Industry sponsorship and research outcome (Review)

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[Methodology Review]

Industry sponsorship and research outcome

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ABSTRACT

Background

Clinical research affecting how doctors practice medicine is increasingly sponsored by companies that make drugs and medical devices. Previous systematic reviews have found that pharmaceutical industry sponsored studies are more often favorable to the sponsor's product compared with studies with other sources of sponsorship. This review is an update using more stringent methodology and also investigating sponsorship of device studies.

Objectives

To investigate whether industry sponsored drug and device studies have more favorable outcomes and differ in risk of bias, compared with studies having other sources of sponsorship.

Search methods

We searched MEDLINE (1948 to September 2010), EMBASE (1980 to September 2010), the Cochrane Methodology Register (Issue 4, 2010) and Web of Science (August 2011). In addition, we searched reference lists of included papers, previous systematic reviews and author files.

Selection criteria

Cross-sectional studies, cohort studies, systematic reviews and meta-analyses that quantitatively compared primary research studies of drugs or medical devices sponsored by industry with studies with other sources of sponsorship. We had no language restrictions.

Data collection and analysis

Two assessors identified potentially relevant papers, and a decision about final inclusion was made by all authors. Two assessors extracted data, and we contacted authors of included papers for additional unpublished data. Outcomes included favorable results, favorable conclusions, effect size, risk of bias and whether the conclusions agreed with the study results. Two assessors assessed risk of bias of included papers. We calculated pooled risk ratios (RR) for dichotomous data (with 95% confidence intervals).

Main results

Forty-eight papers were included. Industry sponsored studies more often had favorable efficacy results, risk ratio (RR): 1.24 (95% confidence interval (CI): 1.14 to 1.35), harms results RR: 1.87 (95% CI: 1.54 to 2.27) and conclusions RR: 1.31 (95% CI: 1.20 to 1.44) compared with non-industry sponsored studies. Ten papers reported on sponsorship and effect size, but could not be pooled due to differences in their reporting of data. The results were heterogeneous; five papers found larger effect sizes in industry sponsored studies compared with non-industry sponsored studies and five papers did not find a difference in effect size. Only two papers (including 120 device studies) reported separate data for devices and we did not find a difference between drug and device studies on the association between sponsorship and conclusions (test for interaction, P = 0.23). Comparing industry and non-industry sponsored studies, we did not find a difference in risk of bias from sequence generation, allocation concealment and follow-up. However, industry sponsored studies more often had low risk of bias from blinding, RR: 1.32 (95% CI: 1.05 to 1.65), compared with non-industry sponsored studies. In industry sponsored studies, there was less agreement between the results and the conclusions than in non-industry sponsored studies, RR: 0.84 (95% CI: 0.70 to 1.01).

Authors' conclusions

Sponsorship of drug and device studies by the manufacturing company leads to more favorable results and conclusions than sponsorship by other sources. Our analyses suggest the existence of an industry bias that cannot be explained by standard 'Risk of bias' assessments.

PLAIN LANGUAGE SUMMARY

Industry sponsorship and research outcome

Results from clinical studies on drugs and medical devices affect how doctors practice medicine and thereby the treatments offered to patients. However, clinical research is increasingly sponsored by companies that make these products, either because the companies directly perform the studies, or fully or partially fund them. Previous research has found that pharmaceutical industry sponsored studies tend to favor the sponsors' drugs much more than studies with any other sources of sponsorship. This suggests that industry sponsored studies are biased in favor of the sponsor's products.

This review is an update of a previous review on this topic that looked only at drug studies. It uses more rigorous methodology and also investigates sponsorship of medical device studies. The primary aim of the review was to find out whether the published results and overall conclusions of industry sponsored drug and device studies were more likely to favor the sponsors' products, compared with studies with other sources of sponsorship. The secondary aim was to find out whether such industry sponsored studies used methods that increase the risk of bias, again compared with studies with other sources of sponsorship. We did a comprehensive search of all relevant papers published before September 2010 and included 48 papers in our review.

Industry sponsored drug and device studies more often had favorable efficacy results, (risk ratio (RR): 1.24, 95% confidence interval (CI): 1.14 to 1.35), harms results (RR: 1.87, 95% CI: 1.54 to 2.27) and overall conclusions (RR: 1.31, 95% CI: 1.20 to 1.44), compared with non-industry sponsored drug and device studies. We did not find a difference between industry and non-industry sponsored studies with respect to standard factors that may increase the risk of bias, except for blinding: industry sponsored studies reported satisfactory blinding more often than non-industry sponsored studies. We did not find a difference between drug and device studies on the association between sponsorship and conclusions. In industry sponsored studies, there was less agreement between the results and the conclusions than in non-industry sponsored studies, RR: 0.84 (95% CI: 0.70 to 1.01). Our analysis suggests that industry sponsored drug and device studies are more often favorable to the sponsor's products than non-industry sponsored drug and device studies due to biases that cannot be explained by standard 'Risk of bias' assessment tools.

BACKGROUND

Description of the problem or issue

Clinical research sponsored by the pharmaceutical industry affects how doctors practice medicine (PhRMA 2008; Wyatt 1991). An increasing number of clinical trials at all stages in a product's life cycle are funded by the pharmaceutical industry, and the industry now spends more on medical research than do the National Institutes of Health in the United States (Dorsey 2010). Results and conclusions that are unfavorable to the sponsor (i.e. studies that find an expensive drug similarly or less effective or more harmful than drugs used to treat the same condition) can pose considerable financial risks to companies.

Several systematic reviews have documented that pharmaceutical industry sponsorship of drug studies is associated with findings that are favorable to the sponsor's product (Bekelman 2003; Lexchin 2003; Schott 2010; Sismondo 2008a). There are several ways that industry can sponsor a study, including single-source sponsorship, shared sponsorship, and provision of free drugs or devices only. There are also several potential ways that industry sponsors can influence the outcome of a study, including the framing of the question, the design of the study, the conduct of the study, how data are analyzed, selective reporting of favorable results, and spin in reporting conclusions (Bero 1996; Lexchin 2011; Sismondo 2008b). Although some journals now require that the role of the sponsor in the design, conduct and publication of the study be described, this practice is not widespread (Tuech 2005).

Why it is important to do this review

This systematic review is the update of an original systematic review by two of the authors (Lexchin 2003), which investigated whether sponsorship by industry is associated with the publication of outcomes favorable to the sponsor. That review is now out of date and included pharmacoeconomic papers. We therefore updated it. Recent developments, such as the adoption of trial registration could lessen the bias associated with industry sponsorship, as publication bias can be more readily detected (DeAngelis 2004). On the other hand, the release of internal industry documents as a result of settlement agreements resulting from litigation against drug companies has revealed examples of industry manipulation of the conduct and publication of studies (Fugh-Berman 2010; Ross 2008; Steinman 2006; Vedula 2009). In addition, the scope of the review is now expanded to include device studies, as they are subject to the same biases as drug studies and are also often sponsored by companies with a financial interest in the outcome.

OBJECTIVES

The objectives were to investigate whether:

- sponsorship of drug and device studies by the pharmaceutical and device industries is associated with outcomes, including conclusions, that are favorable to the sponsor;

- drug and device studies sponsored by the pharmaceutical and device industries differ in their risk of bias compared with studies with other sources of sponsorship.

METHODS

Criteria for considering studies for this review

Types of studies

This review includes reports of studies that investigate samples of primary research studies. To avoid confusion we will use the terms 'studies' for the primary research studies and 'papers' for the reports of studies of primary research studies. We will use the term trials to describe studies of a randomized clinical trial design.

We included papers of cross-sectional studies, cohort studies, systematic reviews or meta-analyses that quantitatively compared primary research of drug or medical device studies sponsored by the pharmaceutical or device industry with studies that had other sources of sponsorship. Drugs were defined as medications that require approval by a regulatory authority as a prescription drug, recognizing that these approval standards vary worldwide. Devices were defined based on the Food and Drug Administration (FDA) definition as instruments intended for use in the diagnosis, treatment or prevention of disease.

We excluded papers without quantitative data. We excluded papers of the effects of sponsorship by non-pharmaceutical or non-device (e.g. tobacco, food or chemical) industries, and papers that evaluated the effectiveness of herbal supplements or medical procedures. Papers of mixed interventions (e.g. pharmaceuticals and educational interventions) were included if drug or device data were reported separately or could be obtained from the authors.

We excluded papers that quantitatively compared the association of sponsorship and results of syntheses of research studies (i.e. systematic reviews or meta-analyses) or pharmacoeconomic studies of drugs or devices. We also excluded analyses of pharmacokinetic studies.

Only papers published in full were included; we excluded letters to the editor and published conference presentations. We had no language restrictions.

Types of data

Drug and device papers including human research studies comparing drug to placebo, device to sham, drug to drug, drug to device, device to device, or mixed comparisons where the effectiveness, efficacy or harms of the drug or device were evaluated.

Types of methods

We defined sponsorship as funding or provision of free drug or devices. Drug or device studies with pharmaceutical or device industry funding versus those with other or undisclosed funding were included. We extracted the definition of industry funding verbatim from the included papers (see Data extraction and management) and reported this in the 'Characteristics of included studies' table. For analysis, we grouped the definitions into a variety of categories, including 100% pharmaceutical or device company funding, 100% non-profit funding, mixed funding (e.g. non-profit and industry collaboration), free provision of drug or device only, and undisclosed funding.

We included papers that compared industry sponsored studies with non-industry sponsored studies and also papers that compared studies of products by competing manufacturers (i.e. studies sponsored by the manufacturer of the test treatment with studies sponsored by the manufacturer of the control treatment); we analyzed the two types of papers separately.

Types of outcome measures

Primary outcomes

We included two primary outcomes:

1. Whether the results were favorable to the sponsor.
2. Whether the conclusions were favorable to the sponsor.

We used the definition of favorable results as described in the methods of the included papers. For efficacy results, most papers considered favorable results to be those that were statistically significant (e.g. $P < 0.05$ or 95% confidence interval excluding the possibility of no difference) in favor of the sponsor's product. Based on the previous review (Lexchin 2003), which found very few studies that reported results unfavorable to the sponsor, unfavorable results were combined with studies that reported results that were neutral or not statistically significant. For harms results, most papers regarded favorable results to be those where harms were not statistically significant (e.g. $P > 0.05$ or 95% confidence interval including the possibility of no difference) or results that had a statistically significant higher number of harms in the comparator group.

Conclusions in which the sponsor's product was preferred over the control treatment were considered favorable to the sponsor. For conclusions we did not distinguish between efficacy and harms, as conclusions are often overall qualitative judgements based on a benefit to harm balance.

Secondary outcomes

We included three secondary outcomes.

1. The size of the effect estimate in industry sponsored studies versus those with other sources of sponsorship.
2. The risk of bias in industry sponsored studies versus those with other sources of sponsorship.
3. The concordance between study results and conclusions, i.e. whether the conclusions agreed with the study results, in industry sponsored studies versus those with other sources of sponsorship.

We included papers that reported at least one of these secondary outcomes, even if it reported neither of the primary outcomes.

Search methods for identification of studies

Electronic searches

We searched Ovid MEDLINE (R) In-Process and other non-indexed citations and Ovid MEDLINE (R) (1948 to September 2010), Ovid EMBASE (1980 to September 2010) and the Cochrane Methodology Register (Issue 4, 2010) (Wiley InterScience Online). We searched the Web of Science (August 2011) for papers that cited any of the papers included in our review.

Search strategy

We used the strategy shown in Appendix 1 for Ovid MEDLINE and adapted it for the other databases.

Searching other resources

Other sources of data included author files, searches of reference lists of included papers and previous systematic reviews.

Data collection and analysis

Selection of studies

Two assessors (AL and OAB) screened the titles and abstracts, when available, of all retrieved records for obvious exclusions, and assessed the remaining papers based on full text. Potentially eligible papers were sent to the other assessors for final validation of the inclusion criteria. Any disagreements were resolved by consensus and reasons for exclusions of potentially eligible papers are described in the 'Characteristics of excluded studies' table. There was no need for translation of non-English papers.

Data extraction and management

Two assessors (AL and SS) independently extracted data from included papers; differences in data extraction were resolved by consensus.

We extracted data on the following.

- Year published.
- Country of corresponding author.
- Study objective.
- Study design used in the paper (cohort, cross-sectional, systematic review or meta-analysis, other).
- Study domain - descriptive (e.g. oncology drug trials).
- Study domain - category (drug/device class, specific disease, medical specialty/type of diseases, mixed).
- Type of studies (drug, device, drug and device, mixed).
- Type of comparisons (drug versus drug, drug versus placebo, device versus device, device versus sham, device versus drug, mixed, other).
- Sample strategy used to locate research studies (electronic search only, electronic plus other, sampling of journals, sampling by venue (e.g. conference abstracts)).
- Whether there were language restrictions on the search.
- Number of studies included in the sample.
- Time period covered by studies in the paper.
- Sponsorship categories coded in the paper. Categories were:
  - 100% pharmaceutical/device company funded;
  - 100% non-profit funded;
  - mixed funding - e.g. non-profit and industry collaboration;
  - provision of drug or device only; and
  - undisclosed funding.
- Sponsorship categories used in analysis in the paper (e.g. 100% industry funded grouped with mixed funding for industry category).
- Data on association between author conflicts of interest and outcomes.
- Description of role of the sponsor (if any). For example, definition of the sponsor's role in the design, implementation or reporting in the sample of studies.
- Criteria used to assess risk of bias of the studies included in the paper.
- Primary purpose of the study.
- Whether the paper commented on appropriateness of comparators.
- Data on sponsorship and results.
- Data on sponsorship and conclusions.
- Data on sponsorship and effect size.
- Data on sponsorship and risk of bias.
- Data on sponsorship and concordance between study results and conclusions.
- Additional relevant data.

Assessment of risk of bias in included studies

Since there are no validated criteria for assessing risk of bias in these types of papers, we developed our own criteria. We reviewed papers for high, low or unclear risk of bias for each of four criteria. If a criterion was met it was regarded as having low risk of bias, and high risk of bias otherwise. If we could not determine whether a criterion was met, we coded it as unclear. We used the following criteria:

- whether explicit and well defined criteria that could be replicated by others were used to select studies for inclusion/exclusion;
- whether there was an adequate study inclusion method, with two or more assessors selecting studies;
- whether the search for studies was comprehensive; and
- whether methodological differences and other characteristics that could introduce bias were controlled for or explored.

Measures of the effect of the methods

We performed a meta-analysis of the papers that reported the association of sponsorship with favorable study outcomes in cases where a pooled risk ratio (RR) and its 95% confidence interval could be computed.

The definition of a favorable outcome varied among papers. In some papers it was stated that favorable outcomes were outcomes favorable to the sponsor's product and in others favorable to the test treatment. This difference in terminology did not matter when the comparison was between active treatment and placebo, since the sponsor was related to the active treatment and not placebo. For head-to-head comparisons, however, the sponsor could be either the manufacturer of the test treatment or the control treatment. In these cases, when data were available, we recoded outcomes as to whether they were favorable to the sponsor's product.

We separately analyzed papers of industry sponsored head-to-head studies, comparing studies sponsored by the manufacturer of the test treatment with studies sponsored by the manufacturer of the comparator treatment. This was done by assigning the newest treatment (most recent FDA approval date) as the 'test' treatment and the older treatment as the 'comparator' treatment using similar methods as described by Bero et al. (Bero 2007) and comparing the number of studies favorable to the test treatment in the two groups (i.e. sponsor produces test treatment or sponsor produces comparator treatment).

At the time many of the papers were conducted, the approach was to assess the methodological quality of studies as opposed to an assessment of the risk of bias of studies. We therefore recoded the data on methodological quality into 'Risk of bias' categories. So, for example, a trial with adequate concealment of allocation was coded as low risk of bias and a trial with inadequate concealment of allocation as high risk of bias. Some papers assessed risk of bias by summarizing the information of individual domains in an

overall methodological quality score (i.e. a scale approach). There are substantial methodological problems related to quality scales (Jüni 1999) and their use is not recommended. We therefore did not combine the results obtained with these scales, but report the results descriptively.

Dealing with missing data

We contacted authors of the original papers in an attempt to obtain missing data. If papers included studies reporting conflicts of interest, but not the source of funding, we contacted the authors in order to obtain separate data for funding. In total we contacted authors of 36 papers and received additional data for 18 of these papers.

Assessment of heterogeneity

We assessed heterogeneity using I^2. In our initial protocol we intended to use a random-effects model when P was < 0.10 for the Chi^2 test. However, since this is not in line with current recommendations in the *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (Higgins 2011a), we instead used a random-effects model when statistical heterogeneity was substantial, defined as an I^2 > 50%.

Data synthesis

We used Review Manager (RevMan 2011) to analyze data. For dichotomous data we used the Mantel-Haenszel fixed-effect model to create a pooled RR. However, when substantial heterogeneity was observed, we used a DerSimonian-Laird random-effects model.

Subgroup analysis and investigation of heterogeneity

We considered the following factors as potential explanations for heterogeneity and investigated them in separate subgroup analyses.

1. We hypothesized that the association of industry sponsorship and favorable outcomes may be larger in high risk of bias papers. We assessed overall risk of bias of the included papers using the criteria described in 'Assessment of risk of bias in included studies'. We regarded papers with adequate study inclusion, a comprehensive search and controlling for bias as having a low risk of bias; others as having a high risk. We compared low risk of bias papers with high risk of bias papers in a subgroup analysis.
2. We compared papers of drug studies with device studies, as the mechanisms of influencing study outcomes may differ between the industries. For example, drug trials are more regulated than device trials, which could have an influence on biases in the design, conduct and reporting of the trials. We compared this in a subgroup analysis.
3. As the study domain might contribute to heterogeneity, we compared papers on specific treatments or diseases with papers of mixed domains in another subgroup analysis.

Sensitivity analysis

We undertook the following sensitivity analyses to test the robustness of our findings.

1. The primary analyses compared the number of favorable results and conclusions in papers with industry sponsorship to those with other sources of sponsorship; 'industry sponsorship' included 100% pharmaceutical/device company funding, mixed funding and provision of drug or device only. 'Non-industry sponsorship' included 100% government funding, 100% non-profit funding and undisclosed funding. In a sensitivity analysis, we excluded those studies with mixed funding sources and those with funding consisting solely of free product from the 'industry sponsorship' category, and excluded studies with undisclosed funding from the category of 'non-industry sponsorship', to determine if these had an impact on the initial analysis. As noted under 'Data extraction and management' we were reliant on how the studies in our review defined 'funding'.
2. Originally we had intended a sensitivity analysis restricted to papers with a low risk of bias using estimates adjusted for confounders (e.g. adjusted for sample size and concealment of allocation using logistic regression). However, because few papers with low risk of bias reported adjusted estimates in a way that we could use in our analysis, we decided to base our analysis on both low and high risk of bias papers reporting adjusted estimates. We used the generic inverse variance method to pool adjusted odds ratios in a fixed-effect model.
3. Due to the variability in study characteristics and methodology between papers, a random-effects model may be preferred, even if no statistical heterogeneity is observed. We therefore also undertook a sensitivity analysis where all analyses were based on a random-effects model.

RESULTS

Description of studies

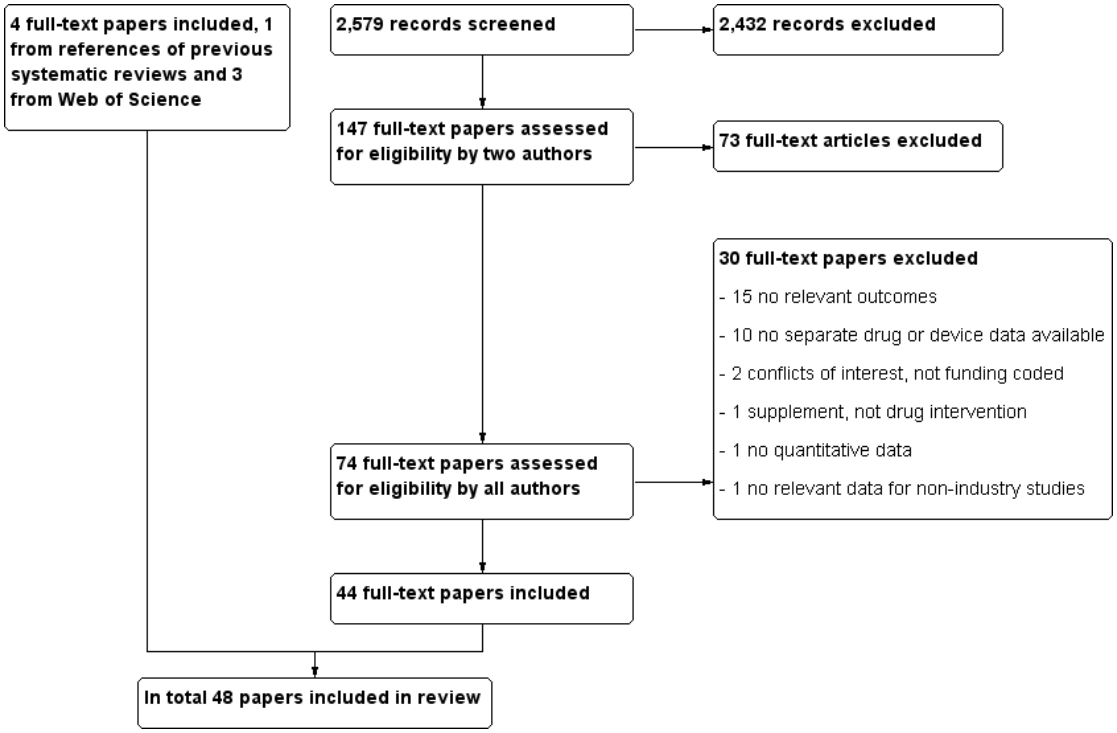
See: Characteristics of included studies; Characteristics of excluded studies.

See:Characteristics of included studies; Characteristics of excluded studies.

Results of the search

See: Figure 1

Figure 1. Study flow diagram.



