



# Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias

Kerry Dwan, Douglas G. Altman, Juan A. Arnaiz, Jill Bloom, An-Wen Chan, Eugenia Cronin, Evelyne Decullier, Philippa J. Easterbrook, Erik Von Elm, Carrol Gamble, Davina Ghera, John P. A. Ioannidis, John Simes, Paula R. Williamson.<sup>1</sup>

Centre for Medical Statistics and Health Evaluation, School of Health Sciences, University of Liverpool, UK.

Email: kerry.dwan@liverpool.ac.uk

## 1. BACKGROUND:

The increased application of meta-analysis in systematic reviews of healthcare interventions has highlighted several types of bias that can arise during the completion of a randomised controlled trial (RCT). Study publication bias has been recognised as a potential threat to the validity of meta-analysis and can make the readily available evidence unreliable for decision making. Until recently, outcome reporting bias has received less attention.

## 2. AIMS AND OBJECTIVES:

We review and summarise the evidence from a series of cohort studies that have assessed study publication bias and outcome reporting bias in randomised controlled trials.

## 3. METHODS:

We included research that assessed an inception cohort of RCTs for study publication bias and/or outcome reporting bias. Cohorts based on prevalence archives were excluded. Both cohorts containing exclusively RCTs or containing a mix of RCTs and non-RCTs were eligible. The assessment of RCTs in the included studies had to involve comparison of the protocol against all publications or information from trialists. MEDLINE, SCOPUS and the Cochrane Methodology Register were searched. Additional steps were taken to complement electronic database searches. The methodological quality of the included studies was assessed. Flow diagrams (Figure 1) to show the status of approved protocols was completed for each empirical study.

This review provides a descriptive summary of the included empirical studies. We refrained from statistically combining results from the different cohorts due to the differences in their design.

## 4. RESULTS:

Sixteen studies were eligible of which only two followed the cohort all the way from protocol approval to information regarding publication of outcomes. An example of this is shown in Figure 1.

### Study publication bias

Eleven of the studies investigated study publication bias and the results consistently show that positive studies are more likely to be published compared to negative studies (Table 1).

### Outcome reporting bias

Five of the studies investigated outcome reporting bias. Four empirical studies that examined the association between outcome reporting bias and statistical significance found that statistically significant outcomes were more likely to be completely reported than non-significant outcomes (range of odds ratios: 2.2 to 4.7). In comparing trial publications to protocols, we found that 40-62% of studies had at least one primary outcome that was changed, introduced, or omitted. Other comparisons of the primary outcome between protocol and publication were made (Table 2).

## 5. CONCLUSIONS:

Several studies have shown evidence of publication bias and recent work provides direct empirical evidence for the existence of outcome reporting bias. There is strong evidence of an association between significant results and publication; studies that report positive or significant results are more likely to be published and outcomes that are statistically significant have higher odds of being fully reported. Publications have been found to be inconsistent with their protocols. Researchers need to be aware of the problems of both types of bias and efforts should be concentrated on improving the reporting of trials.

## REFERENCES:

1. Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan A-W, et al. (2008) Systematic Review of the empirical evidence of study publication bias and outcome reporting bias. PLoS ONE 3(8): e3081. doi:10.1371/journal.pone.0003081
2. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG (2004) Empirical Evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 291 (20): 2457-2465.

