



Publication standards of systematic reviews and meta-analysis of preclinical studies: Meta bias

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'I Don't Think I'm Biased'



Research & Bias



- All research is susceptible to bias
- Systematic reviews and meta-analyses
 - Developing field of research with a number of different approaches to its conduct and reporting
 - provide empirical evidence to spur the field to improve the rigor of the conduct and reporting of preclinical research
- Our worst bias is meta
 - being more aware of biases makes us more willing to assume that others' biases, and not ours, are responsible for our disagreement



Caesar's wife must be above suspicion

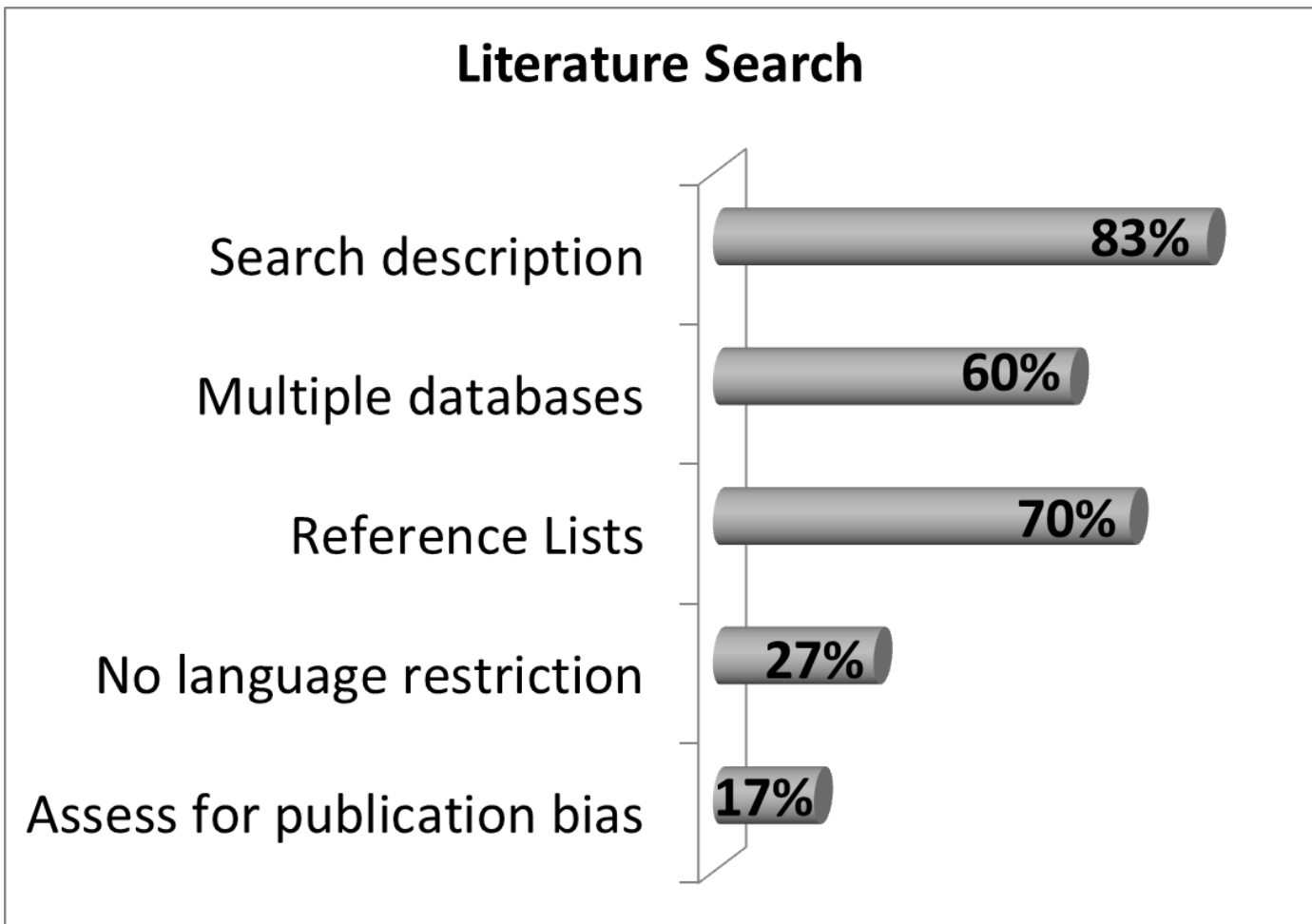
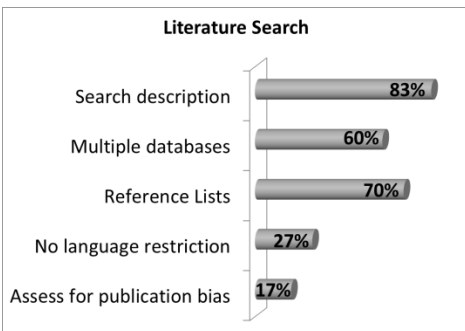
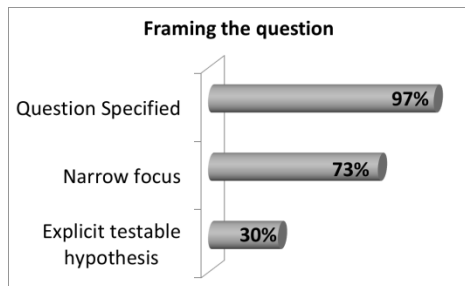