After removal of duplicates, 2579 references were identified. From reading titles and abstracts, 2432 were eliminated as being not relevant to the review. Full-text papers were obtained for 147 references. From these 147 papers, 73 papers were excluded and 74 were retained for assessment by all assessors. Of these 74 papers, 30 were excluded (see Characteristics of excluded studies) and 44 included (see Characteristics of included studies). One additional paper (Chard 2000) was included as a result of searching reference lists of previous systematic reviews and three from searching Web of Science for papers citing any of the included papers (Jones 2010; Lubowitz 2007; Pengel 2009).

Included studies

See: Characteristics of included studies

The 48 papers were published between 1986 and 2010. Forty-six papers included mainly published studies, one included studies presented at a conference, and one included studies submitted to a medical journal. Thirty-seven papers included only drug studies, one only device studies, one drug and device studies and nine included different types of interventions (e.g. drugs, devices, behavioral interventions). Nineteen papers included studies related to specific drug classes, 13 related to specific medical specialties or types of diseases (e.g. endocrinology), six related to a specific disease, one related to a specific type of device, eight included all types of research studies and one did not state the domain. Various aspects of medicine were covered, but 10 (21%) papers were restricted to psychiatric diseases or drugs. Thirty-five papers included only clinical trials, two only observational studies, and 11 both clinical trials and observational studies. Eight papers included only drug versus drug comparisons, three only drug versus placebo, 34 mixed comparisons (e.g. drug versus drug, drug versus placebo) and three did not describe the kind of comparisons. The median number of included studies per paper was 137 (range: nine to 930). Of the 48 papers, 16 reported data on both favorable outcomes and risk of bias, 28 on favorable outcomes only and four on risk of bias only.

Risk of bias in included studies

See: Figure 2; Figure 3

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

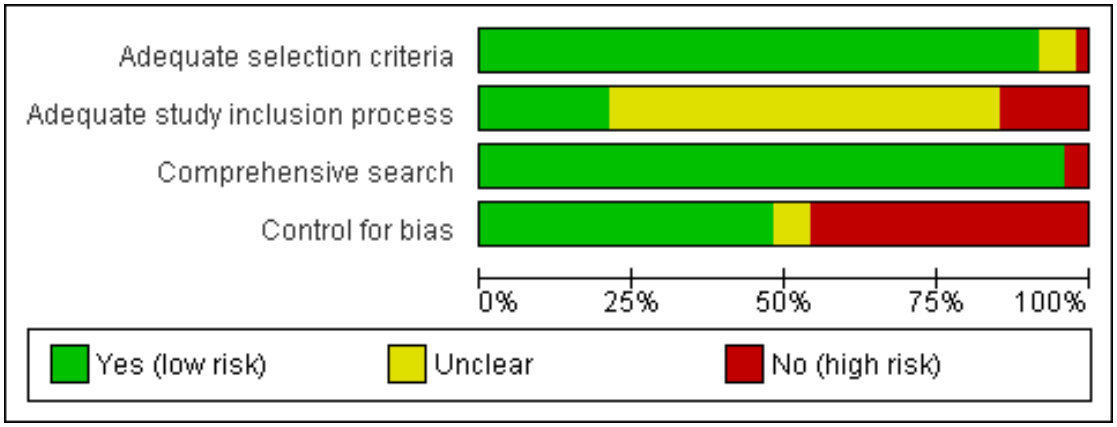
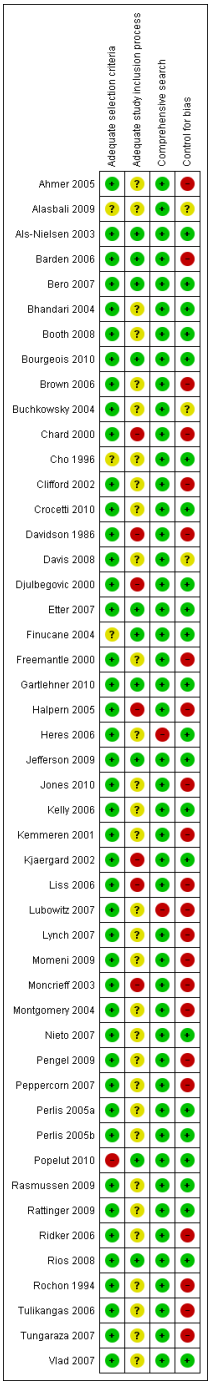


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Forty-four papers had low risk of bias for the selection criteria for inclusion of studies, three were unclear and one had high risk. Ten papers had low risk of bias for the study inclusion process, 31 were unclear and seven had high risk. Forty-six papers had low risk of bias from the search and two had high risk. Twenty-three papers had low risk of bias due to lack of control for bias in the studies, three were unclear and 22 had high risk. Nine papers were regarded as having an overall low risk of bias and 39 as a high risk of bias according to our criteria.

Effect of methods

Favorable results: industry sponsored versus non-industry sponsored studies

Fifteen papers, including 1746 studies (all drug studies), reported on sponsorship and efficacy results, and 14 could be combined in a pooled analysis. An analysis based on these 14 papers, including 1588 studies, found that industry sponsored studies more often had favorable efficacy results (e.g. those with significant P values) compared with non-industry sponsored studies, risk ratio (RR): 1.24 (95% confidence interval (CI): 1.14 to 1.35), I^2: 35% (Analysis 1.1). The paper that could not be included in the pooled analysis (Bhandari 2004), which had included 158 drug studies in general medicine, found similar results, odds ratio (OR): 1.6 (95% CI: 1.1 to 2.8).

Three papers, including 561 studies, found that industry sponsored studies more often had favorable harms results compared with non-industry sponsored studies, RR: 1.87 (95% CI: 1.54 to 2.27). No heterogeneity was observed (Analysis 1.2). The analysis was driven by one study (Nieto 2007) that contributed 97% of the weight in the analysis.

Favorable results: industry sponsorship by test treatment company versus industry sponsorship by comparator treatment company

Three papers, including 151 trials (all drug trials), compared efficacy results of trials sponsored by the manufacturer of the test treatment with trials sponsored by the manufacturer of the comparator treatment, and two could be combined in a pooled analysis. An analysis based on these two papers (Bero 2007; Rattinger 2009), which included 131 industry sponsored trials of statins and thiazolidinediones, found that trials were much more likely to favor the test treatment when they were sponsored by the manufacturer of the test treatment than when they were sponsored by the manufacturer of the comparator treatment, RR: 4.64 (95% CI: 2.08 to 10.32), I^2: 50% (Analysis 2.1). The paper that could not be included in the pooled analysis, which had included 20 selective serotonin reuptake inhibitor head-to-head trials, found that two trials favored the sponsor's drug, 18 had similar efficacy and none favored the comparator drug (Gartlehner 2010).

Favorable conclusions: industry sponsored versus non-industry sponsored studies

Twenty-four papers, including 4616 studies (4403 drug studies and 213 device studies), reported on sponsorship and conclusions, and 21 could be combined in a pooled analysis. An analysis based on these 21 papers, including 3941 studies (3821 drug studies and 120 device studies), found that industry sponsored studies more often had favorable conclusions than non-industry sponsored studies, RR: 1.31 (95% CI: 1.20 to 1.44), I^2: 83% (Analysis 3.1). Three papers could not be included in the pooled analysis. Of these, one paper of 301 psychiatric drug studies (Kelly 2006) found that industry sponsored studies more often had favorable conclusions than non-industry sponsored studies ($P < 0.001$) and similar findings were reported in a paper of 59 trials of antipsychotics ($P = 0.02$) (Montgomery 2004). A paper of 315 gastroenterology trials (222 drug trials and 93 device trials) did not find a difference in conclusions between industry sponsored trials and non-industry sponsored trials (industry: 86% favorable, non-industry: 83% favorable; $P = 0.57$) (Brown 2006).

Favorable conclusions: industry sponsorship by test treatment company versus sponsorship by comparator treatment company

Five papers, including 348 drug trials, compared conclusions of studies sponsored by the manufacturer of the test treatment with studies sponsored by the manufacturer of the comparator treatment, and three could be combined in a pooled analysis. An analysis based on these three papers (Bero 2007; Heres 2006; Rattinger 2009) including 154 industry sponsored trials of statins, antipsychotics and thiazolidinediones, found that trials were much more likely to favor the test treatment when they were sponsored by the manufacturer of the test treatment than when they were sponsored by the manufacturer of the control treatment, RR: 5.90 (95% CI: 2.79 to 12.49). No heterogeneity was observed (Analysis 4.1). A paper of 138 psychiatric drug studies (Kelly 2006) had similar findings, RR 2.80 (95% CI: 2.02 to 3.88), and a paper of 56 non-steroidal anti-inflammatory drug (NSAID) trials (Rochon 1994) found that 16 trials favored the sponsor's drug, 40 concluded that the drugs had similar effect and none favored the comparator drug.

Effect size: industry sponsored versus non-industry sponsored studies

Ten papers, including 906 studies (865 drug studies and 41 device studies), reported on sponsorship and effect size, but could not be pooled due to differences in their reporting of data. The results were heterogeneous.

Five papers, including 798 drug studies, did not find a difference in effect size between industry sponsored studies and non-industry sponsored studies. One paper including 370 drug trials (Als-Nielsen 2003) found mean z-scores of -1.48 (95% CI: -1.19 to -1.77) in industry sponsored trials, -1.77 (95% CI: -1.35 to -2.28) in trials with mixed sponsorship and -1.20 (95% CI: -0.59 to -1.81) in non-industry sponsored trials, which were not statistically significantly different. Similarly, a paper of 176 trials of drugs for acute pain and migraine (Barden 2006) did not find a difference in number of patients with pain relief between industry sponsored trials and non-industry sponsored trials. A paper of 124 trials comparing second-generation antipsychotics with first-generation antipsychotics (Davis 2008) did not find a difference in effect size between industry sponsored trials and non-industry sponsored trials (P = 0.57). A paper of 105 trials comparing selective serotonin reuptake inhibitors with alternative antidepressants (Freemantle 2000) also did not find a difference in effect size between industry sponsored trials and non-industry sponsored trials. A paper of 23 studies of chondrocyte implantation (Lubowitz 2007) did not find a difference in effect size between industry sponsored studies and non-industry sponsored studies for various outcomes.

In contrast, four papers found higher effects in industry sponsored studies. A paper including nine trials comparing clozapine with conventional antipsychotics (Moncrieff 2003) found that the treatment effect was higher in industry sponsored trials than in non-industry sponsored trials, standardized mean difference (SMD): -0.83 (95% CI: -1.06 to -0.61) versus SMD: -0.21 (95% CI: -0.34 to -0.07) (P < 0.001). Similarly, a paper of 41 dental implant trials (Popelut 2010) found that the failure rates were lower in industry sponsored trials compared with non-industry sponsored trials, OR: 0.21 (95% CI: 0.12 to 0.38). A paper including 15 trials of glucosamine (Vlad 2007) found that the effect size was higher in industry sponsored trials than in non-industry sponsored trials, SMD: 0.47 (95% CI: 0.24 to 0.70) versus SMD: 0.05 (95% CI: -0.32 to 0.41) (P = 0.05). One paper including 34 nicotine replacement drug trials (Etter 2007) found higher effects in industry sponsored trials compared with non-industry sponsored trials, OR: 1.90 versus OR 1.61 (P = 0.06).

Only one paper assessed effect size of harms (Kemmeren 2001). It included nine observational studies that compared third generation with second-generation oral contraceptives and found that the risk of thrombosis was lower in industry sponsored studies compared with non-industry sponsored studies, OR: 1.3 (95% CI: 1.0 to 1.7) versus OR 2.3 (95% CI: 1.7 to 3.2).

Risk of bias: industry sponsored versus non-industry sponsored studies

Nine papers, including 1505 studies (1327 drug studies, 178 device studies), measured risk of bias using five different composite quality scales (Brown, Cho, Cochrane, Jadad or Sackett) and the results were heterogeneous. Four papers did not find a difference in risk of bias between industry sponsored and non-industry sponsored studies (Cho 1996; Jefferson 2009; Lynch 2007; Vlad 2007), whereas five papers found lower risk of bias (i.e. higher methodological quality scores) in industry sponsored studies (Brown 2006; Djulbegovic 2000; Montgomery 2004; Pengel 2009; Perlis 2005a).

Three papers, including 487 drug trials, did not find a difference in low risk of bias from sequence generation in industry sponsored trials compared with non-industry sponsored trials, RR: 0.85 (95% CI: 0.52 to 1.41), I^2: 86% (Analysis 5.1). Ten papers, including 1311 drug trials, did not find a difference in low risk of bias from concealment of allocation in industry sponsored trials compared with non-industry sponsored trials, RR: 1.09 (95% CI: 0.86 to 1.38), I^2: 54% (Analysis 5.2). Nine papers, including 1216 drug trials, found that industry sponsored trials more often had low risk of bias from blinding compared with non-industry sponsored trials, RR: 1.32 (95% CI: 1.05 to 1.65), I^2: 74% (Analysis 5.3). Two papers, including 118 drug trials, did not find a difference in low risk of bias from loss to follow-up in industry sponsored trials compared with non-industry sponsored trials, RR: 0.98 (95% CI: 0.84 to 1.16). No heterogeneity was observed (Analysis 5.4).

Concordance between study results and conclusions: industry sponsored versus non-industry sponsored studies

Five papers, including 667 drug studies, reported on concordance between study efficacy results (e.g. as judged by their P values) and conclusions. Industry sponsored studies were less concordant than non-industry sponsored studies, RR: 0.84 (95% CI: 0.70 to 1.01), I^2: 67% (Analysis 6.1). One paper (Alasbali 2009), including 39 drug studies, found markedly higher lack of concordance in industry studies than the other four papers, and this was the reason for the high heterogeneity between papers.

One paper, of 211 corticosteroid studies with statistically significant harms results, found that industry sponsored studies more often concluded that the drug was safe than non-industry sponsored studies, RR: 3.68 (95% CI: 2.14 to 6.33) (Nieto 2007).

Subgroup analysis and investigation of heterogeneity

Because only three papers with efficacy results data had low risk of bias (Bero 2007; Bourgeois 2010; Etter 2007) and only four with conclusions data had low risk of bias (Als-Nielsen 2003; Bero 2007; Finucane 2004; Jefferson 2009) our comparison of low and high risk of bias papers was limited. Nonetheless, the association between industry sponsorship and favorable results was stronger in the low risk of bias group than in the high risk of bias group, RR: 1.50 (95% CI: 1.30 to 1.74) versus 1.14 (95% CI: 1.03 to 1.25) (test for subgroup differences P = 0.002) (Analysis 7.1). For conclusions, the differences between the groups went in the same

direction, RR: 1.54 (95% CI: 1.24 to 1.91) versus 1.26 (95% CI: 1.14 to 1.39), (test for subgroup differences P = 0.10) (Analysis 7.2).

Similarly, as only two papers (Lynch 2007; Ridker 2006) had data on device studies, the comparison between drug and device studies was limited. We did not find a difference in the association between sponsorship and conclusions in drug studies compared with device studies (Analysis 7.3). Only two papers with results data (Bourgeois 2010; Clifford 2002) and four with conclusion data (Buchkowsky 2004; Cho 1996; Davidson 1986; Kjaergard 2002) were of mixed domain. We did not find a difference in the association between sponsorship and results or conclusion in studies limited to specific treatments or diseases compared with studies of mixed domains (Analysis 7.4; Analysis 7.5).

Sensitivity analysis

Our re-analyses of the outcomes using variations in definition of sponsorship categories gave similar results as our main analyses for results, conclusions, sequence generation, concealment of allocation and blinding (Analysis 8.1; Analysis 8.2; Analysis 8.3; Analysis 8.4; Analysis 8.5). Our analyses based on pooling adjusted odds ratios confirmed our findings that industry sponsored trials compared with non-industry sponsored trials more often had favorable results, OR: 3.86 (95% CI: 1.93 to 7.70) and favorable conclusions, OR: 4.15 (95% CI: 2.40 to 7.19). No heterogeneity was observed (Analysis 8.6; Analysis 8.7). Similarly, the change from a fixed-effect model to a random-effects model did not affect our analyses (Analysis 8.8; Analysis 8.9; Analysis 8.10; Analysis 8.11; Analysis 8.12).

DISCUSSION

Summary of main results

We found that drug and device studies sponsored by the manufacturing company more often had favorable results (e.g. those with significant P values) and conclusions than those that were sponsored by other sources. The findings were consistent across a wide range of diseases and treatments. We did not find any differences in risk of bias of drug and device trials sponsored by industry compared with non-industry sponsored trials, except in relation to blinding, where industry sponsored trials seemed to have lower risk of bias. The evidence from device studies was limited, but the association between sponsorship and outcomes was similar to drug studies.

Reasons for observed heterogeneity

For the association between sponsorship and favorable results of drug and device studies the data had acceptable heterogeneity, but heterogeneity for conclusions was substantial with an I^2 of 83%. One reason for this was likely that the coding of favorable results was similar across the different papers, using statistical significance as the cut-off, but coding varied for conclusions. Some papers did not describe what they considered a favorable conclusion and others used scales, but for similar scales the cut-off varied between papers. For example, on the same six-point scale one paper used four as cut-off (Djulbegovic 2000) and another six as cut-off (Als-Nielsen 2003).

Also, the proportion of studies with favorable conclusions in the non-industry sponsored group might have contributed to the size of the association and thereby the heterogeneity. For example, while the Chard and Liss papers (Chard 2000; Liss 2006) had a similar proportion of favorable industry sponsored studies (both 98%), they reported very different proportions of favorable non-industry sponsored studies (32% and 97%) and this explains why the risk ratios reported in the two studies were not the same: 3.03 in Liss and 1.01 in Chard. Variations in study domain or definition of favorable conclusions might explain why the risk ratios reported in the two papers were not similar. For example, in the Chard paper, a conclusion was coded as favorable if the study authors supported the use of the treatment, even in the absence of a statistical significant result. Our subgroup analysis to test for differences in the association of sponsorship and results or conclusions between studies of mixed domains and studies related to specific treatments or diseases did not show different results, though this was a simplistic comparison.

Our data for the relationship between sponsorship and effect size showed mixed results, with most not finding a difference. All but one of these papers were restricted to specific treatments, which may explain the different findings. A recent study of systematic reviews of nine different drugs found that the influence of reporting biases on effect sizes varied considerably between drugs (Hart 2012). Furthermore, one paper found that even when adjusting for effect size, industry sponsored studies more often had favorable conclusions, compared with non-industry sponsored studies (Als-Nielsen 2003). Therefore, while the direction of the relationship between sponsorship and favorable outcomes was consistent, the size of the effect likely varies depending on domains.

Reasons for favorable outcomes in industry sponsored studies

The pharmaceutical and medical device industries have strong interests in scientific publications that present their products positively, as publications are the basis of regulatory, purchasing, and medical decisions. These interests can influence the design, conduct and publication of studies in ways that make the sponsor's product appear better than the comparator product (Bero 1996).

Several possible factors can explain the relationship between industry sponsorship and favorable outcomes. It has been argued that since many industry sponsored studies are undertaken to fulfill regulatory requirements, industry sponsored studies could have a lower risk of bias than non-industry sponsored studies (Rosefsky 2003). Even if this were true, it would not explain the association of industry sponsorship and favorable results and conclusions. In addition, we did not find evidence for differences in risk of bias except in relation to blinding, where industry sponsored trials tended to have a lower risk of bias, even when restricted to head-to head trials (Bero 2007). The papers comparing blinding between trials with different sponsorship often used a description of double blinding as an indicator for low risk of bias. Double blinding is an inconsistent term and does not ensure that, for example, outcome assessors are blinded (Devereaux 2001). The more frequent use of double blinding may therefore be a reporting issue, with industry trials being better reported. This is further substantiated by the fact that nearly all the papers finding a higher methodological quality score in industry studies used the Jadad scale, a scale which has been criticized for having more focus on the quality of reporting than on methodological quality (Lundh 2008).

On the other hand, evidence suggests that for non-industry trials, companies may prevent proper blinding by restricting access to placebo drugs (Christensen 2012) and therefore differences in adequate blinding may be real. In addition, double blinding can be used as a proxy for low risk of bias and trials without double blinding are on average more likely to have favorable results (Pildal 2007). The effect of this bias is in the opposite direction of our findings, as it would lead to industry sponsored studies having less favorable results and conclusions, and our findings can therefore, not be explained by differences in risk of bias between industry and non-industry sponsored studies.

Another possible explanation for our findings could be that industry studies have larger sample sizes, and would have a higher chance of achieving statistically significant results. Although industry trials seem in general to be of larger size (Als-Nielsen 2003; Booth 2008; Bourgeois 2010; Etter 2007; Perlis 2005a), when we restricted our analysis to studies controlling for sample size and other confounders, the relationship between industry sponsorship and favorable results or conclusions was still present.

Industry argues that the trials they sponsor are more likely to have favorable results because they fund research that has a high chance of achieving success (Palmer 2003). However, when independent investigators conduct non-industry sponsored trials, they in most cases test treatments that have been approved based on favorable industry trial results. Non-industry sponsored trials would therefore also be expected to achieve successful results, unless they are designed to answer different questions than industry sponsored trials. For example testing a new treatment against a well-established treatment instead of against placebo or against an outdated, inferior treatment.

Accordingly, it seems most plausible that industry achieves overly positive results through a variety of biasing choices in the design, conduct and reporting of their studies. For example, industry protocols might include inferior comparators that will increase the chance of their product's success. Djulbegovic et al. (Djulbegovic 2003) have argued that industry sponsored studies violate equipoise by choosing inferior competing treatment alternatives. Previous studies have found that industry sponsored trials more often use placebo control (Als-Nielsen 2003; Djulbegovic 2000; Estellat 2012; Katz 2006; Lathyris 2010), active comparators in inferior doses (Rochon 1994; Safer 2002) or inappropriate administration of the drugs (Johansen 1999). Or, industry sponsored studies may be biased in the coding of events and their data analysis (Furukawa 2004; Psaty 2008; Psaty 2010). Industry and its sponsored investigators also may selectively report favorable outcomes, fail to publish whole studies with unfavorable results, or publish studies with favorable results multiple times (Chan 2004; Dwan 2008; Gøtzsche 2011; McGauran 2010; Melander 2003; Rising 2008; Vedula 2009). While such biases in analyses and reporting have been documented in a number of cases, the papers included in this review focused on comparisons of published studies. Therefore, we are unable to determine the extent to which selective analysis or reporting contribute to our findings.

