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# BMJ Open

## Reporting of Drug Trial Funding Sources and Author Financial Conflicts of Interest in Cochrane and non-Cochrane Meta-analyses: A Cross-sectional Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035633
Article Type:	Original research
Date Submitted by the Author:	08-Nov-2019
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Keywords:	EPIDEMIOLOGY, STATISTICS & RESEARCH METHODS, MEDICAL ETHICS

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Manuscripts



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3 **1 Reporting of Drug Trial Funding Sources and Author Financial Conflicts of Interest in**  
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5 **2 Cochrane and non-Cochrane Meta-analyses: A Cross-sectional Study**  
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51 45  
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53 46 **Word count:** 4,048  
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3 47 **ABSTRACT**  
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5 48 **Objective:** To (1) investigate the extent to which recently published meta-analyses report trial  
6  
7 49 funding, author-industry financial ties, and author-industry employment from included RCTs,  
8  
9 50 comparing Cochrane and non-Cochrane meta-analyses; (2) examine characteristics of meta-  
10  
11 51 analyses independently associated with reporting funding sources of included RCTs; and (3)  
12  
13 52 compare reporting among recently published Cochrane meta-analyses to Cochrane reviews  
14  
15 53 published in 2010.  
16  
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18

19 54 **Design:** Review of consecutive sample of recently published meta-analyses.  
20

21 55 **Data sources:** MEDLINE database via PubMed searched on October 19, 2018.  
22

23 56 **Eligibility criteria for selecting articles:** We selected the 250 most recent meta-analyses listed  
24  
25 57 in PubMed that included a documented search of at least one database, statistically combined  
26  
27 58 results from  $\geq 2$  RCTs, and evaluated the effects of a drug or class of drugs.  
28  
29

30 59 **Results:** 90 of 107 (84%) Cochrane meta-analyses reported funding sources for some or all  
31  
32 60 included trials compared with 21 of 143 (15%) non-Cochrane meta-analyses, a difference of 69%  
33  
34 61 (95% confidence interval [CI], 59% to 77%). Percent reporting was also higher for Cochrane  
35  
36 62 meta-analyses compared with non-Cochrane meta-analyses for trial author-industry financial ties  
37  
38 63 (44% versus 1%; 95% CI for difference, 33% to 52%) and employment (17% versus 1%; 95%  
39  
40 64 CI for difference, 9% to 24%). In multivariable analysis, compared with Cochrane meta-  
41  
42 65 analyses, the odds ratio for reporting trial funding was  $\leq 0.11$  for all other journal category and  
43  
44 66 impact factor combinations. Compared with Cochrane reviews from 2010, reporting of funding  
45  
46 67 sources of included RCTs among recently published Cochrane meta-analyses improved by 54%  
47  
48 68 (95% CI, 42% to 63%), and reporting of trial author-industry financial ties and employment  
49  
50 69 improved by 37% (95% CI, 26% to 47%) and 10% (95% CI, 2% to 19%).  
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3 70 **Conclusions:** Reporting of trial funding sources, trial author-industry financial ties, and trial  
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5 71 author-industry employment in Cochrane meta-analyses has improved since 2010 and is higher  
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7 72 than in non-Cochrane meta-analyses.  
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3 73 **Strengths and limitations of this study**  
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- 5 74
- 6 • We assessed reporting in 250 recently published meta-analyses, including 107  
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8 75 Cochrane meta-analyses.
  - 9  
10 76 • The meta-analyses selected for inclusion in our study were representative of the  
11  
12 77 spectrum of meta-analyses of drug interventions and the journals where they were  
13  
14 78 published in 2016-2018.
  - 15  
16  
17 79 • We compared reporting practices among Cochrane and non-Cochrane meta-  
18  
19 80 analyses and recent Cochrane meta-analyses with Cochrane systematic reviews  
20  
21 81 from 2010.
  - 22  
23  
24 82 • Most meta-analyses of drug trials are published as Cochrane reviews or in  
25  
26 83 relatively low-impact specialty medicine journals. Thus, we were unable to  
27  
28 84 examine whether meta-analyses published in different types of journals or  
29  
30 85 journals with different impact factors are more or less likely to report on financial  
31  
32 86 conflicts of interest from included trials.
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35 87 • Our study examined only disclosed financial conflicts of interest and did not  
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37 88 attempt to identify non-disclosed conflicts.
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3 89 Financial conflicts of interest (FCOIs) can introduce bias in drug trials by influencing  
4  
5 90 how a trial is designed, inclusion and exclusion criteria, choice of drug dosages and comparators,  
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7 91 selection of trial outcomes, how analyses are conducted, interpretation of findings, which  
8  
9  
10 92 outcomes are reported, and whether trial results are published.<sup>1-9</sup> Drug trials funded by industry  
11  
12 93 are approximately 30% more likely to report favourable efficacy findings than non-industry  
13  
14 94 trials,<sup>8</sup> and drug trials with principal investigators with FCOIs have higher odds of reporting  
15  
16 95 favourable outcomes than those led by principal investigators without FCOIs, even after  
17  
18 96 controlling for trial funding sources.<sup>7</sup>  
19  
20

21 97 Previous studies that have examined meta-analyses of drug trials published in high-  
22  
23 98 impact journals and Cochrane systematic reviews of drug trials have found that funding sources  
24  
25 99 and author FCOIs of included randomized controlled trials (RCTs) were rarely reported.<sup>10, 11</sup> A  
26  
27  
28 100 2011 study found that only 2 of a sample of 29 (7%) meta-analyses on the effects of drug  
29  
30 101 interventions published in high-impact journals in 2009 reported the funding sources of included  
31  
32 102 drug trials and that none reported trial author-industry financial ties or author-industry  
33  
34 103 employment.<sup>10</sup> A second study, published in 2012, examined Cochrane systematic reviews of  
35  
36 104 drug trials and found that only 46 of 151 (30%) eligible reviews published in 2010 reported  
37  
38 105 information on the funding source of some or all included trials, 11 (7%) provided any  
39  
40 106 information on author-industry financial ties, and 10 (7%) provided any information on author-  
41  
42 107 industry employment from included trials.<sup>11</sup>  
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45

46 108 In 2012, the Cochrane Collaboration began to require that Cochrane reviews report trial  
47  
48 109 funding sources and FCOIs of the primary researchers of all included trials in the characteristics  
49  
50 110 of included studies table (Methodological Expectations of Cochrane Intervention Reviews  
51  
52 111 (MECIR), standards R69 and R70).<sup>12-13</sup> The Preferred Reporting Items for Systematic Reviews  
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3 112 and Meta-analyses (PRISMA) statement, however, has not been updated since its publication in  
4  
5 113 2009<sup>14, 15</sup> and does not address the reporting of trial funding or author FCOIs of trials included in  
6  
7  
8 114 systematic reviews and meta-analyses.

