A Systematic Analysis of Peer Reviewers' Responses in Five EBM Studies: Do We Need Newer Evidence Synthesis Approaches?

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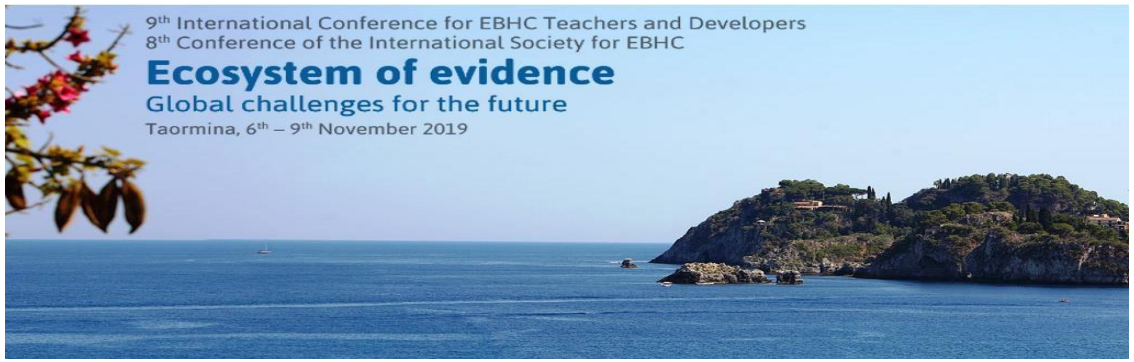


Background

- Systematic reviews & meta-analyses are considered the highest level of evidence for assessing the effectiveness and safety of therapy.

- Clinical trials may be biased in favour of type 1 error, and ‘spin’ is prevalent in published articles where the effectiveness is less clear.
  Khan MS. JAMA 2019: e192622.

- Medical literature places strong emphasis on efficacy and economic considerations, but less addressing risk of harm.

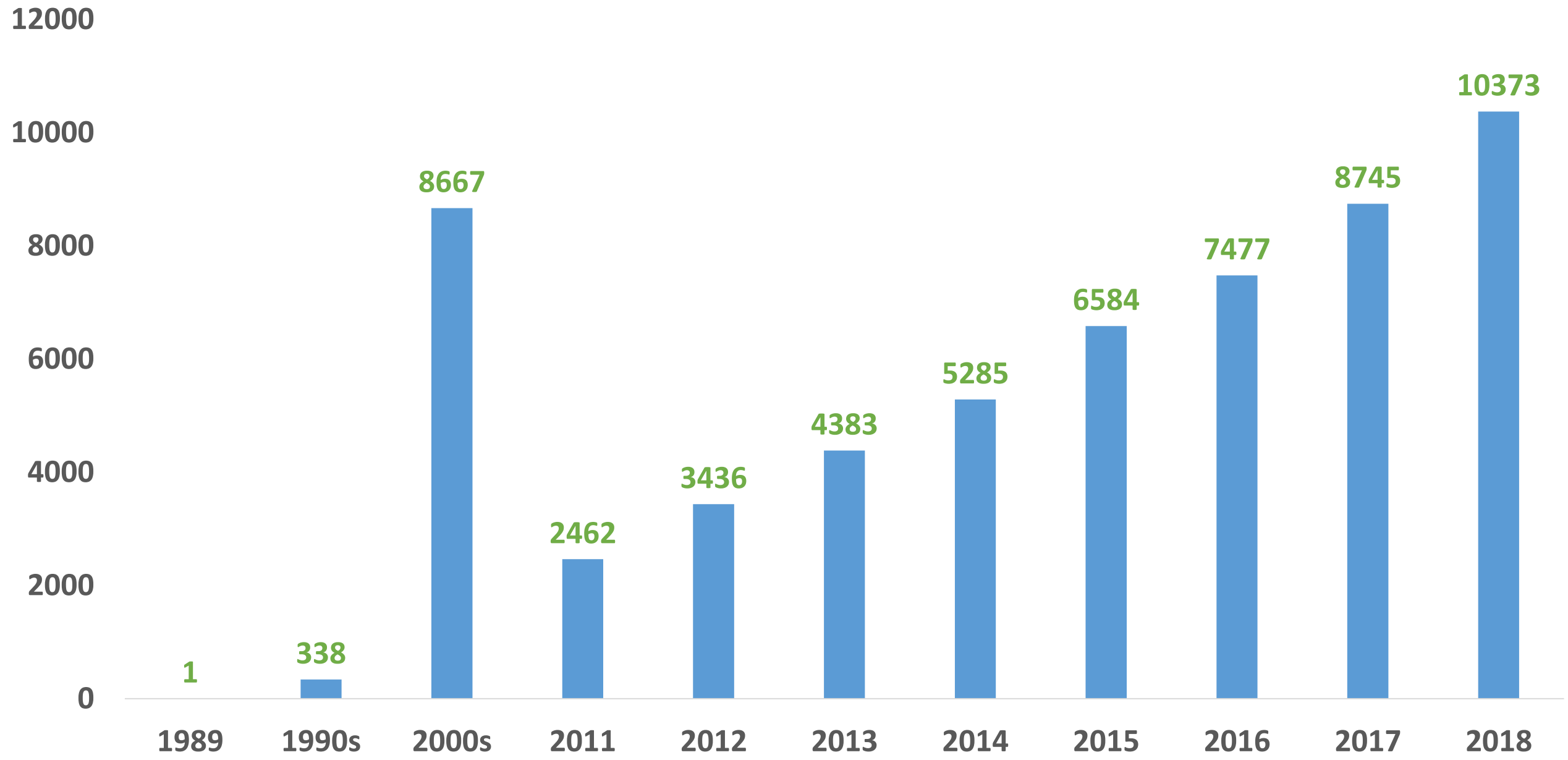
Levels of Evidence for Therapeutic Studies*