The finding that industry sponsored studies are more likely to have favorable conclusions could be explained by use of spin in conclusions (Boutron 2010). It should also be noted that some studies in the non-industry group likely had authors with conflicts of interest, which may have influenced their interpretation of study results (Stelfox 1998; Wang 2010) thereby diluting the measured effect of industry bias on study conclusions. Also, we coded studies as non-industry sponsored if they did not state who sponsored the study. As some of these studies were likely industry sponsored, this misclassification will have led to similar bias towards the null. In our sensitivity analyses, we excluded studies without sponsorship statements and did not see a change in results, but the confidence intervals were wide and did not exclude a possible bias towards the null.

Further evidence for industry bias stems from our comparison of studies sponsored by the manufacturer of the test treatment with those sponsored by the manufacturer of the control treatment. These studies had the advantage of comparing like with like, as they are restricted to specific drug classes or types of devices and have similar methodologies. Though limited to only three papers on drug trials, the findings show associations that are stronger than the comparison between industry and non-industry sponsored studies. These comparisons are restricted to drugs competing for the same market, which may put pressure on companies to influence outcomes to a greater degree than what is needed in placebo controlled trials to present the drug in a good light.

In sum, the industry bias associated with favorable results and conclusions may be mediated by factors other than traditional measures of the risk of bias (e.g. lack of concealment of allocation, blinding and drop-out) and sample size. This industry bias may

be partially mediated by such factors as the choice of comparators, dosing and timing of comparisons, selective analysis, and selective reporting.

Quality of the evidence

The majority of included papers were regarded as having a high risk of bias. Many lacked information on study conduct and did not control for confounders that could influence the relationship. Nevertheless, we did identify nine papers with low risk of bias and analyses restricted to these papers actually strengthened the relationship between sponsorship and outcomes. In general, there is convincing and consistent evidence for the existence of an industry bias in studies; however, the evidence for device studies is not as strong as for drug studies. While papers, including studies of devices and other interventions, have been published in the surgical field (Cunningham 2007; Khan 2008; Leopold 2003; Roach 2008; Shah 2005; Yao 2007), the papers do not report separate data for device studies.

Potential biases in the review process

We did a comprehensive search, our methods were based on prespecified criteria in a protocol as outlined in *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (Higgins 2011a) and our review has substantially increased the number of included papers from our previous review (Lexchin 2003). Nevertheless, there are some limitations. First, we decided only to include published papers. In our previous review (Lexchin 2003), we found problems with the completeness and quality of the data in conference abstracts and letters and therefore decided not to include them in this review. In our searches, we identified five conference abstracts and five letters that otherwise seemed to fit our inclusion criteria (Bond 2009; Djulbegovic 1999; Esquitin 2010; Higgins 2005; Koepp 1999; Mandelkern 1999; Thomas 2002; Vandenbroucke 2000; Wagena 2003; Wahlbeck 1999). Most were small (including a median of 30 studies, range 12 to 567 studies). Data from four papers could be included in a pooled analysis and gave similar findings for the association between sponsorship and study conclusions, RR: 1.57 (95% CI: 1.21 to 2.03), and RR: 1.32 (95% CI: 1.21 to 1.45) when they were added to the published papers (data available from authors on request). This makes publication bias unlikely to have influenced our results.

Second, our assessment of risk of bias in the included papers was not based on validated criteria similar to 'Risk of bias' assessment for clinical trials (Higgins 2011b). As no validated assessment tools exist for these type of papers, we developed our own criteria and included items similar to assessment tools for systematic reviews (Oxman 1991; Shea 2007).

Third, one item not included in our assessment of risk of bias in the papers was whether coders of outcomes were blinded to the sponsorship status of the studies. If these types of papers were undertaken by authors with a particular view on the drug industry, knowledge of sponsorship status could introduce bias in the assessment of whether outcomes were favorable, particularly for conclusions, as this is an outcome that is qualitative in nature. Some of the included papers were written by authors who had published multiple times in the area, and as such could be at increased risk of bias. These papers used coders who were both blinded and unblinded to the sponsorship status of the studies. The agreement in coding was high, suggesting a lack of bias (Als-Nielsen 2003; Bero 2007; Kjaergard 2002). Likewise, most of us (AL, JL, LB, SS) have published several times in the field and one of us (LB) is the author of four of the included papers (Bero 2007; Cho 1996; Rasmussen 2009; Rattinger 2009), which could have introduced bias. Because of the way data were presented in the papers, it was not possible to blind our data extraction process, so instead data extraction was undertaken by two of us with modest experience in the field and who were not authors of the original review or any of the included papers (AL, SS). Furthermore, our data extraction of outcomes did not involve any qualitative interpretation as we extracted actual numbers.

Fourth, if the papers included in this review included some of the same studies, their findings would not be independent. It was not possible to assess the potential overlap of studies as most papers did not provide a reference list of included studies. However, any overlap of included studies is likely to be very small and unimportant, as the disease and intervention topics of the included papers varied widely.

Agreements and disagreements with other studies or reviews

Our results are in agreement with previous systematic reviews (Bekelman 2003; Lexchin 2003; Schott 2010; Sismondo 2008a), though the risk ratios for the associations are less than previous quantitative estimates. Previous reviews did not distinguish between favorable results or conclusions, but looked at the association between sponsorship and outcomes. Bekelman found OR 3.60 (95% CI: 2.63 to 4.91) and Lexchin OR 4.05 (95% CI: 2.98 to 5.51). Translated to odds ratios, we found 2.15 (95% CI: 1.70 to 2.72) for results and 2.67 (95% CI 2.02 to 3.53) for conclusions in our review. This difference could be due to chance or it could be because the earlier reviews also included pharmacoeconomic analyses, non-drug studies, letters and conference presentations. It is also possible that the degree of industry bias has diminished over time, for example with a decrease in reporting bias due to trial registration. However, we do not find it likely. First, a recent study found that reporting bias is also prevalent in registered trials (Mathieu 2009). Second, one of the most recent papers (Bourgeois 2010) sampled drug trials registered at clinicaltrials.gov and conducted between 2000 and 2006 and found OR: 4.50 (95% CI:

2.60 to 7.80) for results, suggesting that industry bias has not changed over time.

AUTHORS' CONCLUSIONS

Implication for systematic reviews and evaluations of healthcare

Sponsorship of drug and device studies by the manufacturing company leads to more favorable results (e.g. those with significant P values) and conclusions than studies sponsored by other sources. Our analyses suggest the existence of an industry bias that cannot be explained by standard 'Risk of bias' assessments.

The findings resonate with current calls for access to full protocols and raw data when assessing drug and device interventions, for example while producing guidelines or systematic reviews, as relying on the published evidence of industry sponsored trials alone leads to too positive results, on average (Doshi 2012; Godlee 2009; Gøtzsche 2011; Krleza-Jeric 2005). To improve transparency, guidelines and systematic reviews should always report the source of sponsorship of trials, even when other risks of bias are assessed; this is currently not the case, neither in Cochrane reviews, nor elsewhere (Roseman 2011; Roseman 2012). We also suggest that the robustness of the results be assessed in a sensitivity analysis limited to non-industry sponsored studies with low risk of bias. Such requirements also necessitate proper reporting of funding in the original trial publications.

Journals should consider requiring independent statistical analysis, as is the case for JAMA (DeAngelis 2010), and that trial protocols and the raw data be posted on websites. Governments and non-commercial sponsors should also increase funds for independent drug and device trials and consider making submission of data from independent trials a mandatory requirement for gaining drug and device approval from regulatory agencies (Lexchin 2011). Independently sponsored trials should focus on testing innovative and essential treatments, as well as comparisons with existing effective treatments, thus shifting the resources spent on drug and device trials away from trials with a marketing purpose to those that are clinically important. Lastly, clinicians, guideline developers and others who rely on systematic reviews to aid decision-making should be aware of the influence of industry bias on research results and conclusions.

Implication for methodological research

Currently, the *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* acknowledges problems in relation to sponsorship, but does not recommend assessing industry sponsorship as a separate domain in the 'Risk of bias' assessment (Higgins 2011b). The assumption is that the influence of the sponsor will be mediated through the mechanisms of bias that are currently assessed, such as selective reporting of favorable outcomes. A Cochrane review that examined the association of sponsorship and selective outcome reporting bias (Dwan 2011) found uncertain evidence for the association; however, assessment of selective outcome reporting is complex and bias may be difficult to detect (Kirkham 2010). Some studies that have documented the extensive selective reporting of favorable outcomes have examined only industry sponsored studies (Rising 2008; Vedula 2009), thus making comparison with non-industry sponsored studies impossible.

Our data suggest that the more favorable outcomes in industry sponsored studies are mediated by factors other than those documented in the 'Risk of bias' assessment tool in Cochrane reviews. It has been suggested that industry bias should be regarded as a meta-bias, as industry sponsorship in itself is not a bias-producing process - as for example lack of concealment of allocation is - but a risk factor for bias (Goodman 2011). However, the characteristics currently assessed in the standard risk of bias approach in Cochrane reviews likely do not capture the additional risk of bias in industry sponsored studies. For example, the *Handbook* states that design issues, such as dosage of comparators are not issues of bias, but of generalizability. Yet, pharmacological interventions have dose-response curves, and testing drugs that are not in comparable places on their dose-response curves sets up a systematic, unfair and biased comparison (Safer 2002).

Consequently, our data suggest that industry sponsorship should be treated as bias-inducing and industry bias should be treated as a separate domain. There are many subtle mechanisms through which sponsorship may influence outcomes, and an assessment of sponsorship should therefore be used as a proxy for these mechanisms. Interestingly, the AMSTAR tool for methodological quality assessment of systematic reviews includes funding and conflicts of interest as a domain (Shea 2007). Methods for reporting, assessing and handling industry bias and other biases in future systematic reviews must be developed. Specifically, further methodological research should focus on how industry bias is handled in Cochrane reviews.

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REFERENCES

References to studies included in this review

Ahmer 2005 *{published and unpublished data}*
Ahmer S, Arya P, Anderson D, Faruqui R. Conflict of interest in psychiatry. *The Psychiatrist* 2005;**29**(8):302–4.

Alasbali 2009 *{published and unpublished data}*
Alasbali T, Smith M, Geffen N, Trope GE, Flanagan JG, Jin Y, et al. Discrepancy between results and abstract conclusions in industry- vs nonindustry-funded studies comparing topical prostaglandins. *American Journal of Ophthalmology* 2009;**147**(1):33–8.e2.

Als-Nielsen 2003 *{published data only (unpublished sought but not used)}*
Als-Nielsen B, Chen W, Gluud C, Kjaergard LL. Association of funding and conclusions in randomized drug trials: a reflection of treatment effect or adverse events?. *JAMA* 2003;**290**(7):921–8.

Barden 2006 *{published data only}*
Barden J, Derry S, McQuay HJ, Moore RA. Bias from industry trial funding? A framework, a suggested approach, and a negative result. *Pain* 2006;**121**(3):207–18.

Bero 2007 *{published and unpublished data}*
Bero L, Oostvogel F, Bacchetti P, Lee K. Factors associated with findings of published trials of drug-drug comparisons: why some statins appear more efficacious than others. *PLoS Medicine* 2007;**4**(6):e184.

Bhandari 2004 *{published data only (unpublished sought but not used)}*
Bhandari M, Busse JW, Jackowski D, Montori VM, Schünemann H, Sprague S, et al. Association between industry funding and statistically significant pro-industry findings in medical and surgical randomized trials. *CMAJ* 2004;**170**(4):477–80.

Booth 2008 *{published data only (unpublished sought but not used)}*
Booth CM, Cescon DW, Wang L, Tannock IF, Krzyzanowska MK. Evolution of the randomized controlled trial in oncology over three decades. *Journal of Clinical Oncology* 2008;**26**(33):5458–64.

Bourgeois 2010 *{published and unpublished data}*
Bourgeois FT, Murthy S, Mandl KD. Outcome reporting among drug trials registered in ClinicalTrials.gov. *Annals of Internal Medicine* 2010;**153**(3):158–66.

Brown 2006 *{published data only (unpublished sought but not used)}*
Brown A, Kraft D, Schmitz SM, Sharpless V, Martin C, Shah R, et al. Association of industry sponsorship to published outcomes in gastrointestinal clinical research. *Clinical Gastroenterology and Hepatology* 2006;**4**(12):1445–51.

Buchkowsky 2004 *{published data only}*
Buchkowsky SS, Jewesson PJ. Industry sponsorship and authorship of clinical trials over 20 years. *The Annals of Pharmacotherapy* 2004;**38**(4):579–85.

Chard 2000 *{published and unpublished data}*
Chard JA, Tallon D, Dieppe PA. Epidemiology of research into interventions for the treatment of osteoarthritis of the knee joint. *Annals of the Rheumatic Diseases* 2000;**59**(6):414–8.

Cho 1996 *{published data only (unpublished sought but not used)}*
Cho MK, Bero LA. The quality of drug studies published in symposium proceedings. *Annals of Internal Medicine* 1996;**124**(5):485–9.

Clifford 2002 *{published data only (unpublished sought but not used)}*
Clifford TJ, Barrowman NJ, Moher D. Funding source, trial outcome and reporting quality: are they related? Results of a pilot study. *BMC Health Services Research* 2002;**2**(1):18.

Crocetti 2010 *{published and unpublished data}*
Crocetti MT, Amin DD, Scherer R. Assessment of risk of bias among pediatric randomized controlled trials. *Pediatrics* 2010;**126**(2):298–305.

Davidson 1986 *{published data only (unpublished sought but not used)}*
Davidson RA. Source of funding and outcome of clinical trials. *Journal of General Internal Medicine* 1986;**1**(3):155–8.

Davis 2008 *{published data only}*
Davis JM, Chen N, Glick ID. Issues that may determine the outcome of antipsychotic trials: industry sponsorship and extrapyramidal side effect. *Neuropsychopharmacology* 2008;**33**(5):971–5.

Djulbegovic 2000 *{published data only (unpublished sought but not used)}*
Djulbegovic B, Lacevic M, Cantor A, Fields KK, Bennett CL, Adams JR, et al. The uncertainty principle and industry-sponsored research. *Lancet* 2000;**356**(9230):635–8.

Etter 2007 *{published data only (unpublished sought but not used)}*
Etter JF, Burri M, Stapleton J. The impact of pharmaceutical company funding on results of randomized trials of nicotine replacement therapy for smoking cessation: a meta-analysis. *Addiction* 2007;**102**(5):815–22.

Finucane 2004 *{published data only}*
Finucane TE, Boult CE. Association of funding and findings of pharmaceutical research at a meeting of a medical professional society. *The American Journal of Medicine* 2004;**117**(11):842–5.

Freemantle 2000 *{published data only (unpublished sought but not used)}*
Freemantle N, Anderson IM, Young P. Predictive value of pharmacological activity for the relative efficacy of antidepressant drugs. Meta-regression analysis. *The British Journal of Psychiatry* 2000;**177**:292–302.

Gartlehner 2010 *{published data only}*
Gartlehner G, Morgan L, Thieda P, Fleg A. The effect of study sponsorship on a systematically evaluated body of evidence of head-to-head trials was modest: secondary

analysis of a systematic review. *Journal of Clinical Epidemiology* 2010;**63**(2):117–25.

Halpern 2005 ***{published data only}***
Halpern SD, Barton TD, Gross R, Hennessy S, Berlin JA, Strom BL. Epidemiologic studies of adverse effects of anti-retroviral drugs: how well is statistical power reported. *Pharmacoepidemiology and Drug Safety* 2005;**14**(3):155–61.

Heres 2006 ***{published data only}***
Heres S, Davis J, Maino K, Jetzinger E, Kissling W, Leucht S. Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: An exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. *American Journal of Psychiatry* 2006;**163**(2):185–94.

Jefferson 2009 ***{published and unpublished data}***
Jefferson T, Di Pietrantonj C, Debalini MG, Rivetti A, Demicheli V. Relation of study quality, concordance, take home message, funding, and impact in studies of influenza vaccines: systematic review. *BMJ* 2009;**338**:b354.

Jones 2010 ***{published data only}***
Jones R, Younie S, Macallister A, Thornton J. A comparison of the scientific quality of publicly and privately funded randomized controlled drug trials. *Journal of Evaluation in Clinical Practice* 2010;**16**(6):1322–5.

Kelly 2006 ***{published and unpublished data}***
Kelly RE Jr, Cohen LJ, Semple RJ, Bialer P, Lau A, Bodenheimer A, et al. Relationship between drug company funding and outcomes of clinical psychiatric research. *Psychological Medicine* 2006;**36**(11):1647–56.

Kemmeren 2001 ***{published data only}***
Kemmeren JM, Algra A, Grobbee DE. Third generation oral contraceptives and risk of venous thrombosis: meta-analysis. *BMJ* 2001;**323**(7305):131–4.

Kjaergard 2002 ***{published and unpublished data}***
Kjaergard LL, Als-Nielsen B. Association between competing interests and authors' conclusions: Epidemiological study of randomised clinical trials published in the BMJ. *BMJ* 2002; **325**(7358):249–52.

Liss 2006 ***{published data only (unpublished sought but not used)}***
Liss H. Publication bias in the pulmonary/allergy literature: effect of pharmaceutical company sponsorship. *Israel Medical Association Journal:IMAJ* 2006;**8**(7):451–4.

Lubowitz 2007 ***{published data only}***
Lubowitz JH, Appleby D, Centeno JM, Woolf SK, Reid JB 3rd. The relationship between the outcome of studies of autologous chondrocyte implantation and the presence of commercial funding. *The American Journal of Sports Medicine* 2007;**35**(11):1809–16.

Lynch 2007 ***{published and unpublished data}***
Lynch JR, Cunningham MR, Warme WJ, Schaad DC, Wolf FM, Leopold SS. Commercially funded and United States-based research is more likely to be published; good-quality studies with negative outcomes are not. *The Journal of Bone and Joint Surgery* 2007;**89**(5):1010–8.

Momeni 2009 ***{published and unpublished data}***
Momeni A, Becker A, Bannasch H, Antes G, Blümle A, Stark GB. Association between research sponsorship and study outcome in plastic surgery literature. *Annals of Plastic Surgery* 2009;**63**(6):661–4.

Moncrieff 2003 ***{published and unpublished data}***
Moncrieff J. Clozapine v. conventional antipsychotic drugs for treatment-resistant schizophrenia: A re-examination. *British Journal of Psychiatry* 2003;**183**:161–6.

Montgomery 2004 ***{published data only (unpublished sought but not used)}***
Montgomery JH, Byerly M, Carmody T, Li B, Miller DR, Varghese F, et al. An analysis of the effect of funding source in randomized clinical trials of second generation antipsychotics for the treatment of schizophrenia. *Controlled Clinical Trials* 2004;**25**(6):598–612.

Nieto 2007 ***{published data only}***
Nieto A, Mazon A, Pamies R, Linana JJ, Lanuza A, Jiménez FO, et al. Adverse effects of inhaled corticosteroids in funded and nonfunded studies. *Archives of Internal Medicine* 2007;**167**(19):2047–53.

Pengel 2009 ***{published and unpublished data}***
Pengel LH, Barcena L, Morris PJ. The quality of reporting of randomized controlled trials in solid organ transplantation. *Transplant International* 2009;**22**(4):377–84.

Peppercorn 2007 ***{published data only (unpublished sought but not used)}***
Peppercorn J, Blood E, Winer E, Partridge A. Association between pharmaceutical involvement and outcomes in breast cancer clinical trials. *Cancer* 2007;**109**(7):1239–46.

Perlis 2005a ***{published data only (unpublished sought but not used)}***
Perlis CS, Harwood M, Perlis RH. Extent and impact of industry sponsorship conflicts of interest in dermatology research. *Journal of the American Academy of Dermatology* 2005;**52**(6):967–71.

Perlis 2005b ***{published and unpublished data}***
Perlis RH, Perlis CS, Wu Y, Hwang C, Joseph M, Nierenberg AA. Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry. *The American Journal of Psychiatry* 2005;**162**(10):1957–60.

Popelut 2010 ***{published and unpublished data}***
Popelut A, Valet F, Fromentin O, Thomas A, Bouchard P. Relationship between sponsorship and failure rate of dental implants: a systematic approach. *PLoS ONE* 2010;**5**(4): e10274.

Rasmussen 2009 ***{published and unpublished data}***
Rasmussen N, Lee K, Bero L. Association of trial registration with the results and conclusions of published trials of new oncology drugs. *Trials* 2009;**10**:116.

Rattinger 2009 ***{published and unpublished data}***
Rattinger G, Bero L. Factors associated with results and conclusions of trials of thiazolidinediones. *PLoS ONE* 2009;**4**(6):e5826.

Ridker 2006 ***{published data only (unpublished sought but not used)}***
Ridker PM, Torres J. Reported outcomes in major cardiovascular clinical trials funded by for-profit and not-for-profit organizations: 2000-2005. *JAMA* 2006;**295**(19): 2270–4.

Rios 2008 ***{published and unpublished data}***
Rios LP, Odueyungbo A, Moitri MO, Rahman MO, Thabane L. Quality of reporting of randomized controlled trials in general endocrinology literature. *The Journal of Clinical Endocrinology and Metabolism* 2008;**93**(10): 3810–6.

Rochon 1994 ***{published data only (unpublished sought but not used)}***
Rochon PA, Gurwitz JH, Simms RW, Fortin PR, Felson DT, Minaker KL, et al. A study of manufacturer-supported trials of nonsteroidal anti-inflammatory drugs in the treatment of arthritis. *Archives of Internal Medicine* 1994;**154**(2):157–63.