9  
10 115 We do not know of any studies that have compared reporting among Cochrane meta-  
11  
12 116 analyses with meta-analyses published in other journals or examined whether reporting in  
13  
14  
15 117 Cochrane reviews has improved since Cochrane implemented its reporting policy. The objectives  
16  
17 118 of the present study were to (1) investigate the extent to which Cochrane and non-Cochrane  
18  
19 119 meta-analyses of drug trials report trial funding sources, author-industry financial ties, and  
20  
21 120 author-industry employment; (2) examine characteristics of meta-analyses that are independently  
22  
23 121 associated with reporting funding sources of included RCTs; and (3) compare reporting among  
24  
25 122 recently published Cochrane meta-analyses to reporting from Cochrane systematic reviews  
26  
27 123 published in 2010,<sup>11</sup> prior to implementation of Cochrane's reporting policy.

## 30 124 **METHODS**

31  
32  
33 125 The methods for the present study were based on our previous study of reporting of  
34  
35 126 funding sources, author-industry financial ties, and author-industry employment from trials  
36  
37 127 included in Cochrane systematic reviews published in 2010; however in the present study, we  
38  
39 128 included only Cochrane reviews that contained a meta-analysis, whereas in the previous study all  
40  
41 129 Cochrane reviews that included results from at least one RCT were eligible.<sup>11</sup> Because of this  
42  
43 130 difference, in our comparison, in addition to main analyses, we conducted sensitivity analyses  
44  
45 131 that only included systematic reviews with meta-analyses from the previous study. A study  
46  
47 132 protocol was developed prior to initiating the present study and was posted on the Open Science  
48  
49 133 Framework (<https://osf.io/njk5w/>).

### 50 134 **Selection of meta-analyses**

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3 135 Meta-analyses in any language were eligible if they (1) included a documented search for  
4  
5 136 eligible RCTs using at least one database, (2) statistically combined results from  $\geq 2$  RCTs, and  
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7  
8 137 (3) evaluated the efficacy/effectiveness or harm of a drug or class of drugs against an alternative  
9  
10 138 treatment (e.g., placebo, alternative drug, non-pharmacological treatment) or no treatment. Meta-  
11  
12 139 analyses that only assessed different methods of administration, dosages, or dosage schedules of  
13  
14 140 the same drug were excluded. Drugs were defined broadly to include biologics and vaccines, but  
15  
16  
17 141 not nutritional supplements or medical devices without a drug component. Meta-analyses that  
18  
19 142 investigated a combination of pharmacological and non-pharmacological interventions or  
20  
21 143 interventions which may or may not involve a drug (e.g., amnioinfusion) were included if a study  
22  
23 144 group was exclusively given a drug intervention or if the meta-analysis assessed the addition of a  
24  
25 145 drug to a treatment received by both intervention and control groups. Interventions were  
26  
27  
28 146 classified as having a drug component if any form of the active ingredient (e.g., dosage, route,  
29  
30  
31 147 strength, compound) was listed as an approved or discontinued brand name, generic drug or  
32  
33 148 therapeutic biological product by the US Food and Drug Administration (FDA) as listed in the  
34  
35 149 Drugs@FDA database at the time of review.<sup>16</sup> If an agent was not listed in the Drugs@FDA  
36  
37  
38 150 database and was classified by the FDA as a non-drug (e.g., food additive, supplement), then it  
39  
40 151 was not considered a drug. If an agent was not regulated as a drug and was not listed as a non-  
41  
42 152 drug by the FDA, drug status was determined based on consensus among investigators using  
43  
44  
45 153 publicly available sources that provided information on the agent.

46  
47 154 We searched the MEDLINE database via PubMed on October 19, 2018 using a search  
48  
49 155 developed by a medical librarian (see eMethods1 for strategy). Citations were uploaded into the  
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51 156 systematic review software DistillerSR (Evidence Partners, Ottawa, Canada), which was used to  
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54 157 code and track results. Two investigators independently evaluated titles and abstracts for  
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3 158 potential eligibility. Full texts of titles and abstracts deemed potentially eligible by either  
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5 159 investigator were then reviewed by two investigators independently. Disagreements at the full-  
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7 160 text level were resolved through consensus with a third investigator consulted as necessary.  
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10 161 Because we sought to include the most recently published meta-analyses that met eligibility  
11  
12 162 criteria, prior to reviewing, citations were organized by PubMed reference identification numbers  
13  
14 163 with the most recent first. Title and abstract and full-text reviews were conducted sequentially  
15  
16  
17 164 until we obtained our desired number of included meta-analyses based on our power analysis.  
18