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence intervals)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual Cohort study (including low quality RCT, e.g. <80% follow-up)
2C	"Outcomes" research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual Case-control study
4	Case series (and poor quality cohort and case-control study
5	Expert opinion without explicit critical appraisal or based on physiology bench research or "first principles"

* From the Centre for Evidence-Based Medicine, http://www.cebm.net.

Burns PB. Plast Reconstr Surg 2011;128:305-310.

Systematic Reviews and Meta-Analyes in PubMed



‘Evidence-based Medicine’

Pfeffer MA. Bowler MB NEJM 2001; 365:1-3

“The medical and legal systems both strive for truth while acknowledging that there are no absolutes”

“Both systems require evidence, which they categorize in a hierarchy of levels, on which to base decisions that can have major effects on the quality and even the quantity of peoples lives”

“Clinicians are well aware… information regarding drug safety does not have to reach the same level of certainty that we demand for demonstrating efficacy”

Study Aims

- Our experience of attempting to publish systematic reviews and meta-analysis of clinical trials to address medication safety, shows some reviewers questioned the validity and applicability of our methods, and widespread anchor bias.

- We performed a systematic analysis of our experience of the peer review process concerning evidence synthesis studies of medication related adverse events, and the relevance to the current paradigm of evidence based medicine

Methods

- We included all electronic responses from the medical journals (Impact Factor >3.0) to whom we submitted manuscripts for review.

- We used published critical views of the current evidence synthesis philosophy from the scientific literature to classify responses

- Details and content of the peer review process were extracted by two authors (A.I & R.C), and consequently analysed

- 5 manuscripts underwent peer review 22 times over a 7 year period.
- 55% (12) submissions were rejected by editors without a review.
- 45% (10) provided a formal review of the manuscript resulting in 191 responses from 29 reviewers.
- The mean duration from first submission to successful publication was 11.4 months (342 days), (SD: 5.08)