Tulikangas 2006 ***{published data only}***
Tulikangas PK, Ayers A, O'Sullivan DM. A meta-analysis comparing trials of antimuscarinic medications funded by industry or not. *BJU International* 2006;**98**(2):377–80.

Tungaraza 2007 ***{published data only (unpublished sought but not used)}***
Tungaraza T, Poole R. Influence of drug company authorship and sponsorship on drug trial outcomes. *The British Journal of Psychiatry* 2007;**191**:82–3.

Vlad 2007 ***{published data only (unpublished sought but not used)}***
Vlad SC, LaValley MP, McAlindon TE, Felson DT. Glucosamine for pain in osteoarthritis: why do trial results differ?. *Arthritis and Rheumatism* 2007;**56**(7):2267–77.

References to studies excluded from this review

Chowers 2009 ***{published data only}***
Chowers MY, Gottesman BS, Leibovici L, Pielmeier U, Andreassen S, Paul M. Reporting of adverse events in randomized controlled trials of highly active antiretroviral therapy: systematic review. *Journal of Antimicrobial Chemotherapy* 2009;**64**(2):239–50.

Conen 2008 ***{published data only}***
Conen D, Torres J, Ridker PM. Differential citation rates of major cardiovascular clinical trials according to source of funding a survey from 2000 to 2005. *Circulation* 2008;**118** (13):1321–7.

Cunningham 2007 ***{published data only (unpublished sought but not used)}***
Cunningham MR, Warme WJ, Schaad DC, Wolf FM, Leopold SS. Industry-funded positive studies not associated with better design or larger size. *Clinical Orthopaedics and Related Research* 2007;**457**:235–41.

Friedman 2004 ***{published data only (unpublished sought but not used)}***
Friedman LS, Richter ED. Relationship between conflicts of interest and research results. *Journal of General Internal Medicine* 2004;**19**(1):51–6.

Glick 2006 ***{published data only}***
Glick N, MacDonald I, Knoll G, Brabant A, Gourishankar S. Factors associated with publication following presentation at a transplantation meeting. *American Journal of Transplantation* 2006;**6**(3):552–6.

Hall 2007 ***{published data only}***
Hall R, de Antueno C, Webber A, Canadian Research Ethics Board. Publication bias in the medical literature: A review by a Canadian Research Ethics Board. *Canadian Journal of Anesthesia* 2007;**54**(5):380–8.

Hill 2007 ***{published data only}***
Hill CL, Buchbinder R, Osborne R. Quality of reporting of randomized clinical trials in abstracts of the 2005 annual meeting of the American College of Rheumatology. *Journal of Rheumatology* 2007;**34**(12):2476–80.

Jagsi 2009 ***{published data only (unpublished sought but not used)}***
Jagsi R, Sheets N, Jankovic A, Motomura AR, Amarnath S, Ubel PA. Frequency, nature, effects, and correlates of conflicts of interest in published clinical cancer research. *Cancer* 2009;**115**(12):2783–91.

Khan 2008 ***{published data only (unpublished sought but not used)}***
Khan SN, Mermer MJ, Myers E, Sandhu HS. The roles of funding source, clinical trial outcome, and quality of reporting in orthopedic surgery literature. *American Journal of Orthopedics* 2008;**37**(12):E205–12.

Kjaergard 1999 ***{published data only (unpublished sought but not used)}***
Kjaergard LL, Nikolova D, Gluud C. Randomized clinical trials in HEPATOLOGY: predictors of quality. *Hepatology* 1999;**30**(5):1134–8.

Krzyzanowska 2003 ***{published data only}***
Krzyzanowska MK, Pintilie M, Tannock IF. Factors associated with failure to publish large randomized trials presented at an oncology meeting. *JAMA* 2003;**290**(4): 495–501.

Kulier 2004 ***{published data only}***
Kulier R, Helmerhorst FM, Maitra N, Gülmezoglu AM. Effectiveness and acceptability of progestogens in combined oral contraceptives - A systematic review. *Reproductive Health* 2004;**1**(1):1.

Kulkarni 2007 ***{published data only}***
Kulkarni AV, Busse JW, Shams I. Characteristics associated with citation rate of the medical literature. *PLoS ONE* 2007;**2**(5):e403.

Lai 2006 ***{published data only (unpublished sought but not used)}***
Lai R, Chu R, Fraumeni M, Thabane L. Quality of randomized controlled trials reporting in the primary treatment of brain tumors. Journal of Clinical Oncology 2006; Vol. 24, issue 7:1136–44.

Leopold 2003 ***{published data only (unpublished sought but not used)}***
Leopold SS, Warme WJ, Fritz Braunlich E, Shott S. Association between funding source and study outcome in orthopaedic research. *Clinical Orthopaedics and Related Research* 2003;**415**:293–301.

Leucht 2009a ***{published data only}***
Leucht S, Corves C, Arbter D, Engel RR, Li C, Davis JM. Second-generation versus first-generation antipsychotic

drugs for schizophrenia: a meta-analysis. *The Lancet* 2009; **373**(9657):31–41.

Leucht 2009b ***{published data only}***
Leucht S, Komossa K, Rummel-Kluge C, Corves C, Hunger H, Schmid F, et al. A meta-analysis of head-to-head comparisons of second-generation antipsychotics in the treatment of schizophrenia. *American Journal of Psychiatry* 2009;**166**(2):152–63.

McLennan 2008 ***{published data only}***
McLennan M, Leong FC, Steele A, Harris J. The influence of industry sponsorship on the acceptance of abstracts and their publication. *American Journal of Obstetrics and Gynecology* 2008;**198**(5):579.e1–4.

Montori 2005 ***{published data only}***
Montori VM, Devereaux PJ, Adhikari NK, Burns KE, Eggert CH, Briel M, et al. Randomized trials stopped early for benefit: a systematic review. *JAMA* 2005;**294**(17): 2203–9.

Nkansah 2009 ***{published data only}***
Nkansah N, Nguyen T, Iraninezhad H, Bero L. Randomized trials assessing calcium supplementation in healthy children: relationship between industry sponsorship and study outcomes. *Public Health Nutrition* 2009;**12**(10):1931–7.

Okike 2007 ***{published data only (unpublished sought but not used)}***
Okike K, Kocher MS, Mehlman CT, Bhandari M. Conflict of interest in orthopaedic research: An association between findings and funding in scientific presentations. *The Journal of Bone and Joint Surgery* 2007;**89**(3):608–13.

Okike 2008 ***{published data only}***
Okike K, Kocher MS, Mehlman CT, Heckman JD, Bhandari M. Nonscientific factors associated with acceptance for publication in The Journal of Bone and Joint Surgery (American Volume). *The Journal of Bone and Joint Surgery* 2008;**90**(11):2432–7.

Procyshyn 2004 ***{published data only (unpublished sought but not used)}***
Procyshyn RM, Chau A, Fortin P, Jenkins W. Prevalence and outcomes of pharmaceutical industry-sponsored clinical trials involving clozapine, risperidone, or olanzapine. *Canadian Journal of Psychiatry* 2004;**49**(9):601–6.

Roach 2008 ***{published data only (unpublished sought but not used)}***
Roach JW, Skaggs DL, Sponseller PD, Macleod LM. Is research presented at the scoliosis research society annual meeting influenced by industry funding?. *Spine* 2008;**33** (20):2208–12.

Sanossian 2006 ***{published data only}***
Sanossian N, Ohanian AG, Saver JL, Kim LI, Ovbiagele B. Frequency and determinants of nonpublication of research in the stroke literature. *Stroke* 2006;**37**:2588–92.

Shah 2005 ***{published data only (unpublished sought but not used)}***
Shah RV, Albert TJ, Bruegel-Sanchez V, Vaccaro AR, Hilibrand AS, Grauer JN. Industry support and correlation to study outcome for papers published in spine. *Spine* 2005; **30**(9):1099–104.

Thomas 2008 ***{published data only}***
Thomas O, Thabane L, Douketis J, Chu R, Westfall AO, Allison DB. Industry funding and the reporting quality of large long-term weight loss trials. *International Journal of Obesity* 2008;**32**(10):1531–6.

Watanabe 2010 ***{published data only}***
Watanabe N, Omori IM, Nakagawa A, Cipriani A, Barbui C, McGuire H, et al. Safety reporting and adverse-event profile of mirtazapine described in randomized controlled trials in comparison with other classes of antidepressants in the acute-phase treatment of adults with depression: systematic review and meta-analysis. *CNS Drugs* 2010;**24** (1):35–53.

Yao 2007 ***{published data only (unpublished sought but not used)}***
Yao F, Singer M, Rosenfeld RM. Randomized controlled trials in otolaryngology journals. *Otolaryngology-Head and Neck Surgery* 2007;**137**(4):539–44.

Yaphe 2001 ***{published data only (unpublished sought but not used)}***
Yaphe J, Edman R, Knishkowy B, Herman J. The association between funding by commercial interests and study outcome in randomized controlled drug trials. *Family Practice* 2001;**18**(6):565–8.

Additional references

Bekelman 2003
Bekelman JE, Li Y, Gross CP. Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA* 2003;**289**(4):454–65.

Bero 1996
Bero LA, Rennie D. Influences on the quality of published drug studies. *International Journal of Technology Assessment in Health Care* 1996;**12**(2):209–37.

Bond 2009
Bond K, Bow S, O'Gorman K, Spooner C, Lemière C, Tjosvold L, et al. The effect of pharmaceutical industry sponsorship on randomized trials for long-acting beta-agonist/inhaled corticosteroid combination therapy for asthma: challenges for estimating comparative effectiveness and safety. 17th Cochrane Colloquium; 2009 Oct 11-14; Singapore. 2009.

Boutron 2010
Boutron I, Dutton S, Ravaud P, Altman DG. Reporting and interpretation of randomized controlled trials with statistically nonsignificant results for primary outcomes. *JAMA* 2010;**303**(20):2058–64.

Chan 2004
Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *JAMA* 2004;**291**(20):2457–65.

Christensen 2012
Christensen M, Knop FK. The unobtainable placebo: control of independent clinical research by industry?. Lancet 2012; Vol. 379, issue 9810:30.

DeAngelis 2004
DeAngelis CD, Drazen JM, Frizelle FA, Haug C, Hoey J, Horton R, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. JAMA 2004; Vol. 292, issue 11:1363–4.

DeAngelis 2010
DeAngelis CD, Fontanarosa PB. The importance of independent academic statistical analysis. *Biostatistics* 2010; **11**(3):383–4.

Devereaux 2001
Devereaux PJ, Manns BJ, Ghali WA, Quan H, Lacchetti C, Montori VM, et al. Physician interpretations and textbook definitions of blinding terminology in randomized controlled trials. *JAMA* 2001;**285**(15):2000–3.

Djulbegovic 1999
Djulbegovic B, Bennett CL, Lyman GH. Violation of the uncertainty principle in conduct of randomized controlled trials (RCTs) of erythropoietin (EPO). *Blood* 1999;**94 (suppl 1)**:399A.

Djulbegovic 2003
Djulbegovic B, Cantor A, Clarke M. The importance of preservation of the ethical principle of equipoise in the design of clinical trials: relative impact of the methodological quality domains on the treatment effect in randomized controlled trials. *Accountability in Research* 2003;**10**(4):301–15.

Dorsey 2010
Dorsey ER, de Roulet J, Thompson JP, Reminick JI, Thai A, White-Stellato Z, et al. Funding of US biomedical research, 2003-2008. *JAMA* 2010;**303**(2):137–43.

Doshi 2012
Doshi P, Jones M, Jefferson T. Rethinking credible evidence synthesis. *BMJ* 2012;**344**:d7898.

Dwan 2008
Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan AW, Cronin E, et al. Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS ONE* 2008;**3**(8):e3081.

Dwan 2011
Dwan K, Altman DG, Cresswell L, Blundell M, Gamble CL, Williamson PR. Comparison of protocols and registry entries to published reports for randomised controlled trials. *Cochrane Database of Systematic Reviews* 2011, Issue 1. [DOI: 10.1002/14651858.MR000031.pub2]

Esquitin 2010
Esquitin R, Aneja A, Shah KA, Razzouk L, Mann DM, Ross JS, et al. The impact of conflicts of interest on adjudication and outcomes in cardiovascular clinical trials. *Journal of American College of Cardiology* 2010;**55**:A132.E1237.

Estellat 2012
Estellat C, Ravaud P. Lack of head-to-head trials and fair control arms: randomized controlled trials of biologic treatment for rheumatoid arthritis. *Archives of Internal Medicine* 2012;**172**(3):237–44.

Fugh-Berman 2010
Fugh-Berman AJ. The haunting of medical journals: how ghostwriting sold "HRT". *PLoS Medicine* 2010;**7**(9): e1000335.

Furukawa 2004
Furukawa TA. All clinical trials must be reported in detail and made publicly available. BMJ 2004; Vol. 329, issue 7466:626.

Godlee 2009
Godlee F. We want raw data, now. *BMJ* 2009;**339**:b5405.

Goodman 2011
Goodman S, Dickersin K. Metabias: a challenge for comparative effectiveness research. Annals of Internal Medicine 2011; Vol. 155, issue 1:61–2.

Gøtzsche 2011
Gøtzsche PC. Why we need easy access to all data from all clinical trials and how to accomplish it. Trials 2011; Vol. 12:249.

Hart 2012
Hart B, Lundh A, Bero L. Effect of reporting bias on meta-analyses of drug trials: reanalysis of meta-analyses. *BMJ* 2012;**344**:d7202.

Higgins 2005
Higgins A, Lord S, Wortley S, Belcher J. Endometrial ablation for heavy menstrual bleeding: the relationship between funding sources and trial outcome. 13th Cochrane Colloquium; 2005 Oct 22-26; Melbourne. 2005.

Higgins 2011a
Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Higgins 2011b
Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Johansen 1999
Johansen HK, Gøtzsche PC. Problems in the design and reporting of trials of antifungal agents encountered during meta-analysis. *JAMA* 1999;**282**(18):1752–9.

Jüni 1999
Juni P, Witschi A, Bloch R, Egger M. The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999; **282**(11):1054–60.

Katz 2006
Katz KA, Karlawish JH, Chiang DS, Bognet RA, Propert KJ, Margolis DJ. Prevalence and factors associated with use of placebo control groups in randomized controlled trials in psoriasis: a cross-sectional study. *Journal of the American Academy of Dermatology* 2006;**55**(5):814–22.

Kirkham 2010
Kirkham JJ, Dwan KM, Altman DG, Gamble C, Dodd S, Smyth R, et al. The impact of outcome reporting bias

in randomised controlled trials on a cohort of systematic reviews. *BMJ* 2010;**340**:c365.

Koepp 1999
Koepp R, Miles SH. Meta-analysis of tacrine for Alzheimer Disease: the influence of industry sponsors. *JAMA* 1999; **281**(24):2287.

Krleza-Jeric 2005
Krleza-Jeric K, Chan AW, Dickersin K, Sim I, Grimshaw J, Gluud C. Principles for international registration of protocol information and results from human trials of health related interventions: Ottawa statement (part 1). *BMJ* 2005;**330**(7497):956–8.

Lathyris 2010
Lathyris DN, Patsopoulos NA, Salanti G, Ioannidis JP. Industry sponsorship and selection of comparators in randomized clinical trials. *European Journal of Clinical Investigation* 2010;**40**(2):172–82.

Lexchin 2011
Lexchin J. Those who have the gold make the evidence: how the pharmaceutical industry biases the outcomes of clinical trials of medications. *Science and Engineering Ethics* 2012;**18**(2):247–61.

Lundh 2008
Lundh A, Gøtzsche PC. Recommendations by Cochrane Review Groups for assessment of the risk of bias in studies. *BMC Medical Research Methodology* 2008;**8**:22.

Mandelkern 1999
Mandelkern M. Manufacturer support and outcome. The Journal of Clinical Psychiatry 1999; Vol. 60, issue 2:122–3.

Mathieu 2009
Mathieu S, Boutron I, Moher D, Altman DG, Ravaud P. Comparison of registered and published primary outcomes in randomized controlled trials. *JAMA* 2009;**302**(9): 977–84.

McGauran 2010
McGauran N, Wieseler B, Kreis J, Schuler YB, Kolsch H, Kaiser T. Reporting bias in medical research - a narrative review. *Trials* 2010;**11**:37.

Melander 2003
Melander H, Ahlqvist-Rastad J, Meijer G, Beermann B. Evidence b(i)ased medicine--selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications. *BMJ* 2003;**326**(7400):1171–3.

Oxman 1991
Oxman AD, Guyatt GH, Singer J, Goldsmith CH, Hutchison BG, Milner RA, et al. Agreement among reviewers of review articles. *Journal of Clinical Epidemiology* 1991;**44**(1):91–8.

Palmer 2003
Palmer RH. Results of clinical trials sponsored by for-profit vs nonprofit entities. JAMA 2003; Vol. 290, issue 23:3070.

PhRMA 2008
PhRMA. Pharmaceutical marketing in perspective: its value and role as one of many factors informing prescribing. http://www.phrma.org/issues/sales-marketing (accessed 22 February 2012).

Pildal 2007
Pildal J, Hróbjartsson A, Jørgensen KJ, Hilden J, Altman DG, Gøtzsche PC. Impact of allocation concealment on conclusions drawn from meta-analyses of randomized trials. *International Journal of Epidemiology* 2007;**36**(4):847–57.

Psaty 2008
Psaty BM, Kronmal RA. Reporting mortality findings in trials of rofecoxib for Alzheimer disease or cognitive impairment: a case study based on documents from rofecoxib litigation. *JAMA* 2008;**299**(15):1813–7.

Psaty 2010
Psaty BM, Prentice RL. Minimizing bias in randomized trials: the importance of blinding. *JAMA* 2010;**304**(7): 793–4.

RevMan 2011
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Rising 2008
Rising K, Bacchetti P, Bero L. Reporting bias in drug trials submitted to the Food and Drug Administration: review of publication and presentation. *PLoS Medicine* 2008;**5**(11): e217.

Rosefsky 2003
Rosefsky JB. Results of clinical trials sponsored by for-profit vs nonprofit entities. JAMA 2003; Vol. 290, issue 23: 3070–1.

Roseman 2011
Roseman M, Milette K, Bero LA, Coyne JC, Lexchin J, Turner EH, et al. Reporting of conflicts of interest in meta-analyses of trials of pharmacological treatments. *JAMA* 2011;**305**(10):1008–17.

Roseman 2012
Roseman M, Turner EH, Lexchin J, Coyne JC, Bero LA, Thombs BD. Reporting of conflicts of interest from drug trials in Cochrane reviews: cross sectional study. *BMJ* 2012; **345**:e5155.

Ross 2008
Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest authorship and ghostwriting in publications related to rofecoxib: a case study of industry documents from rofecoxib litigation. *JAMA* 2008;**299**(15):1800–12.

Safer 2002
Safer DJ. Design and reporting modifications in industry-sponsored comparative psychopharmacology trials. *The Journal of Nervous and Mental Disease* 2002;**190**(9):583–92.

Schott 2010
Schott G, Pachl H, Limbach U, Gundert-Remy U, Ludwig WD, Lieb K. The financing of drug trials by pharmaceutical companies and its consequences. Part 1: a qualitative, systematic review of the literature on possible influences on the findings, protocols, and quality of drug trials. *Deutsches Arzteblatt International* 2010;**107**(16):279–85.

Shea 2007
Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology* 2007;**7**:10.

Sismondo 2008a
Sismondo S. Pharmaceutical company funding and its consequences: a qualitative systematic review. *Contemporay Clinical Trials* 2008;**29**(2):109–13.

Sismondo 2008b
Sismondo S. How pharmaceutical industry funding affects trial outcomes: causal structures and responses. *Social Science & Medicine* 2008;**66**(9):1909–14.

Steinman 2006
Steinman MA, Bero LA, Chren M-M, Landefeld S. The promotion of gabapentin: an analysis of internal industry documents. *Annals of Internal Medicine* 2006;**145**(4): 284–93.

Stelfox 1998
Stelfox HT, Chua G, O'Rourke K, Detsky AS. Conflict of interest in the debate over calcium-channel antagonists. *The New England Journal of Medicine* 1998;**338**(2):101–6.

Thomas 2002
Thomas PS, Tan KS, Yates DH. Sponsorship, authorship, and accountability. Lancet 2002; Vol. 359, issue 9303:351.

Tuech 2005
Tuech JJ, Moutel G, Pessaux P, Thoma V, Schraub S, Herve C. Disclosure of competing financial interests and role of sponsors in phase III cancer trials. *European Journal of Cancer* 2005;**41**(15):2237–40.

Vandenbroucke 2000
Vandenbroucke JP, Helmerhorst FM, Rosendaal FR. Competing interests and controversy about third generation oral contraceptives. BMJ readers should know whose words they read. BMJ 2000; Vol. 320, issue 7231:381–2.

Vedula 2009
Vedula SS, Bero L, Scherer RW, Dickersin K. Outcome reporting in industry-sponsored trials of gabapentin for off-label use. *The New England Journal of Medicine* 2009;**361** (20):1963–71.

Wagena 2003
Wagena EJ, Knipschild PG. The efficacy of bupropion in relation to competing interests and methodological quality. *European Respiratory Journal* 2003;**22**:165.

Wahlbeck 1999
Wahlbeck K, Adams C. Beyond conflict of interest. Sponsored drug trials show more-favourable outcomes. BMJ 1999; Vol. 318, issue 7181:465.

Wang 2010
Wang AT, McCoy CP, Murad MH, Montori VM. Association between industry affiliation and position on cardiovascular risk with rosiglitazone: cross sectional systematic review. *BMJ* 2010;**340**:c1344.

Wyatt 1991
Wyatt J. Use and sources of medical knowledge. *Lancet* 1991;**338**(8779):1368–73.