### 19 165 **Data extraction**

20  
21 166 For each eligible meta-analysis, one reviewer initially extracted all data into a pre-defined  
22  
23 167 form in DistillerSR, and a second reviewer validated all extracted data using the DistillerSR  
24  
25 168 Quality Control function. Discrepancies were resolved by consensus and consultation with a  
26  
27 169 third investigator, if needed. For each included meta-analysis, reviewers extracted first author  
28  
29 170 last name; year of publication; journal name; Clarivate Analytics 2017 journal impact factor;  
30  
31 171 journal speciality area based on Clarivate Analytics classification; whether it was a Cochrane  
32  
33 172 meta-analysis published in the Cochrane Database of Systematic Reviews or elsewhere; funding  
34  
35 173 source for the meta-analysis and author-industry financial ties and employment; reporting in the  
36  
37 174 meta-analysis of trial funding sources, trial author-industry financial ties, and trial author-  
38  
39 175 industry employment; and whether the meta-analysis referenced a published protocol or  
40  
41 176 contained a PROSPERO registration number. If a registration number was not provided, we  
42  
43 177 searched the PROSPERO website (<https://www.crd.york.ac.uk/PROSPERO/>) using key terms  
44  
45 178 from the published article, then attempted to match the principal investigator, funding source,  
46  
47 179 intervention, non-intervention comparator group, and design from the article to registrations  
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52 180 obtained in the search.  
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3 181 To extract information on meta-analysis funding source, meta-analysis author-industry  
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5 182 financial ties, and meta-analysis author-industry employment and to determine whether or not  
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7 183 trial funding sources, trial author-industry financial ties, and trial author-industry employment  
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9  
10 184 were reported in the meta-analysis, for each included meta-analysis, reviewers examined all text,  
11  
12 185 tables, figures, appendices, disclosure statements, acknowledgements and any online  
13  
14  
15 186 supplemental material, published with the manuscript or linked to the manuscript. Funding  
16  
17 187 sources for meta-analyses were classified as (1) non-industry (e.g., public granting agency,  
18  
19 188 private not-for-profit granting agency), (2) pharmaceutical industry, (3) combined  
20  
21 189 pharmaceutical industry and non-industry, (4) no funding or (5) not reported. Financial ties of  
22  
23 190 meta-analysis authors to industry were defined per the International Committee of Medical  
24  
25 191 Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest<sup>17</sup> and included  
26  
27 192 current or former board membership, current or former consultancy, current or former industry  
28  
29 193 employment, expert testimony, industry grants (issued or pending), payment for lectures  
30  
31 194 including service on speakers bureaus, payment for manuscript preparation, patents (planned,  
32  
33 195 pending, or issued), royalties, payment for development of educational presentations, stock or  
34  
35 196 stock options, travel reimbursement, or other relationships with industry, as disclosed in the  
36  
37 197 review. Of these, we specifically coded if industry employees were part of the author group. If a  
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39 198 meta-analysis did not contain a disclosure statement, meta-analysis author-industry financial ties  
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42 199 were coded as not reported.  
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46  
47 200 For reporting of (1) trial funding sources, (2) trial author-industry financial ties, and (3)  
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49 201 trial author-industry employment, meta-analyses were coded as (1) reporting for all included  
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51 202 trials; (2) reporting for some, but not all, included trials; or (3) not reporting. Meta-analyses that  
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53 203 included data from a pharmaceutical industry database or noted that trial drugs were supplied by  
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3 204 the manufacturers for certain trials, but that did not make any explicit statement of trial funding  
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5 205 sources, were coded as not reporting. For meta-analyses that reported information on funding  
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7 206 sources or author FCOIs from included trials, either fully or partially, we recorded where in the  
8  
9 207 meta-analysis the information was reported. Specifically, we recorded whether the information  
10  
11 208 was reported in the abstract, lay summary, risk of bias material (text, figure or table, both), main  
12  
13 209 text other than risk of bias, elsewhere in the main document (e.g., characteristics of included  
14  
15 210 studies table, other table, footnote of a table), or in an online appendix. See eMethods2.

### 19 211 **Power analysis**

21 212 To determine the number of meta-analyses to target, we first calculated the number of  
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23 213 included meta-analyses that would be needed for 80% power to find a statistically significant  
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25 214 difference if there were a 20% difference in reporting trial funding sources based on meta-  
26  
27 215 analysis characteristics, with  $\alpha = 0.05$ . We varied the rates of reporting from 10% versus 30% to  
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29 216 70% versus 90% and considered scenarios where the proportion of reporting meta-analyses with  
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31 217 each characteristic (e.g., high-impact journals versus low-impact journals) was 50% versus 50%  
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33 218 and 30% versus 70%. For a two-tailed binomial test with  $\alpha = 0.05$ , the maximum number of  
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35 219 included meta-analyses needed in any scenario was 239. Because the consequence of  
36  
37 220 overpowering the study was additional labour and not risk to human participants, we rounded  
38  
39 221 this number up to 250 meta-analyses. See eMethods3.

### 44 222 **Statistical analyses**

46 223 We presented characteristics of included meta-analyses descriptively, including funding  
47  
48 224 sources and FCOIs. We determined the proportion of meta-analyses that reported trial funding  
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50 225 source, author-industry financial ties, and author-industry employment of included trials for (1)  
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52 226 all included trials, (2) some, but not all, included trials, and (3) no included trials, along with  
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3 227 95% confidence intervals (CIs). We compared the difference between the proportion of recently  
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5 228 published Cochrane meta-analyses that reported study funding, author-industry financial ties, and  
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7 229 author-industry employment from included RCTs with recently published non-Cochrane meta-  
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9 230 analyses and with Cochrane systematic reviews published in 2010. Because the present study  
10  
11 231 included meta-analyses only, but the previous study of Cochrane reviews included systematic  
12  
13 232 reviews with or without meta-analyses,<sup>11</sup> we conducted a sensitivity analysis in which we  
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15 233 excluded Cochrane systematic reviews from 2010 that did not include a meta-analysis and would  
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17 234 not have been eligible for inclusion in the present study. We calculated 95% CIs for all  
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19 235 differences.<sup>18</sup>

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24 236 To assess the relationship between meta-analysis characteristics and reporting of funding  
25  
26 237 sources for some or all included trials, versus not reporting, we fit unadjusted (bivariate) and  
27  
28 238 adjusted (multivariate) logistic regression models with all predictors using the glm function in R  
29  
30 239 (R version 3.2.3; RStudio Version 1.0.136).<sup>19,20</sup> The predictor variables that were considered in  
31  
32 240 bivariate and adjusted analyses were: (1) combined category (Cochrane, specialty medicine,  
33  
34 241 general medicine, multidisciplinary) and impact factor of the journal in which the meta-analysis  
35  
36 242 was published; and (2) whether there was industry funding for the meta-analysis or any FCOI  
37  
38 243 disclosed by meta-analysis authors. We combined journal category and impact factor because of  
39  
40 244 the small number of journals in some categories and the small number of journals with impact  
41  
42 245 factor greater than that of Cochrane. Thus, meta-analyses were categorized as (1) low-impact ( $\leq$   
43  
44 246 3.0) specialty medicine journals, (2) low-impact ( $\leq$  3.0) general medicine or multidisciplinary  
45  
46 247 journals, (3) medium-impact (3.1 - 6.7) specialty medicine journals, (4) high-impact ( $>$  6.8)  
47  
48 248 specialty medicine or general medicine journals, and (5) Cochrane meta-analyses (impact factor  
49  
50 249 = 6.8; reference category). Because 28 of 33 meta-analyses in general medicine journals were  
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3 250 from a single journal (*Medicine*) and not necessarily representative of general medicine as a  
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5 251 category, and because 9 of the 10 meta-analyses published in multidisciplinary science journals  
6  
7 252 were published in a single journal (*PLOS ONE*), we combined general medicine and  
8  
9 253 multidisciplinary journals.