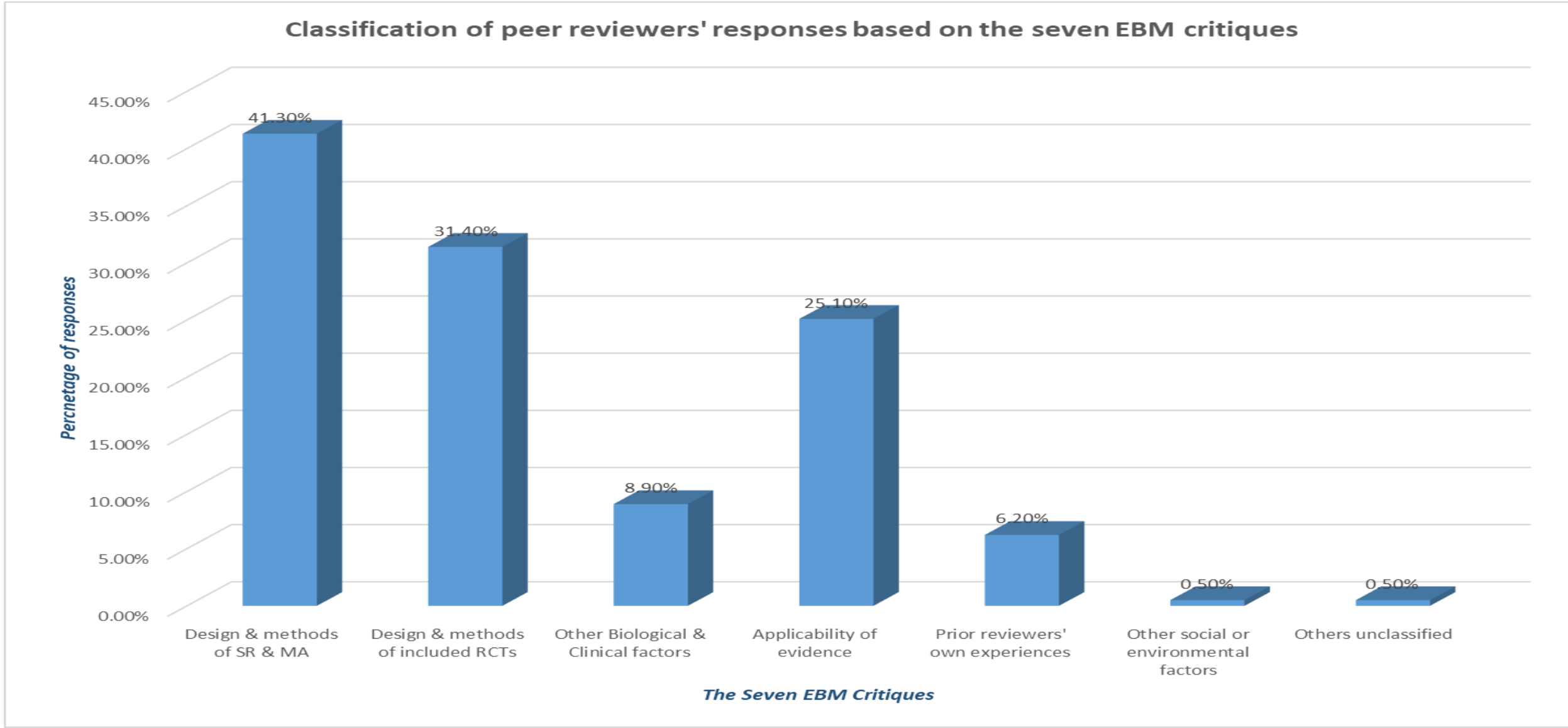
Results

- The majority of peer reviewers' responses (72%) were critiques directed towards limitation of the design & methodology of systematic reviews, meta-analyses, and included clinical trials

- A strong focus on applicability of evidence (in nearly a quarter of responses), and the contradiction of synthesized evidence with peer reviewers own prior experiences (6%) was also noted

- 1 in 4 comments were reviewers' opinions on the topic and had little to do with the design, analysis or validity of the result

Classification of peer reviewers' responses



Solutions?

- More education of reviewers on evidence-based methods?
- Blind reviewers to the name of the intervention, outcome?
- Publish all reviewers comments?
- Different methods (include cohorts) or analyses (Bayesian Modelling)
- Reject reviews that don’t address the fundamentals of the paper?

Conclusions

- Our experience suggests considerable concern remains about the current basis for evidence based medicine in the peer review system and the current evidence based medicine hierarchy.
- The majority of reviewers' responses appropriately addressed specific concerns regarding study design, analysis and conclusions.
- However, more than one quarter of responses were reviewers opinions reflecting personal and pervasive biases.
- Perhaps alternative methods are needed