References to other published versions of this review

Lexchin 2003
Lexchin J, Bero L, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: a systematic review. *BMJ* 2003;**326**(7400):1167–70.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ahmer 2005

Methods	To study the association between study support and outcome in randomized controlled trials (RCTs) of psychotropic drugs. All RCTs published in *Acta Psychiatrica Scandinavica* (APS), *American Journal of Psychiatry* (AJP), *Archives of General Psychiatry* (AGP) and *British Journal of Psychiatry* (BJP) from July 1998 to June 2003.
Data	188 psychotropic drug RCTs (various comparators).
Comparisons	Manufacturer support and no support.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Database and handsearch.
Control for bias?	No	Subgroup analysis, but only of journal name.

Alasbali 2009

Methods	To investigate the relationship between industry vs non-industry funded publications comparing the efficacy of topical prostaglandin analogs by evaluating the correspondence between the statistical significance of the publication's main outcome measure and its abstract conclusions. Studies published from 1966 to November 2007
Data	39 reports of head-to-head comparisons of topical prostaglandins in ophthalmology (various study designs)
Comparisons	Industry and non-industry funding.
Outcomes	Study conclusions, study results and concordance between study results and conclusions
Notes	

Risk of bias

Alasbali 2009 (*Continued*)

Item	Authors' judgement	Description
Adequate selection criteria?	Unclear	Not clear which study designs and whether placebo controlled studies were included, cannot be replicated
Adequate study inclusion process?	Unclear	Three assessors for data extraction, but unclear in relation to study inclusion
Comprehensive search?	Yes	MEDLINE and handsearching.
Control for bias?	Unclear	Not described.

Als-Nielsen 2003

Methods	To explore whether the association between funding and conclusions in randomized drug trials reflects treatment effects or adverse events. All randomized trials included in eligible meta-analyses from a random sample of Cochrane reviews obtained in May 2001 (RCTs from 1971 to 2000)
Data	370 drug RCTs (mixed comparisons).
Comparisons	Funding from non-profit organizations, not reported, both non-profit and for-profit organizations, and for-profit organizations
Outcomes	Study conclusions, effect size and methodological quality (generation of randomization sequence, concealment of allocation and double blinding)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	One assessor screened and two involved in final inclusion.
Comprehensive search?	Yes	Identification via Cochrane reviews.
Control for bias?	Yes	Logistic regression adjusting for treatment effect, adverse events, and other potentially confounding trial variables (methodological quality, sample size, whether preset sample size was estimated and reached, meta-analysis, year of publication, and journal impact factor). Ad-

Als-Nielsen 2003 (*Continued*)

		justed for treatment effect and double blinding in final model

Barden 2006

Methods	To study if industry sponsored trials yield a better result than trials not sponsored by industry, and if a particular drug would perform better as the test drug in trials funded by its manufacturer and worse as the comparator drug in trials funded by a competitor. RCTs from published systematic reviews in acute pain and migraine (reviews from 1999 to 2004)
Data	176 acute pain or migraine drug RCTs (active comparator or placebo controlled)
Comparisons	Industry versus non-industry and manufacturer versus competitor funding
Outcomes	Effect size and methodological quality (Jadad score, 0-5 point scale)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	From Cochrane reviews, seems more than one assessor was used
Comprehensive search?	Yes	Identification via Cochrane reviews.
Control for bias?	No	No control for bias.

Bero 2007

Methods	To examine the associations between research funding source, study design characteristics aimed at reducing bias, and other factors that potentially influence results and conclusions in randomized controlled trials of statin-drug comparisons. All statin RCTs with active comparators from January 1999 to May 2005
Data	192 statin RCTs (active comparators).
Comparisons	Industry, none disclosed/no funding and government/private non-profit funding
Outcomes	Study results, study conclusions, methodological quality (concealment of allocation, blinding and follow-up) and concordance between study results and conclusions
Notes	

Bero 2007 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	Two or more assessors included studies.
Comprehensive search?	Yes	MEDLINE and references.
Control for bias?	Yes	Multivariate logistic regression analysis. Final model controlled for journal Impact Factor, sample size and blinding

Bhandari 2004

Methods	To study the association between industry funding and the statistical significance of results in recently published medical and surgical trials. RCTs from January 1999 to June 2001 in 8 leading surgical journals (*Journal of Bone and Joint Surgery* [American and British volumes], *Clinical Orthopaedics and Related Research*, *Acta Orthopaedica Scandinavica*, *Annals of Surgery*, *American Journal of Surgery*, *Plastic and Reconstructive Surgery and Journal of Neurosurgery*) and 5 medical journals (*Lancet, BMJ, JAMA, Annals of Internal Medicine and New England Journal of Medicine*) .
Data	332 RCTs of drug, surgery, and other types of interventions (no description of comparisons)
Comparisons	Industry-for-profit, not-for-profit and undeclared funding.
Outcomes	Study results and methodological quality (Detsky quality index, 0-21 point scale)
Notes	

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearch and MEDLINE used.
Control for bias?	Yes	Multivariate logistic regression with adjustment for sample size, study quality and type of intervention

Booth 2008

Methods	To describe trends in methodology and reporting of RCTs, in addition to sponsorship, outcomes, and authors' interpretation of results. All RCTs of systemic therapy in breast, colorectal cancer, and non-small-cell lung cancer published during three decades (1975 through 2004) in: *Journal of Clinical Oncology*, *Journal of the National Cancer Institute*, *Cancer Treatment/Chemotherapy Reports*, *New England Journal of Medicine*, *Lancet*, and *JAMA*.
Data	321 drug RCTs (active comparators and placebo controlled).
Comparisons	For-profit/mixed, non-profit and not known funding.
Outcomes	Study results, study conclusions and effect size.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Database and handsearch.
Control for bias?	Yes	Multivariate logistic regression, final model controlled for time to event, effect size and P value

Bourgeois 2010

Methods	To describe characteristics of drug trials listed in ClinicalTrials.gov and examine whether the funding source of these trials is associated with favorable published outcomes. Clinical trials registered from 2000 to 2006 and published up to 2010
Data	546 clinical trials of cholesterol-lowering drugs, antidepressants, antipsychotics, proton-pump inhibitors and vasodilators (active or placebo controlled)
Comparisons	Industry, government and non-profit/non-federal (with or without industry contributions) funding
Outcomes	Study results.
Notes	

Risk of bias

Item	Authors' judgement	Description

Bourgeois 2010 (*Continued*)

Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	Two assessors independently carried out the literature search and disagreements were resolved by consensus
Comprehensive search?	Yes	Four databases, trial registries and contact to investigators and companies
Control for bias?	Yes	Post hoc multivariate logistic regression analysis to assess the association between funding source and trial outcome, while controlling for other trial characteristics (drug class, approval status of indication, study phase, multicenter status, anticipated sample size, age of study population, comparator type, and length of study)

Brown 2006

Methods	To evaluate the trends in the source of funding for gastrointestinal clinical research during the period from 1992 to 2002-2003; to determine whether the source of study funding predicted the likelihood that a study would publish results that favor the drug or device being tested; and to determine whether differences exist in the methodologic quality of the investigational study methods used in studies funded by private industry versus other sources. Clinical trials published in 4 gastrointestinal journals (*Gastroenterology*, *The American Journal of Gastroenterology*, *Hepatology*, and *Gastrointestinal Endoscopy*).
Data	450 clinical trials of drugs and devices in gastroenterology (active or placebo controlled)
Comparisons	Private industry sponsored, federal/state government sponsored, national society/non-profit agency sponsored and not specified
Outcomes	Study conclusions and methodological quality (Brown score, 0 to 5 point scale multiplied by 100)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearching of journals.

Brown 2006 (*Continued*)

Control for bias?	No	No control for bias.

Buchkowsky 2004

Methods	To characterize clinical trial funding, reporting, and sources; investigate author-industry affiliation; and describe clinical outcome trends over time. Random papers from January 1981 to December 2000 from *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet* and *New England Journal of Medicine*.
Data	500 clinical drug trials (drug versus placebo, active comparator or non-drug comparator)
Comparisons	Industry, mixed, non-industry and not stated funding.
Outcomes	Study conclusions
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearching of journals.
Control for bias?	Unclear	Investigates choice of comparators over time, might have assessed other sources of bias

Chard 2000

Methods	To assess the published research base for interventions for osteoarthritis of the knee, and to identify areas in need of further research. Studies from 1950 to 1998
Data	930 studies of different interventions (various study designs with various comparators)
Comparisons	Commercial, government and not stated funding.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**

Chard 2000 (*Continued*)

Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	One assessor on all studies and one on 10% sample, but only 87% agreement indicating two needed for all studies
Comprehensive search?	Yes	MEDLINE, EMBASE, BIDS, The Cochrane Library, previous reviews and experts contacted
Control for bias?	No	No control for bias.

Cho 1996

Methods	To compare the quality, relevance, and structure of drug studies published in symposium proceedings that are sponsored by drug companies with 1) articles from symposia with other sponsors and 2) articles in the peer reviewed parent journals of symposium proceedings; and to study the relation between drug company sponsorship and study outcome. Random selection of symposia from 625 symposia that had been identified for a previous study
Data	127 drug studies (various study designs with various comparators)
Comparisons	Drug company support and no support.
Outcomes	Study conclusions and methodological quality (Cho scale 0-1 point)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Unclear	Not clear enough to replicate how symposia were chosen and how matching papers were chosen
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Comprehensive search within their own database.
Control for bias?	Yes	Subgroup analysis of study design.

Clifford 2002

Methods	To examine the relationship between funding source, trial outcome and reporting quality;100 RCTs from *Annals of Internal Medicine*, *BMJ, JAMA*, *Lancet, New England Journal of Medicine*. From January 1999 to October 2000 with 20 RCTs/journal.
Data	100 drug RCTs (various comparators).
Comparisons	Entirely industry, entirely not-for-profit, mixed and not reported funding
Outcomes	Study results, methodological quality (Jadad score, 0-5 point scale and concealment of allocation)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearching of journals.
Control for bias?	No	No evidence of risk of bias assessment.

Crocetti 2010

Methods	To assess the risk of bias among pediatric RCTs reported in 8 high-impact journals (5 pediatric and 3 general medical) from July 2007 to June 2008
Data	146 pediatric drug, behavioral/educational and nutritional RCTs (various comparators)
Comparisons	Government, industry, internal hospital grant, multiple sources, none and private foundation funding
Outcomes	Methodological quality (sequence generation; allocation concealment; masking of participants, personnel, and outcome assessors; incomplete outcome data reporting; selective outcome reporting; and other sources of bias)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.

Crocetti 2010 (*Continued*)

Comprehensive search?	Yes	MEDLINE search of selected journals.
Control for bias?	Yes	Multivariate logistic regression to test for an association between the presence of a high risk of bias according to domain and the independent variables of funding source, intervention type, author number, and trial registration status

Davidson 1986

Methods	An analysis of the results of clinical trials according to funding source. Clinical trials from 1984 in *New England Journal of Medicine*, *Annals of Internal Medicine*, *the American Journal of Medicine*, *Archives of Internal Medicine*, and the *Lancet.*
Data	107 drug and non-drug clinical trials (various comparators).
Comparisons	Pharmaceutical support and general support.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	Single assessor.
Comprehensive search?	Yes	Journals handsearched.
Control for bias?	No	Control for bias seems unlikely to have been done.

Davis 2008

Methods	The influence of several potentially biasing factors (e.g. industry support, extrapyramidal side effects) on efficacy of studies comparing second-generation antipsychotic with first-generation drugs. Dataset from previously published meta-analysis (search from 1953 to 2002)
Data	124 RCTs of second-generation antipsychotics versus first-generation antipsychotics
Comparisons	Industry and non-industry funding.
Outcomes	Effect size.

Davis 2008 (*Continued*)

Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Comprehensive database search including search for unpublished data
Control for bias?	Unclear	Carried out various sensitivity analysis, but not clear whether they assessed bias in relation to funding and effect size

Djulbegovic 2000

Methods	To evaluate whether the uncertainty principle was upheld, comparison of the number of studies favoring experimental treatments over standard ones according to the source of funding. All RCTs for multiple myeloma from 1996 to 1998	
Data	136 multiple myeloma drug RCTs (various comparators).	
Comparisons	Commercial and public funding.	
Outcomes	Study conclusions and methodological quality (Jadad score, 0-5 point scale)	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	Seems only one author involved in study inclusion.
Comprehensive search?	Yes	Using the Cochrane search strategy to identify trials.
Control for bias?	Yes	Controlled for types of comparator (active versus placebo/no treatment)

Etter 2007

Methods	To assess whether source of funding affected the results of trials of nicotine replacement therapy for smoking cessation. RCTs from 1979 to 2003 identified from Cochrane review
Data	105 RCTs of nicotine replacement therapy (gum or patch versus placebo or no treatment)
Comparisons	Industry/mixed and non-industry/not acknowledged funding.
Outcomes	Study results and effect size.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	From Cochrane review, seems more than one assessors was used
Comprehensive search?	Yes	Identification via Cochrane review.
Control for bias?	Yes	Multivariate logistic regression with adjustment for sample size

Finucane 2004

Methods	To evaluate the association between funding and findings of pharmaceutical research presented at an annual meeting of a clinically oriented US medical professional society
Data	48 presentations of drug studies (observational studies, RCTs and other study designs)
Comparisons	Industry supported and not industry supported.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Unclear	Unclear what "any abstract that reported results about effectiveness or safety of drugs" means. Not clear which study designs and whether reviews were included
Adequate study inclusion process?	Yes	Seems likely that two assessors were used.

Finucane 2004 (*Continued*)

Comprehensive search?	Yes	Comprehensive search within conference.
Control for bias?	Yes	Subgroup analysis of study design.

Freemantle 2000

Methods	To assess whether specific pharmacological characteristics of alternative antidepressants resulted in altered efficacy compared to that of selective serotonin reuptake inhibitors (SSRI) in the treatment of major depression. All RCTs of SSRI versus alternative antidepressants (search from 1966 to 1997)
Data	105 SSRI versus alternative antidepressant RCTs.
Comparisons	Sponsor and not sponsor.
Outcomes	Effect size.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, EMBASE, references and reviews.
Control for bias?	No	No assessment of bias in relation to funding and effect size

Gartlehner 2010

Methods	The objective of this study was to determine the effect of industry bias in a systematically reviewed sample of head-to-head trials. Trials of SSRI head-to-head comparisons from 1993 to 2005
Data	29 SSRI RCTs of head-to-head comparisons.
Comparisons	Sponsor and not sponsor.
Outcomes	Study results and effect size.
Notes	

Risk of bias

Gartlehner 2010 (*Continued*)

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	Two assessors included studies.
Comprehensive search?	Yes	MEDLINE, EMBASE, The Cochrane Library, the International Pharmaceutical Abstracts database, references and reviews and letters to the editor. In addition, the Center for Drug Evaluation and Research database to identify unpublished research submitted to the US Food and Drug Administration (FDA)
Control for bias?	Yes	Sensitivity analysis based on definition of funding.

Halpern 2005

Methods	To determine whether there is a difference in average statistical power between pharmacoepidemiologic studies of anti-retroviral adverse drug effects (ADEs) sponsored by for-profit versus non-profit organizations (drugs approved from 1987 to 1999 and published until 2002)
Data	48 pharmacoepidemiological studies of adverse effects of ani-retroviral drugs
Comparisons	Non-profit, for-profit, charity/institution, none or unable to determine funding
Outcomes	Study results (harms).
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	One assessor only.
Comprehensive search?	Yes	MEDLINE, EMBASE and reference lists.
Control for bias?	No	No control for bias.

Heres 2006

Methods	To review the results of head-to-head studies of second-generation antipsychotics funded by pharmaceutical companies to determine if a relationship exists between the sponsor of the trial and the drug favored in the study's overall outcome. All head-to-head trials of second-generation antipsychotics from 1997 to 2005
Data	42 head-to-head RCTs of second-generation antipsychotics.
Comparisons	Industry only (sponsor of test drug or comparator).
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	No	MEDLINE and screen of selected conference proceedings. Sample of conference proceedings limited to 1999-2004, which may introduce bias due to differences in approval dates for the different drugs
Control for bias?	Yes	Sensitivity analysis of peer-reviewed trials only.

Jefferson 2009

Methods	To explore the relation between study concordance, take home message, funding, and dissemination of comparative studies assessing the effects of influenza vaccines. Studies of various designs from 1961 to 2006
Data	274 studies of influenza vaccine versus placebo/no treatment
Comparisons	Government/private/unfunded, industry/mixed and not stated funding
Outcomes	Study conclusions, methodological quality (Cochrane risk of bias) and concordance between study results and conclusions
Notes	

Risk of bias

Item	Authors' judgement	Description

Jefferson 2009 (*Continued*)

Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	Two assessors included studies.
Comprehensive search?	Yes	MEDLINE, EMBASE, The Cochrane Library, web, and likely references and previous reviews since it is based on Cochrane reviews
Control for bias?	Yes	Sensitivity analysis based on definition of funding and regression analysis of various factors

Jones 2010

Methods	To compare the quality of publicly or privately funded randomized controlled trials. Trials included in Cochrane reviews on hypertension and preterm labour
Data	105 drug trials (mixed comparisons).
Comparisons	Commercial, mixed and non-commercial.
Outcomes	Methodological quality (selection bias, performance bias, detection bias and attrition)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Based on searches from Cochrane reviews.
Control for bias?	No	No control for bias.

Kelly 2006

Methods	To investigate the relationship between industry support and study outcome in the general psychiatric literature. Clinical studies from 1992 and 2002 in *American Journal of Psychiatry, Archives of General Psychiatry,* and *Journal of Clinical Psychopharmacology.*
Data	301 psychiatric drug studies (mixed comparisons).
Comparisons	Non-industry and industry (sponsor of test drug or comparator) funding

Kelly 2006 (*Continued*)

Outcomes	Study results, study conclusions and concordance between study results and conclusions	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Sample of journals.
Control for bias?	Yes	Explanatory analysis of various mediating variables.

Kemmeren 2001

Methods	To evaluate quantitatively articles that compared effects of second- and third-generation oral contraceptives on risk of venous thrombosis. Cohort and case control studies from 1995 to 2000	
Data	12 cohort and case control studies of second- versus third-generation oral contraceptives	
Comparisons	Industry and non-industry funding.	
Outcomes	Study results and effect size.	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, reviews, relevant papers and experts.
Control for bias?	No	Multiple regression used, but not for the association between funding and results or effect size

Kjaergard 2002

Methods	To assess the association between competing interests and authors' conclusions. RCTs published in *BMJ* 1997 to 2001.
Data	159 RCTs of mixed interventions (various comparators).
Comparisons	Profit, non-profit, non-profit and profit, non-profit and free drug, free drug only and no funding/ not stated
Outcomes	Study conclusions and methodological quality (sequence generation, concealment of allocation and blinding)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	Only one assessor included studies.
Comprehensive search?	Yes	MEDLINE journal search.
Control for bias?	Yes	Regression analysis for potential confounders.

Liss 2006

Methods	To determine whether drug studies in the pulmonary/allergy literature also demonstrate a publication bias towards more favorable results when a pharmaceutical company funds the study. Primary research studies of drug interventions published in *Allergy, American Journal of Respiratory and Critical Care Medicine, Annals of Allergy Asthma and Immunology, Chest, European Respiratory Journal, Journal of Allergy and Clinical Immunology, Respiratory Medicine,* and *Thorax* in 2002 to 2003.
Data	Studies of nasal or oral inhaled corticosteroids, long- or short-acting bronchodilators, and leukotriene receptor antagonists (various designs and comparisons)
Comparisons	Pharmaceutically and not pharmaceutically funded.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.

Liss 2006 (*Continued*)

Adequate study inclusion process?	No	Only one assessor included studies.
Comprehensive search?	Yes	Handsearch of journals indirectly described.
Control for bias?	No	No control for bias.

Lubowitz 2007

Methods	To compare outcomes (and levels of evidence) between published Autologous Chondrocyte Implantation outcome studies that were commercially funded and studies that were not commercially funded. Clinical studies from 1994 to 2005
Data	23 studies of chondrocyte implantation (various designs and comparisons)
Comparisons	Commercially funded and not commercially funded.
Outcomes	Effect size.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	No	MEDLINE only, time period not stated and few search terms used
Control for bias?	No	No control for bias.

Lynch 2007

Methods	To test the following hypotheses regarding orthopedic manuscripts submitted for review: (1) non-scientific variables, including receipt of commercial funding, affect the likelihood that a peer-reviewed submission will conclude with a report of a positive study outcome, and (2) positive outcomes and other, non-scientific variables are associated with acceptance for publication. Cohort of manuscripts submitted involving original research on the subject of adult hip or knee reconstruction to *The Journal of Bone and Joint Surgery* (American Volume) between January 2004 and June 2005.
Data	209 studies of knee or hip surgery (various designs, interventions and comparisons)
Comparisons	Commercial, non-funded and noncommercial/philanthropic funding

Lynch 2007 (*Continued*)

Outcomes	Study conclusions and methodological quality (Sackett scale, 0 to 100%)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Sample of papers via journal submission system.
Control for bias?	No	No control for bias.

Momeni 2009

Methods	To investigate if plastic surgical trials with industry-funding are more likely to be associated with statistically significant pro-industry findings. Trials in 4 plastic surgery journals (*Plastic and Reconstructive Surgery, British Journal of Plastic Surgery*, *Annals of Plastic Surgery,* and *Aesthetic Plastic Surgery*) from 1990 to 2005.
Data	346 RCTs and controlled clinical trials (various designs, interventions and comparisons)
Comparisons	Industry, public, university and not specified funding.
Outcomes	Study results.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearch of journals.
Control for bias?	No	No control for bias.

Moncrieff 2003

Methods	To re-evaluate the evidence comparing clozapine with conventional antipsychotics and to investigate sources of heterogeneity. Trials from 1988 to 2001
Data	9 RCTs of clozapine versus conventional antipsychotics.
Comparisons	Industry, other and not declared funding.
Outcomes	Study results and effect size.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	No	Only one assessor included studies.
Comprehensive search?	Yes	MEDLINE, EMBASE and Cochrane review.
Control for bias?	No	Univariate controlled for various predictors in relation to effect size only

Montgomery 2004

Methods	To analyze RCTs of second-generation antipsychotics in schizophrenia with respect to funding source (industry versus non-industry funding). RCTs from 1974 to 2002
Data	86 RCTs of 2nd generation antipsychotics versus other types (various comparisons)
Comparisons	Industry and non-industry.
Outcomes	Study conclusions and methodological quality (Jadad score, 0-5 point scale)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, PsychInfo and references.