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11  
12 254 Our initial protocol indicated that, if possible, we would include in the logistic regression  
13  
14 255 model the year of publication of the meta-analysis and whether there was meta-analysis funding  
15  
16 256 by industry, meta-analysis author-industry financial ties, and meta-analysis author-industry  
17  
18 257 employment, separately. However, 246 of 250 included meta-analyses were published in 2017-  
19  
20 258 2018, and only 3 meta-analyses had industry funding; thus, we did not include year of  
21  
22 259 publication, and we grouped meta-analysis funding source and author FCOIs into a single  
23  
24 260 variable (No FCOIs including funding source versus any FCOI). Additionally, we only  
25  
26 261 conducted a multivariable analysis for the reporting of funding sources of included RCTs and not  
27  
28 262 for reporting of author-industry financial ties and author-industry employment, because there  
29  
30 263 were not enough examples of meta-analyses that reported author-industry financial ties and  
31  
32 264 author-industry employment.

### 33 265 **Patient and Public Involvement**

34  
35 266 Patients and members of the public were not involved in the  
36  
37 267 design, conduct, reporting, or plan for dissemination of our  
38  
39 268 research.

## 40 269 **RESULTS**

### 41 270 **Selection of eligible meta-analyses**

42 271 Our initial search of PubMed without date restrictions retrieved 9,725 unique citations.  
43  
44 272 To select 250 eligible meta-analyses, working backwards from the most recent, a total of 401  
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3 273 citations were screened for eligibility; 64 were excluded at the title and abstract level and 76 at  
4  
5 274 the full-text level. See Figure 1.

6  
7  
8 275 As shown in Table 1, of the 250 included meta-analyses, 107 (43%) were Cochrane  
9  
10 276 reviews, all of which were published in the Cochrane Database of Systematic Reviews. Among  
11  
12 277 the 143 non-Cochrane meta-analyses, 33 (23%) were published in general medicine journals  
13  
14 278 (including 28 in the journal *Medicine*), 100 (70%) in specialty medicine journals, and 10 (7%) in  
15  
16 279 multidisciplinary journals (including 9 in *PLOS ONE*). The mean number of included RCTs for  
17  
18 280 both Cochrane and non-Cochrane meta-analyses was approximately 20. Among the 143 non-  
19  
20 281 Cochrane meta-analyses, 25 (17%) referenced a published protocol or were registered in  
21  
22 282 PROSPERO, and 106 (74%) were published in a journal with impact factor  $\leq 3$ .

23  
24  
25  
26 283 Of the 250 meta-analyses, 3 (1%) reported being funded by industry, 148 (59%) reported  
27  
28 284 funding from non-industry sources, 56 (22%) reported no funding, and 43 (17%) did not report  
29  
30 285 funding source; 3 (1%) had at least 1 author who reported current industry employment, 51  
31  
32 286 (20%) had at least 1 author that reported other financial ties with industry, 187 (75%) reported  
33  
34 287 that there were no authors with FCOIs, and 12 (5%) did not report any information about author  
35  
36 288 FCOIs. Characteristics of each of the 250 included meta-analyses are shown in eTable 1.

### 37 38 39 40 289 **Reporting in meta-analyses of funding sources and author FCOIs from included drug trials**

41  
42 290 As shown in Table 2, 111 of the 250 (44%) included meta-analyses reported the funding  
43  
44 291 sources for some or all included trials, 49 (20%) reported author-industry financial ties for some  
45  
46 292 or all included trials, and 19 (8%) reported author-industry employment for some or all included  
47  
48 293 trials. Of the 107 Cochrane meta-analyses, 90 (84%) reported funding sources for some or all  
49  
50 294 included trials compared with 21 of 143 (15%) non-Cochrane meta-analyses, a difference of 69%  
51  
52 295 (95% CI, 59% to 77%); 47 (44%) Cochrane meta-analyses reported author-industry financial ties  
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3 296 for some or all included trials compared with 2 (1%) non-Cochrane meta-analyses, a difference  
4  
5 297 of 43% (95% CI, 33% to 52%); 18 (17%) Cochrane meta-analyses reported, fully or partially,  
6  
7 298 author-industry employment compared with 1 (1%) non-Cochrane meta-analysis, a difference of  
8  
9 299 16% (95% CI, 9% to 24%).

10  
11  
12 300 Among the 90 Cochrane meta-analyses that reported funding sources for some or all  
13  
14 301 included trials, 77 (86%) provided this information in the characteristics of included studies  
15  
16 302 table, including 23 (26%) that also included it in the assessment of risk of bias of included trials;  
17  
18 303 7 (8%) included it in the risk of bias assessment and at least one other place, but not the  
19  
20 304 characteristics of included studies table, and 6 (7%) reported only as part of the risk of bias  
21  
22 305 assessment. In total, 36 (40%) reported in the context of the risk of bias assessment. See eTable2  
23  
24 306 for reporting for all 250 included meta-analyses.

### 25 26 27 28 307 **Factors associated with reporting FCOIs from included trials in multivariable analysis**

29  
30  
31 308 As shown in Table 3, the odds ratio for reporting funding sources for some or all included  
32  
33 309 RCTs among non-Cochrane meta-analyses was  $\leq 0.11$  compared with Cochrane meta-analyses  
34  
35 310 for all journal category and impact factor combinations. Meta-analyses with any declared FCOI  
36  
37 311 (OR 1.29, 95% CI 0.53 to 3.19) and meta-analyses for which the presence of FCOIs was not  
38  
39 312 reported (OR 1.18, 95% CI 0.40 to 3.44) did not differ significantly in reporting compared with  
40  
41 313 those with no declared FCOIs.