Figure 1 Status of approved protocols for Chan 2004 study<sup>2</sup>

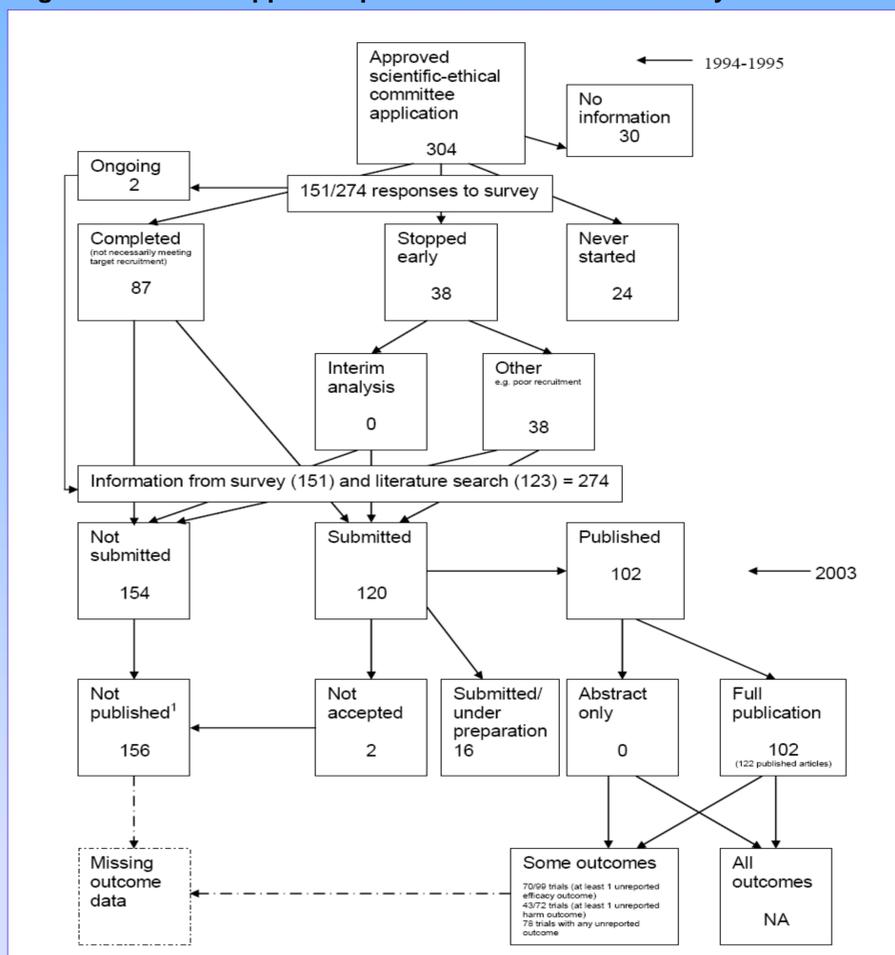


Table 1 Study level comparison of publication and statistical significance

Study	Study level
	Are studies with statistically significant or positive results, more likely to be published than those finding no difference between the study group?
Easterbrook, 1991	OR 2.32, 95% CI; 1.25, 4.28.
Dickersin, 1992	OR 2.54, 95% CI; 1.63, 3.94
Dickersin, 1993	OR 12.30, 95% CI; 2.54, 60
Stern, 1997	HR 2.32, 95% CI; 1.47, 3.66, p=0.0003
Cooper, 1997	p<0.0001 (submission only)
Wormald, 1997	RR 4, 95% CI; 0.6, 32, p=0.10
Ioannidis, 1998	*
Pich, 2003	*
Cronin, 2004	OR 0.53, 95% CI; 0.25, 1.1 p=0.1
Decullier, 2005	OR 4.59, 95% CI; 2.21, 9.54
Decullier, 2006	OR 1.58, 95% CI; 0.37, 6.71

\* The study did not investigate this

Table 2 Comparisons of primary outcome stated in protocol and in publication

Study	Outcome level				
	Primary outcome stated in protocol is the same as in the publication	Primary outcome stated in protocol is downgraded to secondary in the publication	Primary outcome stated in the protocol is omitted from the publication	Non primary outcome in the protocol is changed to primary in the publication	New primary outcome that was not stated in the protocol is included in the publication
Hahn, 2002	27% (4/15)	*	17% (1/6)	*	17% (1/6)
Chan, 2004a	67% (32/ 48)	23% (11/48)	13% (6/48)	9% (4/45)	18% (8/45)
Chan, 2004b	47% (36/76)	34% (26/76)	26% (20/76)	19% (12/63)	17% (11/63)
Ghera, 2006	74% (143/194)	*	16% (31/194)	*	10% (20/194)
Von Elm, 2008	*	*	26% (24/92)	*	11% (11/101)

\* The study did not investigate this