Control for bias?	No	No control for bias.

Nieto 2007

Methods	To evaluate differences between studies funded by the pharmaceutical manufacturer of the drug and those with no pharmaceutical funding regarding the findings and interpretation of adverse effects of inhaled corticosteroids. Studies from 1993 to 2002
Data	504 studies of inhaled corticosteroids (various study designs with various comparators)
Comparisons	Pharmaceutical funded and not pharmaceutical funded.
Outcomes	Study results (harms), study conclusions (harms) and concordance between study results and conclusions (harms)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Sample of journals were identified by MEDLINE.
Control for bias?	Yes	Controlled for confounders using multivariate model.

Pengel 2009

Methods	To examine the quality of reporting of RCTs in solid organ transplantation that were published 2004 to 2006
Data	332 trials in solid organ transplantation (mixed interventions and comparisons)
Comparisons	Commercial, nonprofit, mixed, no funding and not described.
Outcomes	Methodological quality (concealment of allocation and Jadad score, 0-5 point scale)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**

Pengel 2009 (*Continued*)

Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, EMBASE and The Cochrane Library.
Control for bias?	No	No control for bias.

Peppercorn 2007

Methods	To evaluate the correlations between pharmaceutical company involvement, study design, and study outcome and to explore changes in these areas over time. Breast cancer trials of medical therapies that were published in the years 1993, 1998, and 2003 in 10 select English-language medical journals
Data	140 breast cancer drug trials (single arm studies and RCTs).
Comparisons	Pharmaceutical studies versus non-pharmaceutical studies.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearch and MEDLINE used.
Control for bias?	No	Only assessment of differences in study design in relation to funding

Perlis 2005a

Methods	The purpose was to determine the extent and impact of industry sponsorship conflicts of interest in dermatology research. Drug trials from *Journal of Investigative Dermatology, Archives of Dermatology, British Journal of Dermatology,* and *Journal of the American Academy of Dermatology* from 2000 to 2003.
Data	179 RCTs of dermatological drugs (various comparators).

Perlis 2005a (*Continued*)

Comparisons	Industry and non-industry funding.	
Outcomes	Study conclusions and methodological quality (blinding and Jadad score, 0-5 point scale)	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Sample of journals.
Control for bias?	Yes	Multivariate regression analysis adjusted for conflict of interest, Jadad score, and sample size

Perlis 2005b

Methods	To study the extent and implications of industry sponsorship and financial conflicts of interest in psychiatric trials. Drug trials from the *American Journal of Psychiatry, Archives of General Psychiatry, Journal of Clinical Psychiatry, andJournal of Clinical Psychopharmacology* from 2001 to 2003.	
Data	397 psychiatric clinical drug trials (various comparators).	
Comparisons	Industry and non-industry funding.	
Outcomes	Study results.	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Not sure if 3 assessors extracting data were involved in including studies
Comprehensive search?	Yes	MEDLINE and handsearch of journals.
Control for bias?	Yes	Logistic regression adjusted for confounders.

Popelut 2010

Methods	To examine financial sponsorship of dental implant trials, and to evaluate whether research funding sources affects the annual failure rate. Clinical trials from 1988 to 2005
Data	41 clinical trials of dental implants (single arm and active control)
Comparisons	Industry, non-industry and unknown funding.
Outcomes	Effect size.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	No	Inclusion criteria reported, but not possible to decipher and seems subjective
Adequate study inclusion process?	Yes	Two assessors included studies.
Comprehensive search?	Yes	MEDLINE and handsearch.
Control for bias?	Yes	Controlled for confounders using multivariate analysis.

Rasmussen 2009

Methods	To compare the prevalence of favorable results and conclusions among published reports of registered and unregistered RCTs of new oncology drugs. Cohort of trials from 25 drugs granted first-time Food and Drug Administration (FDA) approval for oncology indications in 2000 to 2005 and published in 1996 to 2008
Data	137 RCTs of oncology drugs (placebo or active control).
Comparisons	Industry sponsor and other funding.
Outcomes	Study results, study conclusions, methodological quality (blinding) and concordance between study results and conclusions
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.

Rasmussen 2009 (*Continued*)

Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE and The Cochrane Library.
Control for bias?	Yes	Logistic regression adjusted for confounders.

Rattinger 2009

Methods	To examine the association between research funding source, study design characteristics aimed at reducing bias, and other factors with the results and conclusions of RCTs of thiazolidinediones compared to other oral hypoglycemic agents (search 1996 to 2006)
Data	61 RCTs of thiazolidinediones (active or placebo control).
Comparisons	Test drug company, other drug company, all others and not declared funding
Outcomes	Study results, study conclusions, methodological quality (sequence generation and allocation concealment, blinding and follow-up) and concordance between study results and conclusions
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, The Cochrane Library, references and reviews.
Control for bias?	Yes	Intended multivariate analysis, but due to few associations only univariate performed

Ridker 2006

Methods	To determine in contemporary randomized cardiovascular trials the association between funding source and the likelihood of reporting positive findings. Cardiovascular RCTs published in *JAMA*, *Lancet*, and the *New England Journal of Medicine* in 2000 to 2005.
Data	349 RCTs (mixed interventions and comparators).
Comparisons	For profit, mixed and not for profit funding.
Outcomes	Study conclusions.

Ridker 2006 (*Continued*)

Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Sample of journals identified via MEDLINE.
Control for bias?	No	No control for bias.

Rios 2008

Methods	To assess the reporting quality of RCTs in general endocrinology and to identify predictors for better reporting quality. RCTs published in the *Journal of Clinical Endocrinology* and *Metabolism, Clinical Endocrinology,* and the *European Journal of Endocrinology* in 2005 or 2006.
Data	89 endocrinology drug RCTs (various comparators).
Comparisons	Industry, mixed, non-industry and not stated funding.
Outcomes	Methodological quality (allocation concealment and blinding)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Yes	Two assessors included studies.
Comprehensive search?	Yes	Handsearch of journals.
Control for bias?	Yes	Controlled for confounders using multivariate analysis.

Rochon 1994

Methods	To study the relation between reported drug performance in published trials and support of the trials by the manufacturer of the drug under evaluation. All non-steroidal anti-inflammatory (NSAID) RCTs from September 1987 to May 1990
Data	56 NSAID RCTs (placebo and head-to-head comparisons).
Comparisons	Manufacturer associated only.
Outcomes	Study results (efficacy and harms), study conclusions (efficacy and harms) and methodological quality (Chalmers' scale, 0-100 points)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE searched.
Control for bias?	No	Control for bias seems unlikely to have been done.

Tulikangas 2006

Methods	To determine if there is a significant difference in outcomes of clinical trials funded by industry or not of antimuscarinic medications used to treat overactive bladder symptoms and detrusor overactivity. RCTs from 1980 to 2002
Data	24 RCTs of antimuscarinic drugs (various comparators).
Comparisons	Industry funded and public funded.
Outcomes	Study results.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.

Comprehensive search?	Yes	MEDLINE and references.
Control for bias?	No	No control for bias.

Tungaraza 2007

Methods	To compare drug trials reported in three major psychiatric journals to investigate whether treatments are more likely to report favorable outcomes when they are funded by the pharmaceutical industry. Studies published in the *British Journal of Psychiatry*, *American Journal of Psychiatry* and *Archives of General Psychiatry* from 2000 to 2004.
Data	198 psychiatric drug trials (various designs and comparators)
Comparisons	Industry sponsored, industry authored and independent.
Outcomes	Study conclusions.
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	Handsearch of journals.
Control for bias?	No	No control for bias.

Vlad 2007

Methods	To identify factors that explain heterogeneity in trials of glucosamine. RCTs of glucosamine from 1980 to 2006
Data	15 RCTs of glucosamine versus placebo for osteoarthritis.
Comparisons	Industry funding, industry participation, industry author and independent
Outcomes	Study results, effect size and methodological quality (allocation concealment and Jadad score, 0-5 point scale)
Notes	

Risk of bias

Vlad 2007 (*Continued*)

Item	Authors' judgement	Description
Adequate selection criteria?	Yes	Objective criteria used.
Adequate study inclusion process?	Unclear	Does not describe number of assessors.
Comprehensive search?	Yes	MEDLINE, The Cochrane Library, conference abstracts, references and reviews
Control for bias?	Yes	Exploration of heterogeneity.

RCT: Randomised controlled trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Chowers 2009	No relevant outcomes
Conen 2008	No relevant outcomes
Cunningham 2007	No separate drug or device data
Friedman 2004	Conflicts of interest, not funding
Glick 2006	No relevant outcomes
Hall 2007	No relevant outcomes
Hill 2007	No relevant outcomes (not methodological quality, but reporting quality)
Jagsi 2009	No separate drug or device data
Khan 2008	No separate drug or device data
Kjaergard 1999	No separate drug or device data
Krzyzanowska 2003	No relevant outcomes
Kulier 2004	No quantitative data
Kulkarni 2007	No relevant outcomes
Lai 2006	No separate drug or device data

(*Continued*)

Leopold 2003	No separate drug or device data
Leucht 2009a	No relevant outcomes
Leucht 2009b	No relevant outcomes
McLennan 2008	No relevant outcomes
Montori 2005	No relevant outcomes
Nkansah 2009	Calcium supplementation, not a drug
Okike 2007	Conflicts of interest, not funding
Okike 2008	No relevant outcomes
Procyshyn 2004	No relevant data for non-industry studies
Roach 2008	No separate drug or device data
Sanossian 2006	No relevant outcomes
Shah 2005	No separate drug or device data
Thomas 2008	No relevant outcomes (not methodological quality, but reporting quality)
Watanabe 2010	No relevant outcomes
Yao 2007	No separate drug or device data
Yaphe 2001	No separate drug or device data

DATA AND ANALYSES

Comparison 1. Results: Industry sponsored versus non-industry sponsored studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable efficacy results	14	1588	Risk Ratio (IV, Fixed, 95% CI)	1.24 [1.14, 1.35]
2 Number of studies with favorable harms results	3	561	Risk Ratio (M-H, Fixed, 95% CI)	1.87 [1.54, 2.27]

Comparison 2. Results: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable test treatment efficacy results	2	131	Risk Ratio (M-H, Fixed, 95% CI)	4.64 [2.08, 10.32]

Comparison 3. Conclusions: industry sponsored versus non-industry sponsored studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable conclusions	21	3941	Risk Ratio (IV, Random, 95% CI)	1.31 [1.20, 1.44]

Comparison 4. Conclusions: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable test treatment conclusions	3	154	Risk Ratio (M-H, Fixed, 95% CI)	5.90 [2.79, 12.49]

Comparison 5. Risk of bias: industry sponsored versus non-industry sponsored studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with low risk of bias from sequence generation	3	487	Risk Ratio (IV, Random, 95% CI)	0.85 [0.52, 1.41]
2 Number of studies with low risk of bias from concealment of allocation	10	1311	Risk Ratio (IV, Random, 95% CI)	1.09 [0.86, 1.38]
3 Number of studies with low risk of bias from blinding	9	1216	Risk Ratio (IV, Random, 95% CI)	1.32 [1.05, 1.65]
4 Number of studies with low risk of bias from loss to follow-up	2	118	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.84, 1.16]

Comparison 6. Concordance between study results and conclusions: industry sponsored versus non-industry sponsored studies

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with concordant study results and conclusions	5	667	Risk Ratio (IV, Random, 95% CI)	0.84 [0.70, 1.01]

Comparison 7. Subgroup analysis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable efficacy results	14	1588	Risk Ratio (IV, Fixed, 95% CI)	1.24 [1.14, 1.35]
1.1 High risk of bias	11	962	Risk Ratio (IV, Fixed, 95% CI)	1.14 [1.03, 1.25]
1.2 Low risk of bias	3	626	Risk Ratio (IV, Fixed, 95% CI)	1.50 [1.30, 1.74]
2 Number of studies with favorable conclusions	21	3941	Risk Ratio (IV, Random, 95% CI)	1.31 [1.20, 1.44]
2.1 High risk of bias	17	3062	Risk Ratio (IV, Random, 95% CI)	1.26 [1.14, 1.39]
2.2 Low risk of bias	4	879	Risk Ratio (IV, Random, 95% CI)	1.54 [1.24, 1.91]
3 Number of studies with favorable conclusions	21	3941	Risk Ratio (IV, Random, 95% CI)	1.30 [1.18, 1.42]
3.1 Drug studies	21	3821	Risk Ratio (IV, Random, 95% CI)	1.31 [1.19, 1.44]
3.2 Device studies	2	120	Risk Ratio (IV, Random, 95% CI)	1.09 [0.82, 1.45]
4 Number of studies with favorable efficacy results	14	1588	Risk Ratio (IV, Fixed, 95% CI)	1.24 [1.14, 1.35]

4.1 Specific treatments or diseases	12	1143	Risk Ratio (IV, Fixed, 95% CI)	1.19 [1.08, 1.31]
4.2 Mixed domain	2	445	Risk Ratio (IV, Fixed, 95% CI)	1.39 [1.18, 1.64]
5 Number of studies with favorable conclusions	21	3941	Risk Ratio (IV, Random, 95% CI)	1.31 [1.20, 1.44]
5.1 Specific treatments or diseases	16	2774	Risk Ratio (IV, Random, 95% CI)	1.34 [1.19, 1.51]
5.2 Mixed study domain	5	1167	Risk Ratio (IV, Random, 95% CI)	1.26 [1.08, 1.47]

Comparison 8. Sensitivity analysis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of studies with favorable efficacy results, sponsorship recoded	5	517	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [1.27, 1.76]
2 Number of studies with favorable conclusions, sponsorship recoded	7	951	Risk Ratio (IV, Random, 95% CI)	1.26 [1.06, 1.50]
3 Number of studies with low risk of bias from sequence generation, sponsorship recoded	2	249	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.77, 1.44]
4 Number of studies with low risk of bias from concealment of allocation, sponsorship recoded	7	663	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.90, 1.52]
5 Number of studies with low risk of bias from blinding, sponsorship recoded	5	425	Risk Ratio (M-H, Fixed, 95% CI)	1.54 [1.23, 1.94]
6 Results:Number of studies with favorable efficacy results, analysis adjusted for confounders	2		Odds Ratio (Fixed, 95% CI)	3.86 [1.93, 7.70]
7 Conclusions:Number of studies with favorable conclusions, analysis adjusted for confounders	3		Odds Ratio (Fixed, 95% CI)	4.15 [2.40, 7.19]
8 Number of studies with favorable efficacy results, random-effects model	14	1588	Risk Ratio (IV, Random, 95% CI)	1.26 [1.12, 1.41]
9 Number of studies with favorable harms results, random-effects model	3	561	Risk Ratio (M-H, Random, 95% CI)	1.87 [1.54, 2.27]
10 Number of studies with favorable test treatment efficacy results, random effects-model	2	131	Risk Ratio (M-H, Random, 95% CI)	3.88 [1.26, 11.94]

11 Number of studies with favorable test treatment conclusions, random-effects model	3	154	Risk Ratio (M-H, Random, 95% CI)	5.92 [2.80, 12.54]
12 Number of studies with low risk of bias from loss to follow-up, random-effects model	2	118	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.84, 1.15]

Analysis 1.1. Comparison 1 Results: Industry sponsored versus non-industry sponsored studies, Outcome 1 Number of studies with favorable efficacy results.

Review: Industry sponsorship and research outcome

Comparison: 1 Results: Industry sponsored versus non-industry sponsored studies

Outcome: 1 Number of studies with favorable efficacy results

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Alasbali 2009	7/29	2/10		0.3 %	1.21 [0.30, 4.88]
Bero 2007	65/94	48/97		11.5 %	1.40 [1.10, 1.78]
Booth 2008	49/120	50/165		6.8 %	1.35 [0.98, 1.85]
Bourgeois 2010	222/260	48/85		18.1 %	1.51 [1.25, 1.83]
Clifford 2002	46/66	21/34		7.1 %	1.13 [0.83, 1.54]
Etter 2007	25/49	9/41		1.7 %	2.32 [1.23, 4.40]
Kelly 2006	12/13	4/8		1.3 %	1.85 [0.91, 3.76]
Momeni 2009	20/24	69/85		15.9 %	1.03 [0.84, 1.26]
Moncrieff 2003	2/2	2/7		0.5 %	2.67 [0.85, 8.39]
Perlis 2005b	93/113	37/49		20.7 %	1.09 [0.91, 1.31]
Rasmussen 2009	66/109	14/28		4.2 %	1.21 [0.81, 1.81]
Rattinger 2009	26/36	18/25		6.7 %	1.00 [0.73, 1.38]
Tulikangas 2006	15/15	7/9		5.0 %	1.29 [0.89, 1.87]
Vlad 2007	5/11	0/4		0.1 %	4.58 [0.31, 68.24]
Total (95% CI)	**941**	**647**		**100.0 %**	**1.24 [1.14, 1.35]**

Total events: 653 (Industry), 329 (Non-industry)

Heterogeneity: Chi^2 = 20.09, df = 13 (P = 0.09); I^2 =35%

Test for overall effect: Z = 5.11 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Results: Industry sponsored versus non-industry sponsored studies, Outcome 2 Number of studies with favorable harms results.

Review: Industry sponsorship and research outcome

Comparison: 1 Results: Industry sponsored versus non-industry sponsored studies

Outcome: 2 Number of studies with favorable harms results

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Halpern 2005	1/3	10/45		1.4 %	1.50 [0.28, 8.14]
Kemmeren 2001	3/4	2/5		2.0 %	1.88 [0.56, 6.31]
Nieto 2007	180/275	80/229		96.6 %	1.87 [1.54, 2.28]
Total (95% CI)	**282**	**279**		**100.0 %**	**1.87 [1.54, 2.27]**

Total events: 184 (Industry), 92 (Non-industry)

Heterogeneity: $Chi^2 = 0.07$, df = 2 (P = 0.97); $I^2 = 0.0\%$

Test for overall effect: Z = 6.35 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Results: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company, Outcome 1 Number of studies with favorable test treatment efficacy results.

Review: Industry sponsorship and research outcome

Comparison: 2 Results: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company

Outcome: 1 Number of studies with favorable test treatment efficacy results

Study or subgroup	Test treatment sponsor n/N	Comparator treatm sponsor n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bero 2007	43/65	3/30		55.2 %	6.62 [2.23, 19.63]
Rattinger 2009	22/30	2/6		44.8 %	2.20 [0.70, 6.96]
Total (95% CI)	**95**	**36**		**100.0 %**	**4.64 [2.08, 10.32]**

Total events: 65 (Test treatment sponsor), 5 (Comparator treatm sponsor)

Heterogeneity: $Chi^2 = 2.02$, df = 1 (P = 0.16); $I^2 = 50\%$

Test for overall effect: Z = 3.76 (P = 0.00017)

Test for subgroup differences: Not applicable

Analysis 3.1. Comparison 3 Conclusions: industry sponsored versus non-industry sponsored studies, Outcome 1 Number of studies with favorable conclusions.

Review: Industry sponsorship and research outcome

Comparison: 3 Conclusions: industry sponsored versus non-industry sponsored studies

Outcome: 1 Number of studies with favorable conclusions

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Ahmer 2005	125/138	39/50		6.1 %	1.16 [0.99, 1.36]
Alasbali 2009	26/29	2/10		0.5 %	4.48 [1.29, 15.58]
Als-Nielsen 2003	92/197	43/173		4.2 %	1.88 [1.39, 2.53]
Bero 2007	66/94	39/97		4.5 %	1.75 [1.32, 2.30]
Booth 2008	66/118	55/153		4.6 %	1.56 [1.19, 2.03]
Buchkowsky 2004	138/181	224/319		6.7 %	1.09 [0.97, 1.21]
Chard 2000	106/108	373/383		7.3 %	1.01 [0.98, 1.04]
Cho 1996	39/40	89/112		6.7 %	1.23 [1.10, 1.36]
Davidson 1986	32/36	31/49		4.9 %	1.41 [1.10, 1.79]
Djulbegovic 2000	26/35	50/95		4.5 %	1.41 [1.07, 1.85]
Finucane 2004	30/30	12/18		3.9 %	1.50 [1.08, 2.07]
Jefferson 2009	64/76	131/194		6.3 %	1.25 [1.09, 1.43]
Kjaergard 2002	28/38	16/22		4.0 %	1.01 [0.74, 1.39]
Liss 2006	62/63	12/37		2.6 %	3.03 [1.90, 4.84]
Lynch 2007	26/34	49/65		5.0 %	1.01 [0.80, 1.28]
Peppercorn 2007	52/67	48/73		5.4 %	1.18 [0.96, 1.46]
Perlis 2005a	87/102	47/77		5.5 %	1.40 [1.15, 1.70]
Rasmussen 2009	83/109	15/28		3.5 %	1.42 [0.99, 2.04]
Rattinger 2009	31/36	21/25		5.3 %	1.03 [0.83, 1.27]
Ridker 2006	121/189	21/51		3.7 %	1.55 [1.10, 2.20]
Tungaraza 2007	124/146	28/44		5.0 %	1.33 [1.06, 1.69]
Total (95% CI)	**1866**	**2075**		**100.0 %**	**1.31 [1.20, 1.44]**

Total events: 1424 (Industry), 1345 (Non-industry)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 115.75$, df = 20 ($P<0.00001$); $I^2 = 83\%$

Test for overall effect: $Z = 5.70$ ($P < 0.00001$)

Test for subgroup differences: Not applicable

Analysis 4.1. Comparison 4 Conclusions: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company, Outcome 1 Number of studies with favorable test treatment conclusions.