### 42 43 44 314 **Comparison of recent Cochrane meta-analyses versus Cochrane reviews published in 2010**

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46  
47 315 Reporting of funding sources for some or all included trials improved from 30% in  
48  
49 316 Cochrane reviews of drug trials published in 2010 to 84% in recently published Cochrane meta-  
50  
51 317 analyses, an improvement of 54% (95% CI, 42% to 63%). Reporting of author-industry financial  
52  
53 318 ties for some or all included trials improved from 7% in 2010 to 44% in recent meta-analyses, a

319 37% change (95% CI, 26% to 47%). Reporting of author-industry employment for some or all  
320 included trials improved from 7% in 2010 to 17% in recent meta-analyses (10%; 95% CI, 2% to  
321 19%). Results did not change when the comparison was restricted to Cochrane reviews published  
322 in 2010 that included a meta-analysis. See Table 2. Figure 2 summarizes reporting among  
323 recently published Cochrane and non-Cochrane meta-analyses and Cochrane reviews from 2010.

## 324 **DISCUSSION**

### 325 **Principal findings**

326 We reviewed the 250 most recent meta-analyses of drug treatments listed in PubMed at  
327 the time of our search. Of these, 107 (43%) were Cochrane reviews, 100 (40%) were published  
328 in specialty medicine journals, and 43 (17%) were published in general medicine or  
329 multidisciplinary journals, including 28 in *Medicine* and 9 in *PLOS ONE*. Of the 143 non-  
330 Cochrane meta-analyses, 106 (74%) were published in journals with impact factor  $\leq 3$ .

331 Among Cochrane meta-analyses, 84% reported funding sources for some or all included  
332 RCTs compared with 15% of non-Cochrane meta-analyses. Cochrane meta-analyses were also  
333 more likely than non-Cochrane meta-analyses to report author-industry financial ties (44%  
334 versus 1%) and author-industry employment (17% versus 1%).

335 In 2010, only 30% of 151 Cochrane systematic reviews of drug treatments reported trial  
336 funding sources.<sup>11</sup> This improved to 84% among recent Cochrane meta-analyses. Cochrane  
337 reviews also improved reporting of author-industry financial ties and author-industry  
338 employment of included RCTs from 7% to 44% and from 7% to 17%. It is possible that the  
339 reason that few meta-analyses reported author-industry employment is because some may have  
340 assumed that author-industry employment would be considered a type of author-industry

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3 341 financial tie and did not report employment separately, whereas we considered author-industry  
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5 342 financial ties and employment separately.  
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7  
8 343 Among the 90 Cochrane meta-analyses that reported funding sources of included trials in  
9  
10 344 the present study, 86% included the information in the characteristics of included studies table,  
11  
12 345 as required by Cochrane, and 40% included the information in the risk of bias assessment.  
13

#### 14 346 **Findings in context**

15  
16  
17 347 In 2012, soon after our previous results showed that few Cochrane systematic reviews of  
18  
19 348 drug trials reported funding sources and author FCOIs of included trials,<sup>11</sup> the Cochrane  
20  
21 349 Collaboration began to require that trial funding sources and FCOIs be reported for every  
22  
23 350 included RCT in the characteristics of included studies table.<sup>12-13</sup> Reporting of trial funding  
24  
25 351 sources among recent Cochrane meta-analyses has not reached 100%, and work is needed to  
26  
27 352 improve the reporting of other types of author FCOIs, which was under 50% despite being  
28  
29 353 required by Cochrane. Nonetheless, the improvements documented in the present study are  
30  
31 354 substantial, both compared with previous Cochrane reviews and with contemporary non-  
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33 355 Cochrane meta-analyses. Cochrane is a global organization consisting of a large number of  
34  
35 356 different review and methods groups that span numerous fields of health research. This diversity  
36  
37 357 suggests that changes that have occurred likely resulted from change in the mandatory reporting  
38  
39 358 requirements for Cochrane reviews and widespread adoption by the organization. It also suggests  
40  
41 359 the possibility that other journals could improve the transparency of reporting of trial funding  
42  
43 360 and trial author FCOI in evidence syntheses by adopting similar reporting requirements. The  
44  
45 361 current version of the PRISMA statement does not address reporting of  
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47 362 trial funding sources and FCOIs of trial authors by investigators who publish systematic reviews  
48  
49 363 and meta-analyses.<sup>15,16</sup> The forthcoming updated PRISMA statement, however, will require that  
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3 364 trial funding, although not trial author FCOIs, be reported (personal communication, David  
4  
5 365 Moher, May 22, 2019).

6  
7 366 Members of our research team have previously recommended that risk of bias from trial  
8  
9 367 funding and trial author FCOIs be included in the Cochrane Risk of Bias Tool based on evidence  
10  
11 368 that links trial sponsorship and trial author FCOIs to outcomes.<sup>10</sup> This recommendation was  
12  
13 369 debated at a Cochrane Methods Symposium in 2013, but consensus was not reached for  
14  
15 370 inclusion.<sup>12,21</sup> The present study found that 40% of Cochrane meta-  
16  
17 371 analyses that reported on FCOIs from included trials included  
18  
19 372 this as part of a risk of bias assessment, even though this has  
20  
21 373 not been recommended by Cochrane. Currently, a new tool, the Tool  
22  
23 374 for Addressing Conflicts of Interest in Trials (TACIT),<sup>22</sup> which specifically addresses risk of bias  
24  
25 375 from industry sponsorship of trials and author-industry financial ties and employment, is being  
26  
27 376 developed for inclusion in Cochrane reviews. Once the TACIT tool is completed, risk of bias  
28  
29 377 from trial funding and trial author FCOIs will be explicitly considered in Cochrane reviews and,  
30  
31 378 potentially, in non-Cochrane reviews, as well. Meanwhile, authors should, at a minimum,  
32  
33 379 describe FCOIs and discuss the degree to which they may influence confidence in findings.