- Pompeia hosted the festival of the Bona Dea, which no man was permitted to attend
- However, a young man managed to gain admittance disguised as a woman, apparently for the purpose of seducing Pompeia
- He was caught and prosecuted for sacrilege
- Caesar divorced Pompeia, saying that "my wife ought not even to be under suspicion"





Heterogeneity in the conduct of systematic reviews





Why do we need guidelines?



- It is only through clear reporting is it possible to assess risk of bias
 - Are the methodologies sound and interpretations valid?
- Unaware of empirical evidence of the impact of bias in the conduct or reporting of systematic reviews of preclinical studies.
 - Without such data, guidelines have less validity.
- Recommendations may be useful



Impact of other guidelines



- CONSORT Statement (2001+2010)
 - Consolidated Standards of Reporting Trials
- Assessed with journal endorsement impacts the completeness of reporting
 - 81 meta-analyses that had assessed reporting
 - Endorsing vs non-endorsing journals
 - 25/27 checklist items were better reported in endorsed journals
 - Only 5 items significant at $p < 0.01$
 - Reporting is still sub-optimal

Turner *et al* 2012



Impact of other guidelines



- PRISMA
 - Preferred Reporting Items of Systematic reviews and Meta-Analyses
- Assessed the impact on endorsement
 - Endorsement was associated with better reporting
 - Publications citing PRISMA was not improved



Conduct



Points to consider in critical appraisal

1. Does the study follow a protocol
2. Was the research question clearly defined
3. Are the inclusion criteria appropriate
4. How comprehensive was the search strategy
5. Was the data abstraction appropriate
6. Where the data pooled appropriately?



Reporting guidelines



Title: Identify the report as a systematic review and/or meta-analysis of animal experiments

Abstract: structured covering: objectives, data sources, review methods, results and conclusion

Introduction:
Clearly defined and focussed research question



Reporting guidelines - Methods



Protocol: does it exist and where can I find it?

Searching: keywords, search strategy, any restrictions and special efforts to include all available data

Selection: inclusion and exclusion criteria

Quality Assessment: criteria and process used to assess validity

Data abstraction: Processes used

Study characteristics: study characteristics relevant to your research question

Quantitative data synthesis: Measures of effect, method of combining data, how heterogeneity was assessed; any assessment of publication bias



Reporting guidelines - Results



Flow Chart: A meta-analysis profile summarising study flow giving total number of experiments in the meta-analysis

Study Characteristics: Descriptive data for each experiment

Quantitative data synthesis:

Present simple summary results (e.g. forest plot); identify sources of heterogeneity, impact of study quality and publication bias



Reporting guidelines



Discussion: Summarise the main findings; discuss limitations; provide general interpretation of the results in the context of other findings, and implications for future research

Funding: sources of funding for the review and other support. The role of funders should be presented

Conflict of Interest



Conclusions



- Recent years have seen improvements in the conduct and reporting of
 - RCTs after the CONSORT statement.
 - Systematic reviews of clinical studies after PRISMA
- Guidelines would have much more validity with empirical evidence
- It is important that we are able to discern, as we do for primary research studies, the rigor with which the meta-analyses are performed and reported.



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