Review: Industry sponsorship and research outcome

Comparison: 4 Conclusions: Industry sponsorship by test treatment company versus sponsorship by comparator treatment company

Outcome: 1 Number of studies with favorable test treatment conclusions

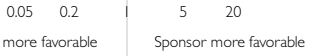
Study or subgroup	Test treatment sponsor n/N	Comparator treatm sponsor n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bero 2007	51/65	4/30		65.9 %	5.88 [2.34, 14.78]
Heres 2006	10/12	1/9		13.8 %	7.50 [1.16, 48.43]
Rattinger 2009	26/32	1/6		20.3 %	4.88 [0.81, 29.40]
Total (95% CI)	**109**	**45**		**100.0 %**	**5.90 [2.79, 12.49]**

Total events: 87 (Test treatment sponsor), 6 (Comparator treatm sponsor)

Heterogeneity: $Chi^2 = 0.11$, df = 2 (P = 0.95); $I^2 = 0.0\%$

Test for overall effect: Z = 4.64 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 5.1. Comparison 5 Risk of bias: industry sponsored versus non-industry sponsored studies, Outcome 1 Number of studies with low risk of bias from sequence generation.

Review: Industry sponsorship and research outcome

Comparison: 5 Risk of bias: industry sponsored versus non-industry sponsored studies

Outcome: 1 Number of studies with low risk of bias from sequence generation

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Als-Nielsen 2003	62/197	43/173		34.0 %	1.27 [0.91, 1.76]
Crocetti 2010	11/32	21/25		28.3 %	0.41 [0.25, 0.68]
Kjaergard 2002	34/38	19/22		37.6 %	1.04 [0.85, 1.26]
Total (95% CI)	**267**	**220**		**100.0 %**	**0.85 [0.52, 1.41]**

Total events: 107 (Industry), 83 (Non-industry)

Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 13.92$, df = 2 (P = 0.00095); $I^2 = 86\%$

Test for overall effect: Z = 0.62 (P = 0.53)

Test for subgroup differences: Not applicable

Analysis 5.2. Comparison 5 Risk of bias: industry sponsored versus non-industry sponsored studies, Outcome 2 Number of studies with low risk of bias from concealment of allocation.

Review: Industry sponsorship and research outcome

Comparison: 5 Risk of bias: industry sponsored versus non-industry sponsored studies

Outcome: 2 Number of studies with low risk of bias from concealment of allocation

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Als-Nielsen 2003	55/197	27/173		12.9 %	1.79 [1.18, 2.70]
Bero 2007	19/95	21/97		9.8 %	0.92 [0.53, 1.60]
Clifford 2002	22/66	14/34		10.3 %	0.81 [0.48, 1.37]
Crocetti 2010	14/32	16/25		11.1 %	0.68 [0.42, 1.12]
Jones 2010	23/31	35/56		16.1 %	1.19 [0.89, 1.59]
Kjaergard 2002	26/38	15/22		14.3 %	1.00 [0.70, 1.44]
Pengel 2009	63/154	34/126		14.7 %	1.52 [1.07, 2.14]
Rattinger 2009	10/36	5/25		4.8 %	1.39 [0.54, 3.57]
Rios 2008	6/42	4/47		3.3 %	1.68 [0.51, 5.54]
Vlad 2007	2/11	3/4		2.6 %	0.24 [0.06, 0.96]
Total (95% CI)	**702**	**609**		**100.0 %**	**1.09 [0.86, 1.38]**

Total events: 240 (Industry), 174 (Non-industry)

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 19.56$, df = 9 (P = 0.02); $I^2 = 54\%$

Test for overall effect: Z = 0.73 (P = 0.46)

Test for subgroup differences: Not applicable

Analysis 5.3. Comparison 5 Risk of bias: industry sponsored versus non-industry sponsored studies, Outcome 3 Number of studies with low risk of bias from blinding.

Review: Industry sponsorship and research outcome

Comparison: 5 Risk of bias: industry sponsored versus non-industry sponsored studies

Outcome: 3 Number of studies with low risk of bias from blinding

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Als-Nielsen 2003	150/197	84/157		16.7 %	1.42 [1.21, 1.68]
Bero 2007	53/95	36/97		13.6 %	1.50 [1.10, 2.06]
Crocetti 2010	28/32	23/25		16.5 %	0.95 [0.80, 1.13]
Jones 2010	16/31	14/56		8.6 %	2.06 [1.17, 3.64]
Kjaergard 2002	26/38	13/22		11.5 %	1.16 [0.77, 1.74]
Perlis 2005a	71/102	27/77		13.2 %	1.99 [1.43, 2.76]
Rasmussen 2009	33/109	3/28		3.4 %	2.83 [0.93, 8.54]
Rattinger 2009	20/36	15/25		11.0 %	0.93 [0.60, 1.43]
Rios 2008	7/42	13/47		5.4 %	0.60 [0.27, 1.37]
Total (95% CI)	**682**	**534**		**100.0 %**	**1.32 [1.05, 1.65]**

Total events: 404 (Industry), 228 (Non-industry)

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 30.72$, df = 8 (P = 0.00016); $I^2 = 74\%$

Test for overall effect: Z = 2.37 (P = 0.018)

Test for subgroup differences: Not applicable

Analysis 5.4. Comparison 5 Risk of bias: industry sponsored versus non-industry sponsored studies, Outcome 4 Number of studies with low risk of bias from loss to follow-up.

Review: Industry sponsorship and research outcome

Comparison: 5 Risk of bias: industry sponsored versus non-industry sponsored studies

Outcome: 4 Number of studies with low risk of bias from loss to follow-up

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crocetti 2010	28/32	22/25		51.1 %	0.99 [0.82, 1.21]
Rattinger 2009	28/36	20/25		48.9 %	0.97 [0.75, 1.26]
Total (95% CI)	**68**	**50**		**100.0 %**	**0.98 [0.84, 1.16]**

Total events: 56 (Industry), 42 (Non-industry)

Heterogeneity: $Chi^2 = 0.02$, df = 1 (P = 0.89); $I^2 = 0.0\%$

Test for overall effect: Z = 0.20 (P = 0.84)

Test for subgroup differences: Not applicable

Analysis 6.1. Comparison 6 Concordance between study results and conclusions: industry sponsored versus non-industry sponsored studies, Outcome 1 Number of studies with concordant study results and conclusions.

Review: Industry sponsorship and research outcome

Comparison: 6 Concordance between study results and conclusions: industry sponsored versus non-industry sponsored studies

Outcome: 1 Number of studies with concordant study results and conclusions

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Alasbali 2009	11/29	10/10		10.1 %	0.40 [0.25, 0.64]
Bero 2007	72/95	80/97		26.6 %	0.92 [0.79, 1.06]
Jefferson 2009	39/66	120/172		21.6 %	0.85 [0.68, 1.06]
Rasmussen 2009	86/109	23/28		23.2 %	0.96 [0.79, 1.17]
Rattinger 2009	27/36	20/25		18.6 %	0.94 [0.71, 1.23]
Total (95% CI)	**335**	**332**		**100.0 %**	**0.84 [0.70, 1.01]**

Total events: 235 (Industry), 253 (Non-industry)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 12.00$, df = 4 (P = 0.02); $I^2 = 67\%$

Test for overall effect: Z = 1.86 (P = 0.063)

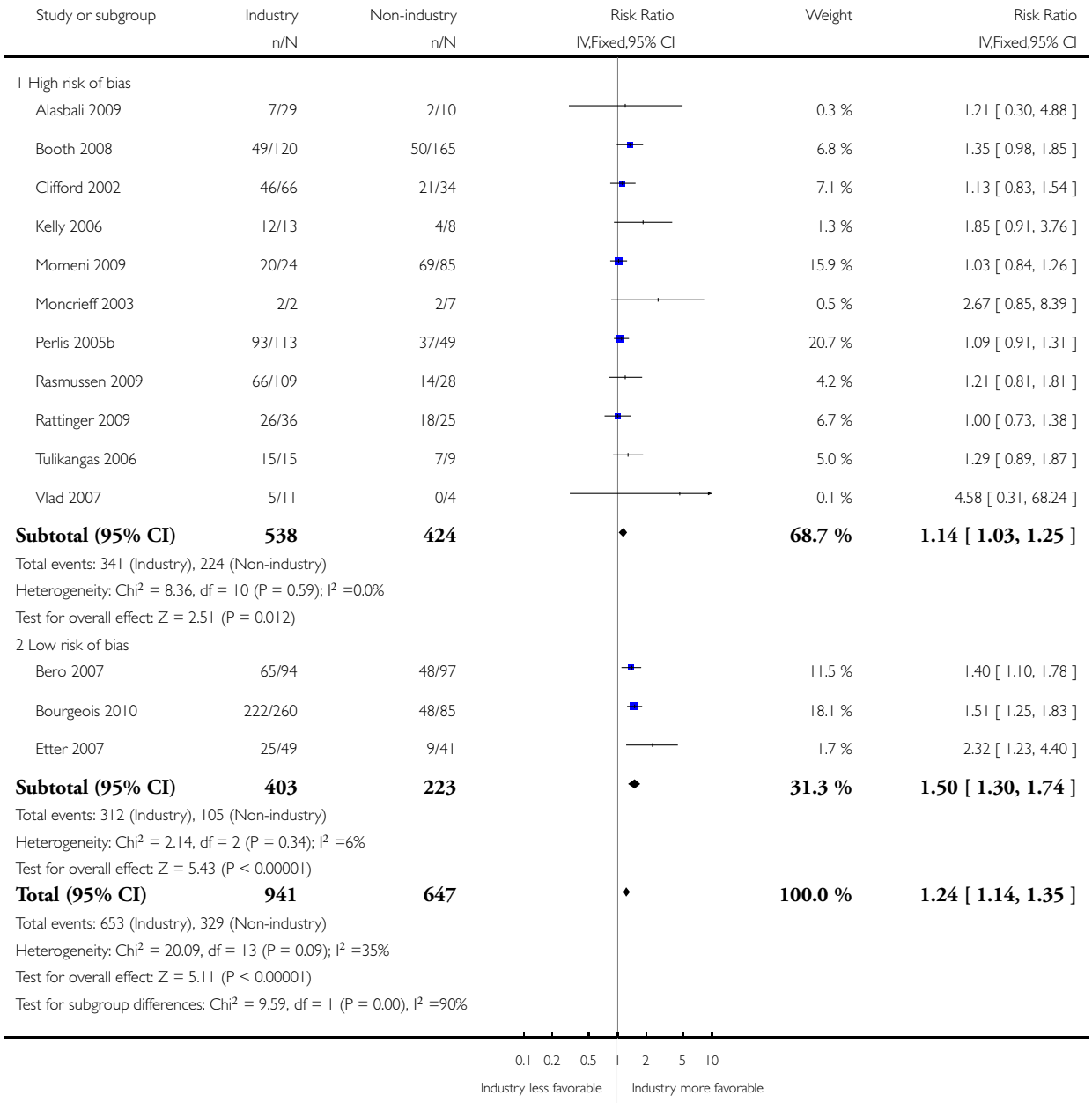
Test for subgroup differences: Not applicable

Analysis 7.1. Comparison 7 Subgroup analysis, Outcome 1 Number of studies with favorable efficacy results.

Review: Industry sponsorship and research outcome

Comparison: 7 Subgroup analysis

Outcome: 1 Number of studies with favorable efficacy results



Analysis 7.2. Comparison 7 Subgroup analysis, Outcome 2 Number of studies with favorable conclusions.

Review: Industry sponsorship and research outcome

Comparison: 7 Subgroup analysis

Outcome: 2 Number of studies with favorable conclusions

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 High risk of bias					
Ahmer 2005	125/138	39/50		6.1 %	1.16 [0.99, 1.36]
Alasbali 2009	26/29	2/10		0.5 %	4.48 [1.29, 15.58]
Booth 2008	66/118	55/153		4.6 %	1.56 [1.19, 2.03]
Buchkowsky 2004	138/181	224/319		6.7 %	1.09 [0.97, 1.21]
Chard 2000	106/108	373/383		7.3 %	1.01 [0.98, 1.04]
Cho 1996	39/40	89/112		6.7 %	1.23 [1.10, 1.36]
Davidson 1986	32/36	31/49		4.9 %	1.41 [1.10, 1.79]
Djulbegovic 2000	26/35	50/95		4.5 %	1.41 [1.07, 1.85]
Kjaergard 2002	28/38	16/22		4.0 %	1.01 [0.74, 1.39]
Liss 2006	62/63	12/37		2.6 %	3.03 [1.90, 4.84]
Lynch 2007	26/34	49/65		5.0 %	1.01 [0.80, 1.28]
Peppercorn 2007	52/67	48/73		5.4 %	1.18 [0.96, 1.46]
Perlis 2005a	87/102	47/77		5.5 %	1.40 [1.15, 1.70]
Rasmussen 2009	83/109	15/28		3.5 %	1.42 [0.99, 2.04]
Rattinger 2009	31/36	21/25		5.3 %	1.03 [0.83, 1.27]
Ridker 2006	121/189	21/51		3.7 %	1.55 [1.10, 2.20]
Tungaraza 2007	124/146	28/44		5.0 %	1.33 [1.06, 1.69]
Subtotal (95% CI)	**1469**	**1593**		**81.2 %**	**1.26 [1.14, 1.39]**
Total events: 1172 (Industry), 1120 (Non-industry)					
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 81.31$, df = 16 (P<0.00001); $I^2 = 80\%$					
Test for overall effect: Z = 4.67 (P < 0.00001)					
2 Low risk of bias					
Als-Nielsen 2003	92/197	43/173		4.2 %	1.88 [1.39, 2.53]
Bero 2007	66/94	39/97		4.5 %	1.75 [1.32, 2.30]

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Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Finucane 2004	30/30	12/18		3.9 %	1.50 [1.08, 2.07]
Jefferson 2009	64/76	131/194		6.3 %	1.25 [1.09, 1.43]
Subtotal (95% CI)	**397**	**482**		**18.8 %**	**1.54 [1.24, 1.91]**
Total events: 252 (Industry), 225 (Non-industry)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 9.02, df = 3 (P = 0.03); I^2 =67%					
Test for overall effect: Z = 3.89 (P = 0.00010)					
Total (95% CI)	**1866**	**2075**		**100.0 %**	**1.31 [1.20, 1.44]**
Total events: 1424 (Industry), 1345 (Non-industry)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 115.75, df = 20 (P<0.00001); I^2 =83%					
Test for overall effect: Z = 5.70 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 2.73, df = 1 (P = 0.10), I^2 =63%					

Analysis 7.3. Comparison 7 Subgroup analysis, Outcome 3 Number of studies with favorable conclusions.

Review: Industry sponsorship and research outcome

Comparison: 7 Subgroup analysis

Outcome: 3 Number of studies with favorable conclusions

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Drug studies					
Ahmer 2005	125/138	39/50		5.8 %	1.16 [0.99, 1.36]
Alasbali 2009	26/29	2/10		0.5 %	4.48 [1.29, 15.58]
Als-Nielsen 2003	92/197	43/173		4.0 %	1.88 [1.39, 2.53]
Bero 2007	66/94	39/97		4.3 %	1.75 [1.32, 2.30]
Booth 2008	66/118	55/153		4.4 %	1.56 [1.19, 2.03]
Buchkowsky 2004	138/181	224/319		6.4 %	1.09 [0.97, 1.21]
Chard 2000	106/108	373/383		7.0 %	1.01 [0.98, 1.04]
Cho 1996	39/40	89/112		6.4 %	1.23 [1.10, 1.36]
Davidson 1986	32/36	31/49		4.7 %	1.41 [1.10, 1.79]

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Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Djulbegovic 2000	26/35	50/95		4.3 %	1.41 [1.07, 1.85]
Finucane 2004	30/30	12/18		3.7 %	1.50 [1.08, 2.07]
Jefferson 2009	64/76	131/194		6.1 %	1.25 [1.09, 1.43]
Kjaergard 2002	28/38	16/22		3.8 %	1.01 [0.74, 1.39]
Liss 2006	62/63	12/37		2.5 %	3.03 [1.90, 4.84]
Lynch 2007	7/8	9/9		3.7 %	0.88 [0.63, 1.21]
Peppercorn 2007	52/67	48/73		5.1 %	1.18 [0.96, 1.46]
Perlis 2005a	87/102	47/77		5.3 %	1.40 [1.15, 1.70]
Rasmussen 2009	83/109	15/28		3.4 %	1.42 [0.99, 2.04]
Rattinger 2009	31/36	21/25		5.1 %	1.03 [0.83, 1.27]
Ridker 2006	98/159	17/43		3.1 %	1.56 [1.06, 2.30]
Tungaraza 2007	124/146	28/44		4.8 %	1.33 [1.06, 1.69]
Subtotal (95% CI)	**1810**	**2011**		**94.5 %**	**1.31 [1.19, 1.44]**
Total events: 1382 (Industry), 1301 (Non-industry)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 116.15, df = 20 (P<0.00001); I^2 =83%					
Test for overall effect: Z = 5.55 (P < 0.00001)					
2 Device studies					
Lynch 2007	19/26	40/56		4.2 %	1.02 [0.77, 1.36]
Ridker 2006	23/30	4/8		1.3 %	1.53 [0.75, 3.15]
Subtotal (95% CI)	**56**	**64**		**5.5 %**	**1.09 [0.82, 1.45]**
Total events: 42 (Industry), 44 (Non-industry)					
Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.05, df = 1 (P = 0.31); I^2 =4%					
Test for overall effect: Z = 0.58 (P = 0.56)					
Total (95% CI)	**1866**	**2075**		**100.0 %**	**1.30 [1.18, 1.42]**
Total events: 1424 (Industry), 1345 (Non-industry)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 117.20, df = 22 (P<0.00001); I^2 =81%					
Test for overall effect: Z = 5.58 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 1.45, df = 1 (P = 0.23), I^2 =31%					

Analysis 7.4. Comparison 7 Subgroup analysis, Outcome 4 Number of studies with favorable efficacy results.

Review: Industry sponsorship and research outcome

Comparison: 7 Subgroup analysis

Outcome: 4 Number of studies with favorable efficacy results

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Specific treatments or diseases					
Alasbali 2009	7/29	2/10		0.3 %	1.21 [0.30, 4.88]
Bero 2007	65/94	48/97		11.5 %	1.40 [1.10, 1.78]
Booth 2008	49/120	50/165		6.8 %	1.35 [0.98, 1.85]
Etter 2007	25/49	9/41		1.7 %	2.32 [1.23, 4.40]
Kelly 2006	12/13	4/8		1.3 %	1.85 [0.91, 3.76]
Momeni 2009	20/24	69/85		15.9 %	1.03 [0.84, 1.26]
Moncrieff 2003	2/2	2/7		0.5 %	2.67 [0.85, 8.39]
Perlis 2005b	93/113	37/49		20.7 %	1.09 [0.91, 1.31]
Rasmussen 2009	66/109	14/28		4.2 %	1.21 [0.81, 1.81]
Rattinger 2009	26/36	18/25		6.7 %	1.00 [0.73, 1.38]
Tulikangas 2006	15/15	7/9		5.0 %	1.29 [0.89, 1.87]
Vlad 2007	5/11	0/4		0.1 %	4.58 [0.31, 68.24]
Subtotal (95% CI)	**615**	**528**		**74.8 %**	**1.19 [1.08, 1.31]**
Total events: 385 (Industry), 260 (Non-industry)					
Heterogeneity: Chi^2 = 15.02, df = 11 (P = 0.18); I^2 =27%					
Test for overall effect: Z = 3.61 (P = 0.00030)					
2 Mixed domain					
Bourgeois 2010	222/260	48/85		18.1 %	1.51 [1.25, 1.83]
Clifford 2002	46/66	21/34		7.1 %	1.13 [0.83, 1.54]
Subtotal (95% CI)	**326**	**119**		**25.2 %**	**1.39 [1.18, 1.64]**
Total events: 268 (Industry), 69 (Non-industry)					
Heterogeneity: Chi^2 = 2.48, df = 1 (P = 0.12); I^2 =60%					
Test for overall effect: Z = 3.96 (P = 0.000075)					
Total (95% CI)	**941**	**647**		**100.0 %**	**1.24 [1.14, 1.35]**
Total events: 653 (Industry), 329 (Non-industry)					
Heterogeneity: Chi^2 = 20.09, df = 13 (P = 0.09); I^2 =35%					
Test for overall effect: Z = 5.11 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 2.59, df = 1 (P = 0.11), I^2 =61%					

Analysis 7.5. Comparison 7 Subgroup analysis, Outcome 5 Number of studies with favorable conclusions.