### 34 **Strengths and limitations**

35  
36 381 A strength of the present study is that we assessed reporting in a large number of recently  
37  
38 382 published meta-analyses, including 107 Cochrane meta-analyses, which allowed us to compare  
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40 383 reporting practices among Cochrane and non-Cochrane meta-analyses and recent Cochrane  
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42 384 meta-analyses with Cochrane systematic reviews from 2010. However, there are limitations that  
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44 385 should be considered. First, since most meta-analyses of drug trials are published as Cochrane  
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46 386 reviews or in relatively low-impact specialty medicine journals, we were not able to conduct

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3 387 robust assessments of whether meta-analyses published in different types of journals or journals  
4  
5 388 with different impact factors are more or less likely to report on trial funding and trial author  
6  
7 389 FCOIs for included drug trials. The vast majority of meta-analyses published in general medicine  
8  
9 390 journals were from a single journal (*Medicine*), which further limited our ability to examine this  
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11 391 factor. On the other hand, the meta-analyses selected for inclusion in our study constituted a  
12  
13 392 consecutive sample of the most recent meta-analyses listed in PubMed and, thus, were  
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15 393 representative of the spectrum of meta-analyses of drug interventions and the journals where  
16  
17 394 they were published in 2016–2018. Second, our study examined only disclosed FCOIs. A  
18  
19 395 surprising finding was that a higher proportion of Cochrane meta-analysis authors indicated that  
20  
21 396 they had FCOIs compared with non-Cochrane authors; it is not known if this reflects greater  
22  
23 397 industry involvement among Cochrane authors or a higher propensity to report transparently and  
24  
25 398 completely among this group of authors. Third, information about FCOIs from included RCTs  
26  
27 399 was not extracted from the RCT publications. Finally, our previous study of Cochrane reviews  
28  
29 400 from 2010 included all systematic reviews, whereas the present study was restricted to reviews  
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31 401 with meta-analyses. However, a sensitivity analysis showed that results did not change when we  
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33 402 compared recent results to those from 2010 that were restricted to reviews with a meta-analysis.  
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### 403 **Conclusions and policy implications**

404 In summary, the percentage of recent Cochrane meta-analyses  
405 on the effects of drug interventions that transparently reported  
406 funding sources and trial author-industry financial ties and  
407 employment for included trials far exceeds reporting in other  
408 journals. It also far exceeds reporting in Cochrane systematic  
409 reviews published in 2010, before the implementation by Cochrane of its policy

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3 410 requiring the reporting of trial funding sources and author-industry FCOIs. These results suggest  
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5 411 that it is possible to achieve more transparent reporting of FCOIs from trials included in meta-  
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7 412 analyses. We encourage the uptake and enforcement of reporting requirements in the  
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10 413 forthcoming updated PRISMA statement.<sup>23</sup> We also encourage the adoption of Cochrane's new  
11  
12 414 TACIT tool<sup>22</sup> by journals and authors in order to assess trial funding sources and author FCOIs  
13  
14 415 as risks of bias. Continued non-disclosure of FCOIs when evidence is synthesized in meta-  
15  
16 416 analyses misleads readers of medical journals into believing that there is not risk of bias from  
17  
18 417 FCOIs to be considered, even though an increasingly robust evidence base tells us that this is  
19  
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21 418 often not the case.<sup>7,8</sup>  
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3 419 **Acknowledgement:** The authors thank Drs. Ian Shrier and Jonathan Kimmelman for providing  
4  
5 420 helpful comments on an earlier version of the manuscript. They were not compensated for their  
6  
7 421 contribution.

8  
9  
10 422 **Contributors:** KAT, MR, JB, LAB, JL, EHT, AB, and BDT were responsible for the study  
11  
12 423 conception and design. KAT, ACJ, CB, and KE were responsible for title and abstract and full-  
13  
14 424 text review. KAT and ACJ were responsible for data extraction and validation. KAT, BL, AB,  
15  
16 425 and BDT analysed and interpreted results. KAT and BDT drafted the  
17  
18 426 manuscript. All authors provided a critical review and approved  
19  
20 427 the final manuscript. BDT is the guarantor.

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13 448 to pay an open access fee—see [http://www.bmj.com/about-](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse)  
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15 449 [bmj/resources-authors/forms-policies-and-checklists/copyright-](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse)  
16  
17 450 [open-access-and-permission-reuse](http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse)). The terms of such open access  
18  
19 451 shall be governed by a Creative Commons licence—details as to  
20  
21 452 which Creative Commons licence will apply to the research  
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23 453 article are set out in our worldwide licence referred to above.  
24  
25  
26 454 **Funding:** Ms. Turner was supported by a Fonds de Recherche Québec - Santé  
27  
28 455 (FRQ-S) masters training award, Ms. Levis was supported by a Canadian Institutes of Health  
29  
30 456 Research doctoral research award, and Drs. Benedetti and Thombs were supported by FRQ-S  
31  
32 457 researcher awards, all outside of the submitted work.  
33  
34  
35 458 **Declaration of Competing Interests:** All authors have completed the ICMJE uniform  
36  
37 459 disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf). Dr. Bero disclosed that she  
38  
39 460 is Senior Editor, Cochrane Public Health and Health Systems, for  
40  
41 461 which the University of Sydney receives remuneration. Dr. Thombs  
42  
43 462 disclosed that he is a content editor with the Cochrane Common  
44  
45 463 Mental Disorders review group (no remuneration received). All  
46  
47 464 other authors declared: no support from any organisation for the submitted work; no  
48  
49 465 financial relationships with any organisations that might have an interest in the submitted work  
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3 466 in the previous three years; no other relationships or activities that could appear to have  
4  
5 467 influenced the submitted work.

6  
7 468 **Ethics Statement:** As this study involved only the review of published articles, research ethics  
8  
9 469 approval was not required.

10  
11 470 **Transparency Declaration:** The manuscript's guarantor affirms that this manuscript is an  
12  
13 471 honest, accurate, and transparent account of the study being reported; that no important aspects  
14  
15 472 of the study have been omitted; and that any discrepancies from the study as planned (and, if  
16  
17 473 relevant, registered) have been explained.

