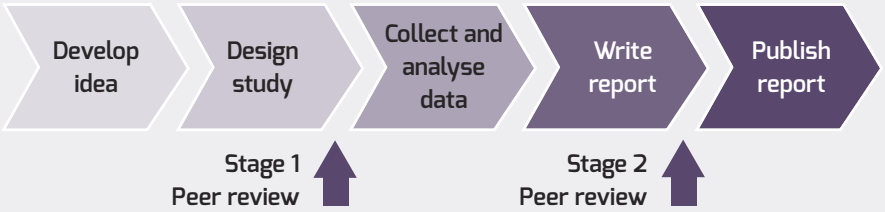
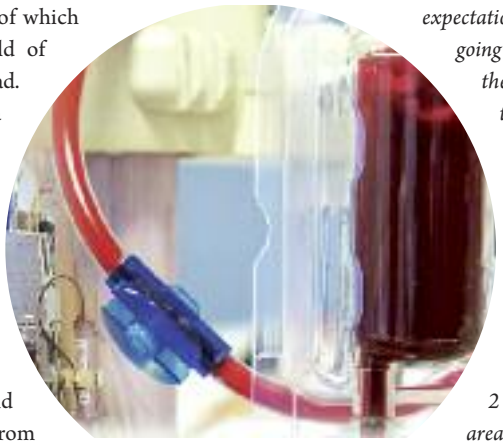


Figure 1. The registered reports model (with permission from the Center for Open Science https://cos.io/rr/)

Real-world data: A complement, not a replacement for randomised controlled trial data

New results were published in 2019 providing arguments for the debate on the generalisation of randomised controlled trials (RCTs). It is often discussed, or even admitted, that patients seen in clinical practice do not reflect those who have been included in RCTs.

Three articles, two of which are applied to the field of dialysis, deserve to be read. These are studies with a lot of data, and these studies have been done well. Rather than detailing or interpreting the data, I am noting the key points of these articles:



1. In a meta-analysis, RCTs from Medline and Cochrane databases from January 2007 to December 2016 were included.[1] These are trials that included at least two sites and more than 100 American adult patients undergoing dialysis for end-stage kidney disease. The RCTs data were compared to the 2011 United States Renal Data System cohort with more than 500,000 patients. Based on median values, the typical study had 211 participants from 15 sites in a single country and a follow-up time from randomisation to final data collection of 7 months.

   Question: *How similar are dialysis-dependent patients recruited to large, multicenter randomized clinical trials compared with the general dialysis-dependent population?*

   Findings: *In this meta-analysis of 189 trials including 80,104 participants, trial participants were significantly younger, more likely to be male, and less likely to have diabetes or diabetic nephropathy than patients in the US national registry. Moreover, the mortality rate of dialysis-dependent patients recruited to large, multicenter randomized trials was substantially lower than that of registry patients, both overall and when only studies recruiting participants from the United States were considered.*

   Meaning: *These findings imply that caution should be exercised when generalizing results from clinical trials to the broader dialysis-dependent patient population.*[1]

The mortality risk was less than half that of the registry patients.

2. Another study, a survey, showed that patients undergoing dialysis often underestimate their disease prognosis, both because of uncertainty as well as optimism.[2] Survey participants were approached between April 2015 and December 2018 from Seattle, Washington, and Nashville, Tennessee.

   Question: What are the prognostic expectations of people undergoing dialysis, and how do these relate to their treatment goals and preferences?

   Findings: *In this cross-sectional survey study of 996 patients receiving maintenance dialysis at nonprofit facilities in 2 US metropolitan areas, most of the respondents were either uncertain about prognosis or had a prognostic expectation of more than 10 years. In adjusted analyses, these groups were less likely than those with a prognostic expectation of fewer than 5 years to report having documented their treatment preferences and to value comfort over life extension, and more likely to want cardiopulmonary resuscitation and mechanical ventilation.*

   Meaning: *Prognostic uncertainty and overly optimistic prognostic expectations among people undergoing dialysis may limit the benefit of advance care planning and contribute to intensive patterns of end-of-life care.*[2]

The editorial accompanying these two papers calls for including older patients and those with serious comorbid illness in RCTs if we want evidence that can be used to inform decision-making for all patients.[3]

3. The objective of another study was to identify the number of trials published in seven high-impact journals in 2017 that could be feasibly replicated using observational data from insurance claims and/or electronic health records (EHRs).[4] The seven journals were: *NEJM, Lancet, JAMA, The BMJ, Annals of Internal Medicine, JAMA Internal Medicine, and PLoS Medicine*. They included 220 US-based trials: 86 had an intervention that could be ascertained from insurance claims and/or EHR data. Among the 86 trials, 62 had an indication that could be ascertained, and 45 of the 62 at least 80% of inclusion and exclusion criteria data that could be ascertained, while 33 of the 45 had at least one primary end point that could be determined.

   Question: *What percentage of clinical trials published in high-impact journals in 2017 generated evidence that could feasibly be replicated using observational methods and data sources?*

   Findings: *In this cross-sectional study of 220 clinical trials published in high-impact journals in 2017, only 15% could feasibly be replicated using currently available real-world data sources.*

   Meaning: *This study suggests that, although the increasing use of real world evidence in medical research presents opportunities to supplement or even replace some clinical trials, observational methods are not likely to obviate the need for traditional clinical trials.*[4]

This debate is complex, with disagreements among experts on the generalisation of RCTs. The societal demand to always analyse real-life data is understandable, but these data can rarely replace data from RCTs!

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