Review: Industry sponsorship and research outcome

Comparison: 7 Subgroup analysis

Outcome: 5 Number of studies with favorable conclusions

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Specific treatments or diseases					
Ahmer 2005	125/138	39/50		6.1 %	1.16 [0.99, 1.36]
Alasbali 2009	26/29	2/10		0.5 %	4.48 [1.29, 15.58]
Bero 2007	66/94	39/97		4.5 %	1.75 [1.32, 2.30]
Booth 2008	66/118	55/153		4.6 %	1.56 [1.19, 2.03]
Chard 2000	106/108	373/383		7.3 %	1.01 [0.98, 1.04]
Djulbegovic 2000	26/35	50/95		4.5 %	1.41 [1.07, 1.85]
Finucane 2004	30/30	12/18		3.9 %	1.50 [1.08, 2.07]
Jefferson 2009	64/76	131/194		6.3 %	1.25 [1.09, 1.43]
Liss 2006	62/63	12/37		2.6 %	3.03 [1.90, 4.84]
Lynch 2007	26/34	49/65		5.0 %	1.01 [0.80, 1.28]
Peppercorn 2007	52/67	48/73		5.4 %	1.18 [0.96, 1.46]
Perlis 2005a	87/102	47/77		5.5 %	1.40 [1.15, 1.70]
Rasmussen 2009	83/109	15/28		3.5 %	1.42 [0.99, 2.04]
Rattinger 2009	31/36	21/25		5.3 %	1.03 [0.83, 1.27]
Ridker 2006	121/189	21/51		3.7 %	1.55 [1.10, 2.20]
Tungaraza 2007	124/146	28/44		5.0 %	1.33 [1.06, 1.69]
Subtotal (95% CI)	**1374**	**1400**		**73.6 %**	**1.34 [1.19, 1.51]**
Total events: 1095 (Industry), 942 (Non-industry)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 90.76$, df = 15 (P<0.00001); $I^2 = 83\%$					
Test for overall effect: Z = 4.77 (P < 0.00001)					
2 Mixed study domain					
Als-Nielsen 2003	92/197	43/173		4.2 %	1.88 [1.39, 2.53]
Buchkowsky 2004	138/181	224/319		6.7 %	1.09 [0.97, 1.21]
Cho 1996	39/40	89/112		6.7 %	1.23 [1.10, 1.36]
Davidson 1986	32/36	31/49		4.9 %	1.41 [1.10, 1.79]
Kjaergard 2002	28/38	16/22		4.0 %	1.01 [0.74, 1.39]

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Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Subtotal (95% CI)	**492**	**675**		**26.4 %**	**1.26 [1.08, 1.47]**
Total events: 329 (Industry), 403 (Non-industry)					
Heterogeneity: Tau^2 = 0.02; Chi^2 = 14.79, df = 4 (P = 0.01); I^2 =73%					
Test for overall effect: Z = 2.91 (P = 0.0036)					
Total (95% CI)	**1866**	**2075**		**100.0 %**	**1.31 [1.20, 1.44]**
Total events: 1424 (Industry), 1345 (Non-industry)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 115.75, df = 20 (P<0.00001); I^2 =83%					
Test for overall effect: Z = 5.70 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.37, df = 1 (P = 0.54), I^2 =0.0%					

Analysis 8.1. Comparison 8 Sensitivity analysis, Outcome 1 Number of studies with favorable efficacy results, sponsorship recoded.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 1 Number of studies with favorable efficacy results, sponsorship recoded

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bero 2007	54/76	10/23		14.4 %	1.63 [1.00, 2.66]
Bourgeois 2010	188/220	48/85		64.9 %	1.51 [1.25, 1.84]
Clifford 2002	30/44	15/28		17.2 %	1.27 [0.85, 1.90]
Moncrieff 2003	2/2	1/6		0.8 %	3.89 [0.86, 17.54]
Rattinger 2009	25/32	1/1		2.7 %	1.03 [0.45, 2.34]
Total (95% CI)	**374**	**143**		**100.0 %**	**1.50 [1.27, 1.76]**
Total events: 299 (Industry), 75 (Non-industry)					
Heterogeneity: Chi^2 = 3.11, df = 4 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 4.88 (P < 0.00001)					
Test for subgroup differences: Not applicable					

Analysis 8.2. Comparison 8 Sensitivity analysis, Outcome 2 Number of studies with favorable conclusions, sponsorship recoded.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 2 Number of studies with favorable conclusions, sponsorship recoded

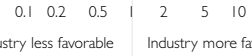
Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Ahmer 2005	75/84	34/43		22.5 %	1.13 [0.95, 1.34]
Als-Nielsen 2003	74/146	11/67		7.1 %	3.09 [1.76, 5.42]
Bero 2007	57/76	10/23		8.9 %	1.73 [1.06, 2.80]
Buchkowsky 2004	76/104	121/180		23.4 %	1.09 [0.93, 1.27]
Jefferson 2009	23/29	89/130		19.7 %	1.16 [0.93, 1.44]
Kjaergard 2002	21/23	10/13		14.4 %	1.19 [0.86, 1.64]
Rattinger 2009	28/32	1/1		3.9 %	1.15 [0.51, 2.59]
Total (95% CI)	**494**	**457**		**100.0 %**	**1.26 [1.06, 1.50]**

Total events: 354 (Industry), 276 (Non-industry)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 14.91$, df = 6 (P = 0.02); $I^2 = 60\%$

Test for overall effect: Z = 2.65 (P = 0.0079)

Test for subgroup differences: Not applicable



Analysis 8.3. Comparison 8 Sensitivity analysis, Outcome 3 Number of studies with low risk of bias from sequence generation, sponsorship recoded.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 3 Number of studies with low risk of bias from sequence generation, sponsorship recoded

Study or subgroup	Industry n/N	Nonindustry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Als-Nielsen 2003	43/146	20/67		68.2 %	0.99 [0.63, 1.54]
Kjaergard 2002	21/23	10/13		31.8 %	1.19 [0.86, 1.64]
Total (95% CI)	**169**	**80**		**100.0 %**	**1.05 [0.77, 1.44]**
Total events: 64 (Industry), 30 (Nonindustry)					
Heterogeneity: Chi^2 = 0.63, df = 1 (P = 0.43); I^2 =0.0%					
Test for overall effect: Z = 0.31 (P = 0.76)					
Test for subgroup differences: Not applicable					

Analysis 8.4. Comparison 8 Sensitivity analysis, Outcome 4 Number of studies with low risk of bias from concealment of allocation, sponsorship recoded.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 4 Number of studies with low risk of bias from concealment of allocation, sponsorship recoded

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Als-Nielsen 2003	38/146	13/67		24.6 %	1.34 [0.77, 2.35]
Bero 2007	17/76	6/24		12.6 %	0.89 [0.40, 2.01]
Clifford 2002	16/44	13/28		21.9 %	0.78 [0.45, 1.37]
Kjaergard 2002	16/23	8/13		14.1 %	1.13 [0.68, 1.88]
Pengel 2009	52/128	11/38		23.4 %	1.40 [0.82, 2.41]
Rattinger 2009	9/32	0/1		1.3 %	1.15 [0.10, 13.47]
Rios 2008	3/16	2/27		2.1 %	2.53 [0.47, 13.57]
Total (95% CI)	**465**	**198**		**100.0 %**	**1.17 [0.90, 1.52]**

Total events: 151 (Industry), 53 (Non-industry)

Heterogeneity: $Chi^2 = 3.90$, df = 6 (P = 0.69); $I^2 = 0.0\%$

Test for overall effect: Z = 1.18 (P = 0.24)

Test for subgroup differences: Not applicable

Analysis 8.5. Comparison 8 Sensitivity analysis, Outcome 5 Number of studies with low risk of bias from blinding, sponsorship recoded.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 5 Number of studies with low risk of bias from blinding, sponsorship recoded

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Als-Nielsen 2003	108/146	32/67		63.5 %	1.55 [1.18, 2.03]
Bero 2007	45/76	5/24		11.0 %	2.84 [1.27, 6.34]
Kjaergard 2002	17/23	9/13		16.6 %	1.07 [0.69, 1.65]
Rattinger 2009	20/32	0/1		1.4 %	2.48 [0.22, 27.81]
Rios 2008	2/16	7/27		7.5 %	0.48 [0.11, 2.04]
Total (95% CI)	**293**	**132**		**100.0 %**	**1.54 [1.23, 1.94]**

Total events: 192 (Industry), 53 (Non-industry)

Heterogeneity: $Chi^2 = 7.61$, df = 4 (P = 0.11); $I^2 = 47\%$

Test for overall effect: Z = 3.71 (P = 0.00021)

Test for subgroup differences: Not applicable

Analysis 8.6. Comparison 8 Sensitivity analysis, Outcome 6 Results:Number of studies with favorable efficacy results, analysis adjusted for confounders.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 6 Results:Number of studies with favorable efficacy results, analysis adjusted for confounders

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Fixed,95% CI	Weight	Odds Ratio IV,Fixed,95% CI
Bourgeois 2010	1.5686 (0.5142)		47.0 %	4.80 [1.75, 13.15]
Etter 2007	1.1569 (0.4846)		53.0 %	3.18 [1.23, 8.22]
Total (95% CI)			**100.0 %**	**3.86 [1.93, 7.70]**

Heterogeneity: $Chi^2 = 0.34$, df = 1 (P = 0.56); $I^2 = 0.0\%$

Test for overall effect: Z = 3.83 (P = 0.00013)

Test for subgroup differences: Not applicable

Analysis 8.7. Comparison 8 Sensitivity analysis, Outcome 7 Conclusions:Number of studies with favorable conclusions, analysis adjusted for confounders.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

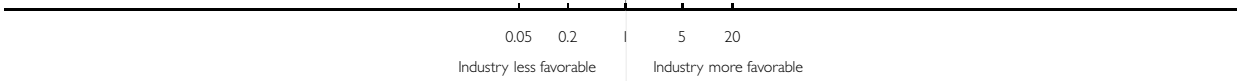
Outcome: 7 Conclusions:Number of studies with favorable conclusions, analysis adjusted for confounders

Study or subgroup	log [Odds Ratio] (SE)	Odds Ratio IV,Fixed,95% CI	Weight	Odds Ratio IV,Fixed,95% CI
Als-Nielsen 2003	1.6677 (0.5082)		30.4 %	5.30 [1.96, 14.35]
Booth 2008	1.2528 (0.3868)		52.5 %	3.50 [1.64, 7.47]
Perlis 2005a	1.5129 (0.6776)		17.1 %	4.54 [1.20, 17.13]
Total (95% CI)			**100.0 %**	**4.15 [2.40, 7.19]**

Heterogeneity: $Chi^2 = 0.44$, df = 2 (P = 0.80); $I^2 = 0.0\%$

Test for overall effect: Z = 5.08 (P < 0.00001)

Test for subgroup differences: Not applicable



Analysis 8.8. Comparison 8 Sensitivity analysis, Outcome 8 Number of studies with favorable efficacy results, random-effects model.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 8 Number of studies with favorable efficacy results, random-effects model

Study or subgroup	Industry n/N	Non-industry n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Alasbali 2009	7/29	2/10		0.7 %	1.21 [0.30, 4.88]
Bero 2007	65/94	48/97		11.6 %	1.40 [1.10, 1.78]
Booth 2008	49/120	50/165		8.5 %	1.35 [0.98, 1.85]
Bourgeois 2010	222/260	48/85		14.2 %	1.51 [1.25, 1.83]
Clifford 2002	46/66	21/34		8.8 %	1.13 [0.83, 1.54]
Etter 2007	25/49	9/41		2.8 %	2.32 [1.23, 4.40]
Kelly 2006	12/13	4/8		2.4 %	1.85 [0.91, 3.76]
Momeni 2009	20/24	69/85		13.5 %	1.03 [0.84, 1.26]
Moncrieff 2003	2/2	2/7		1.0 %	2.67 [0.85, 8.39]
Perlis 2005b	93/113	37/49		15.0 %	1.09 [0.91, 1.31]
Rasmussen 2009	66/109	14/28		6.1 %	1.21 [0.81, 1.81]
Rattinger 2009	26/36	18/25		8.4 %	1.00 [0.73, 1.38]
Tulikangas 2006	15/15	7/9		6.9 %	1.29 [0.89, 1.87]
Vlad 2007	5/11	0/4		0.2 %	4.58 [0.31, 68.24]
Total (95% CI)	**941**	**647**		**100.0 %**	**1.26 [1.12, 1.41]**

Total events: 653 (Industry), 329 (Non-industry)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 20.09$, df = 13 (P = 0.09); $I^2 = 35\%$

Test for overall effect: Z = 3.95 (P = 0.000079)

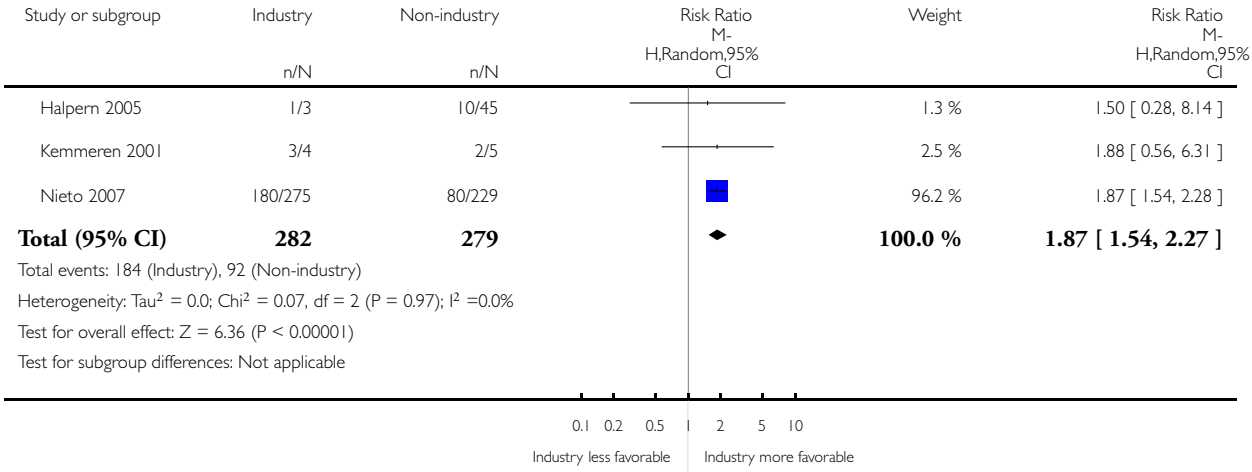
Test for subgroup differences: Not applicable

Analysis 8.9. Comparison 8 Sensitivity analysis, Outcome 9 Number of studies with favorable harms results, random-effects model.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 9 Number of studies with favorable harms results, random-effects model

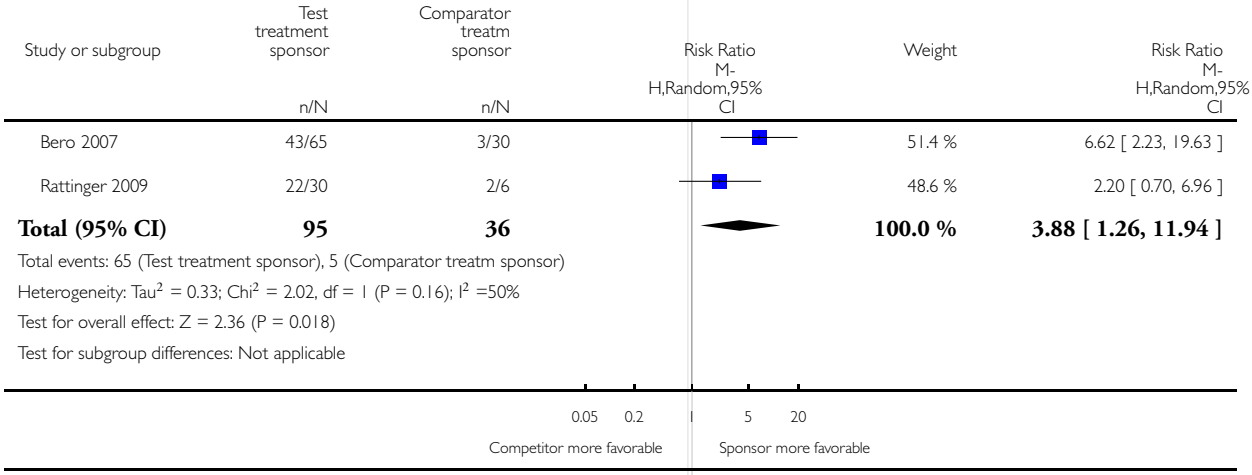


Analysis 8.10. Comparison 8 Sensitivity analysis, Outcome 10 Number of studies with favorable test treatment efficacy results, random effects-model.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 10 Number of studies with favorable test treatment efficacy results, random effects-model

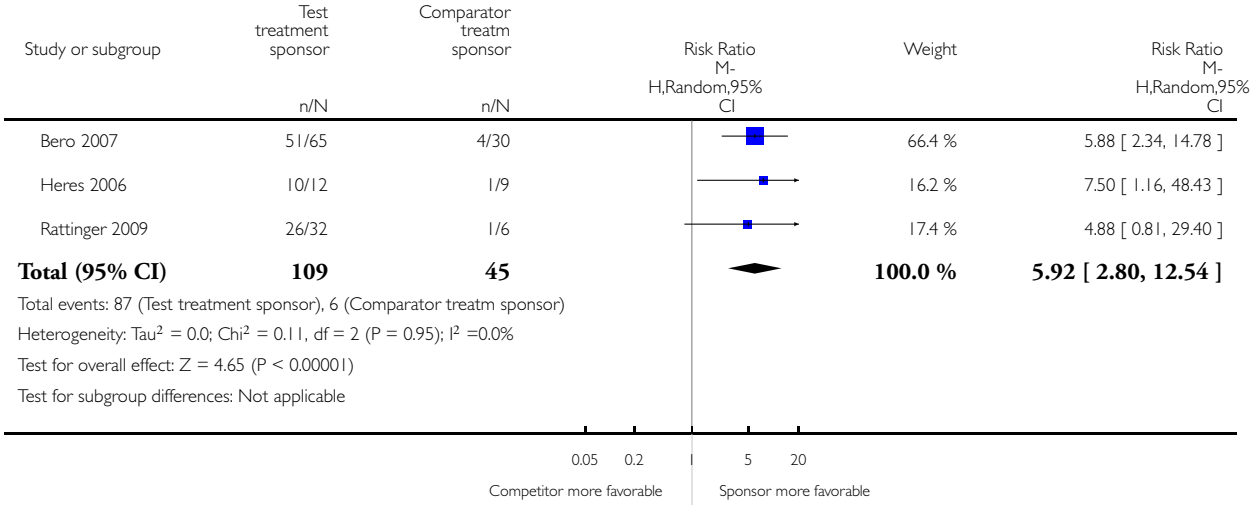


Analysis 8.11. Comparison 8 Sensitivity analysis, Outcome 11 Number of studies with favorable test treatment conclusions, random-effects model.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 11 Number of studies with favorable test treatment conclusions, random-effects model

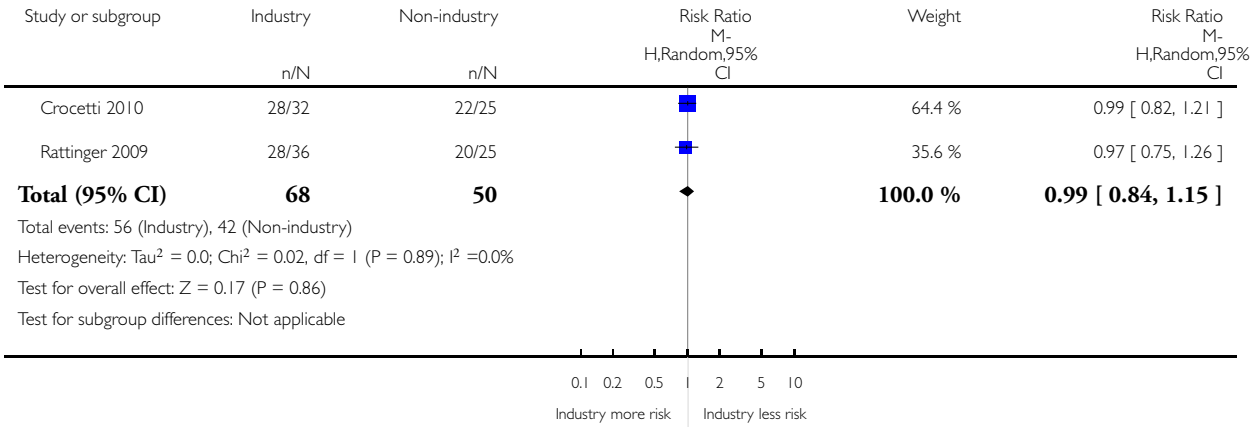


Analysis 8.12. Comparison 8 Sensitivity analysis, Outcome 12 Number of studies with low risk of bias from loss to follow-up, random-effects model.

Review: Industry sponsorship and research outcome

Comparison: 8 Sensitivity analysis

Outcome: 12 Number of studies with low risk of bias from loss to follow-up, random-effects model



APPENDICES

Appendix 1. Search strategy

1. Drug Industry/
2. ((drug$ or pharmaceutical$ or device$ or for-profit) adj (industr$ or company or companies or manufacturer$ or organisation$ or organization$ or agency or agencies)).ti,ab.
3. private industr$.ti,ab.
4. (industr$ or nonindustr$ or non-industr$).ti,ab.
5. 1 or 2 or 3 or 4
6. Conflict of interest/
7. Financial support/
8. Research support as topic/
9. (funded or funding or sponsor$ or support$ or financ$ or involvement).ti,ab.
10. "competing interest$".ti,ab.
11. or/6-10
12. 5 and 11
13. Publication bias/
14. "Bias (Epidemiology)"/
15. bias$.ti,ab.
16. or/13-15
17. 12 and 16
18. Treatment outcome/
19. "Outcome Assessment (Health Care)"/

20. (outcome$ or findings).ti,ab.
21. or/18-20
22. (favor$ or favour$ or positive or significan$ or beneficial or benefit$ or effective or effectual or efficacious).ti,ab.
23. (insignificant$ or nonsignificant$ or negative or adverse or ineffectiv$ or ineffectual or unfavorabl$ or unfavourabl$).ti,ab.
24. 22 or 23
25. 21 and 24
26. 12 and 25
27. ((favor$ or favour$ or positive or significan$ or insignificant$ or nonsignificant$ or negative or unfavorabl$ or unfavourabl$) adj result$).ti,ab.
28. 12 and 27
29. 17 or 26 or 28

HISTORY

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CONTRIBUTIONS OF AUTHORS

Development of protocol (AL, JL, LB and SS); design of the search strategy (AL); initial screening of articles (AL and OAB); final selection of studies (all authors); data extraction (AL and SS); data analysis and interpretation of results (all authors); writing of manuscript (all authors).

DECLARATIONS OF INTEREST

Joel Lexchin, Lisa Bero and Sergio Sismondo are authors of the some of the previous reviews and included studies.

In 2007, Joel Lexchin was retained by a law firm representing Apotex to provide expert testimony about the effects of promotion on the sales of medications. From 2007 to 2008 he was retained as an expert witness by the Canadian federal government in its defense of a lawsuit challenging the ban on direct-to-consumer advertising of prescription drugs in Canada. In 2010 he was a consultant to a law firm acting for the family of a patient who died from an alleged side effect of a drug made by Allergan. He is also on the management group of Healthy Skepticism Inc. and is the chair of the Health Action International - Europe Association Board.

The authors have no other relevant interests.

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The second author was personally salaried by his institution during the period of the review.

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The author was personally salaried by her institution during the period of the review.

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