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19 474 **Data Sharing:** All extracted data are available in the main tables or in eTable1 and eTable2. No  
20  
21 475 additional data were extracted.  
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3 533 **FIGURES**  
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6 534 **Figure 1.** Flow diagram of selection of eligible meta-analyses.  
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9 535 **Figure 2.** Percentage of recently published Cochrane and non-Cochrane meta-analyses and 2010  
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12 536 Cochrane systematic reviews that reported included trial funding source, author-industry  
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14 537 financial ties, and author-industry employment for some or all included trials.  
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**Table 1. Characteristics of included meta-analyses**

	<b>Cochrane Meta-Analyses (N = 107)</b>	<b>Non-Cochrane Meta-Analyses (N = 143)</b>
<b>Year of publication</b>		
2016, <i>N (%)</i>	0	4 (3%)
2017, <i>N (%)</i>	22 (21%)	31 (22%)
2018, <i>N (%)</i>	85 (79%)	108 (76%)
<b>Number of Included RCTs, mean ± SD</b>	21.4 ± 24.4	19.6 ± 46.4
<b>Registered in PROSPERO or Published Protocol, <i>N (%)</i></b>	107 (100%)	25 (17%) <sup>a</sup>
<b>Impact Factor, mean ± SD</b>		
≤ 3	0	106 (74%)
3.1-6.7	0	27 (19%)
6.8	107 (100%)	0
> 6.8	0	10 (7.0%)
<b>Meta-Analysis Funding Sources</b>		
Not reported	4 (4%) <sup>b</sup>	39 (27%)
Industry	0	3 (2%)
Non-Industry	93 (87%)	55 (38%)
No funding	10 (9%)	46 (32%)
<b>Meta-Analysis Author Financial Ties to Industry (Including Employment)<sup>c</sup></b>		
Not reported, <i>N (%)</i>	1 (1%)	11 (8%)
No authors with reported financial ties, <i>N (%)</i>	70 (65%)	117 (81%)

≥ 1 author with reported financial ties, <i>N (%)</i>	36 (34%)	15 (10%)
Proportion of authors with financial ties, <i>mean ± SD<sup>d</sup></i>	11% ± 17%	4% ± 15%

### Journal Category

Cochrane review, <i>N (%)</i>	107 (100%)	0
Specialty medicine <i>N (%)</i>	0	100 (70%)
General medicine (non-Cochrane), <sup>f</sup> <i>N (%)</i>	0	33 (23%)
Multidisciplinary, <sup>g</sup> <i>N (%)</i>	0	10 (7%)

539 <sup>a</sup>One meta-analysis reported that they registered in PROSPERO but did not provide a registration number and one  
540 could not be found. We contacted the authors and they did not provide us with further information; thus this was  
541 coded as not registered. <sup>b</sup>Only 3 included meta-analyses reported author-industry employment and these were  
542 grouped with author-industry financial ties for this table <sup>c</sup>Cochrane reviews typically have a “Sources of Support”  
543 section with funding information. These reviews did not include that section. <sup>d</sup>Proportion of authors with financial  
544 ties or employment of those that reported. <sup>e</sup>Classifications for specialty medicine journals (note that some journals  
545 had more than one classification): Anesthesiology, N = 3; Biochemistry & Molecular Biology, N = 1; Biotechnology  
546 & Applied Microbiology, N = 2; Cardiac & Cardiovascular Systems, N = 7; Cell Biology, N = 1; Chemistry,  
547 Medicinal, N = 4; Chemistry, Multidisciplinary, N = 2; Clinical Neurology, N = 6; Critical Care Medicine, N = 2;  
548 Dermatology, N = 3; Emergency Medicine, N = 2; Endocrinology & Metabolism, N = 2; Gastroenterology &  
549 Hepatology, N = 6; Genetics & Heredity, N = 1; Hematology, N = 2; Immunology, N = 6; Infectious Diseases, N =  
550 = 3; Integrative & Complementary Medicine, N = 1; Medicine, Research & Experimental, N = 3; Microbiology, N =  
551 2; Neurosciences, N = 3; No classification, N = 2; Obstetrics & Gynecology, N = 4; Oncology, N = 11;  
552 Ophthalmology, N = 3; Orthopedics, N = 6; Parasitology, N = 1; Peripheral Vascular Disease, N = 5; Pharmacology  
553 & Pharmacy, N = 13; Physiology, N = 1; Psychiatry, N = 4; Psychology, N = 1; Reproductive Biology, N = 1;  
554 Respiratory System, N = 6; Rheumatology, N = 3; Sport Sciences, N = 1; Surgery, N = 11; Toxicology, N = 2;  
555 Tropical Medicine, N = 1; Urology & Nephrology, N = 1. <sup>f</sup>Of the 33 included general medicine journals, 28 were  
556 published in the journal “Medicine”. <sup>g</sup>Of the 10 journals classified as multidisciplinary, 9 were published in the  
557 journal “PLOS ONE”.



**Table 2. Summary of reporting patterns of disclosed funding source and author-industry FCOI from included RCTs**

	Number of Meta-analyses Reporting Funding Sources of Included RCTs			Number of Meta-analyses Reporting Author Financial Ties of Included RCTs			Number of Meta-analyses Reporting Author-Industry Employment of Included RCTs		
	Full	Partial	Full or Partial	Full	Partial	Full or Partial	Full	Partial	Full or Partial
	<b>Recently Published Meta-analyses:</b>								
Cochrane (N = 107), N (%)	70 (65%)	20 (19%)	90 (84%)	24 (22%)	23 (21%)	47 (44%)	1 (1%)	17 (16%)	18 (17%)
Non-Cochrane (N = 143), N (%)	14 (10%)	7 (5%)	21 (15%)	1 (1%)	1 (1%)	2 (1%)	0	1 (1%)	1 (1%)
<b>Difference in Reporting Between Cochrane and Non-Cochrane Meta-analyses, % (95% CI)</b>	56% (44% to 65%)	14% (6% to 23%)	69% (59% to 77%)	22% (14% to 31%)	21% (13% to 30%)	43% (33% to 52%)	1% (-2% to 5%)	15% (9% to 23%)	16% (9% to 24%)
<b>2010:</b>									
All Cochrane Systematic Reviews (N = 151), N (%) <sup>a</sup>	30 (20%)	16 (11%)	46 (30%)	2 (1%)	9 (6%)	11 (7%)	0	10 (7%)	10 (7%)
<b>Difference in Reporting Between Recently Published Cochrane Meta-analyses versus Cochrane Systematic Reviews Published in 2010, % (95% CI)</b>	46% (34% to 56%)	8% (-1% to 18%)	54% (42% to 63%)	21% (13% to 30%)	16% (7% to 25%)	37% (26% to 47%)	1% (-2% to 5%)	9% (2% to 18%)	10% (2% to 19%)
<b>2010:</b>									
Cochrane Meta-analyses (N = 119),	21 (19%)	15 (13%)	36 (30%)	0 (0%)	7 (6%)	7 (6%)	0 (0%)	7 (6%)	7 (6%)

N (%)

<b>Difference in Reporting Between</b>	48%	6%	54%	22%	16%	38%	1%	10%	11%
<b>Recently Published Cochrane Meta-</b>	(36% to 58%)	(-3% to 16%)	(42% to 63%)	(15% to 31%)	(7% to 25%)	(27% to 48%)	(-2% to 5%0	(2% to 19%)	(3% to 20%)
<b>analyses versus Cochrane Meta-</b>									
<b>analyses Published in 2010, % (95%</b>									
<b>CI)</b>									

558 <sup>a</sup>Results from Roseman et al., 2012.

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**Table 3. Factors associated with reporting funding sources of included RCTs**

	<b>Proportion that reported some or all declared funding sources from included RCTs</b>	<b>Unadjusted odds ratio (95% CI)</b>	<b>Adjusted odds ratio (95% CI)</b>
<b>FCOI of meta-analysis (including meta-analysis funding)</b>			
reference = no FCOI	67/151 (44%)		
Any disclosed FCOI	35/51 (69%)	2.74 (1.42 to 5.49)	1.29 (0.53 to 3.19)
Not reported	9/48 (19%)	0.29 (0.12 to 0.62)	1.18 (0.40 to 3.44)
<b>Impact Factor and Journal Type</b>			
reference = Cochrane	90/107 (84%)		
Specialty impact factor $\leq 3^b$	4/65 (6%)	0.01 (< 0.01 to 0.03)	0.01 (< 0.01 to 0.04)
General (N=31) or Multidisciplinary (N=10) impact factor $\leq 3$	4/41 (10%)	0.02 (< 0.01 to 0.06)	0.02 (< 0.01 to 0.06)
Specialty impact factor 3.1 - 6.7 <sup>c</sup>	10/27 (37%)	0.11 (0.04 to 0.28)	0.11 (0.04 to 0.28)
Specialty (N=8) or General (N=2) impact factor > 6.8	3/10 (30%)	0.08 (0.02 to 0.32)	0.08 (0.02 to 0.32)

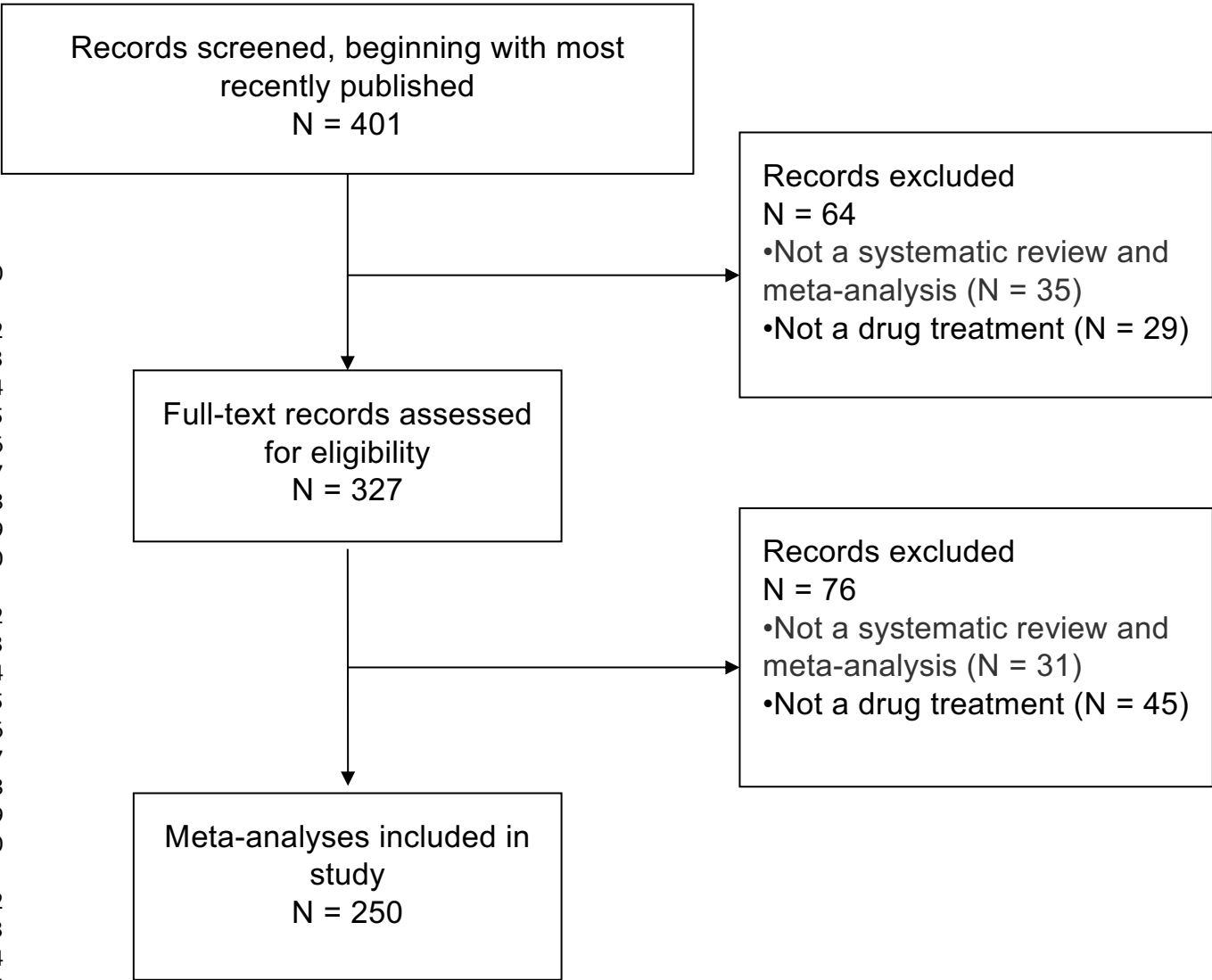
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3 559 <sup>a</sup>Not reported included meta-analyses for which the presence of FCOI could not be determined  
4 560 because either meta-anlaysis funding, meta-analysis author FCOI, or both were not reported.  
5 561 <sup>b</sup> Two meta-analyses were from journals that did not have an impact factor, and these were coded as having an impact factor of 0.5 for our  
6 562 analyses.  
7 563 <sup>c</sup> There were no multidisciplinary or general medicine journals with an impact factor of 3.1-6.7.  
8 564 FCOI = financial conflicts of interest

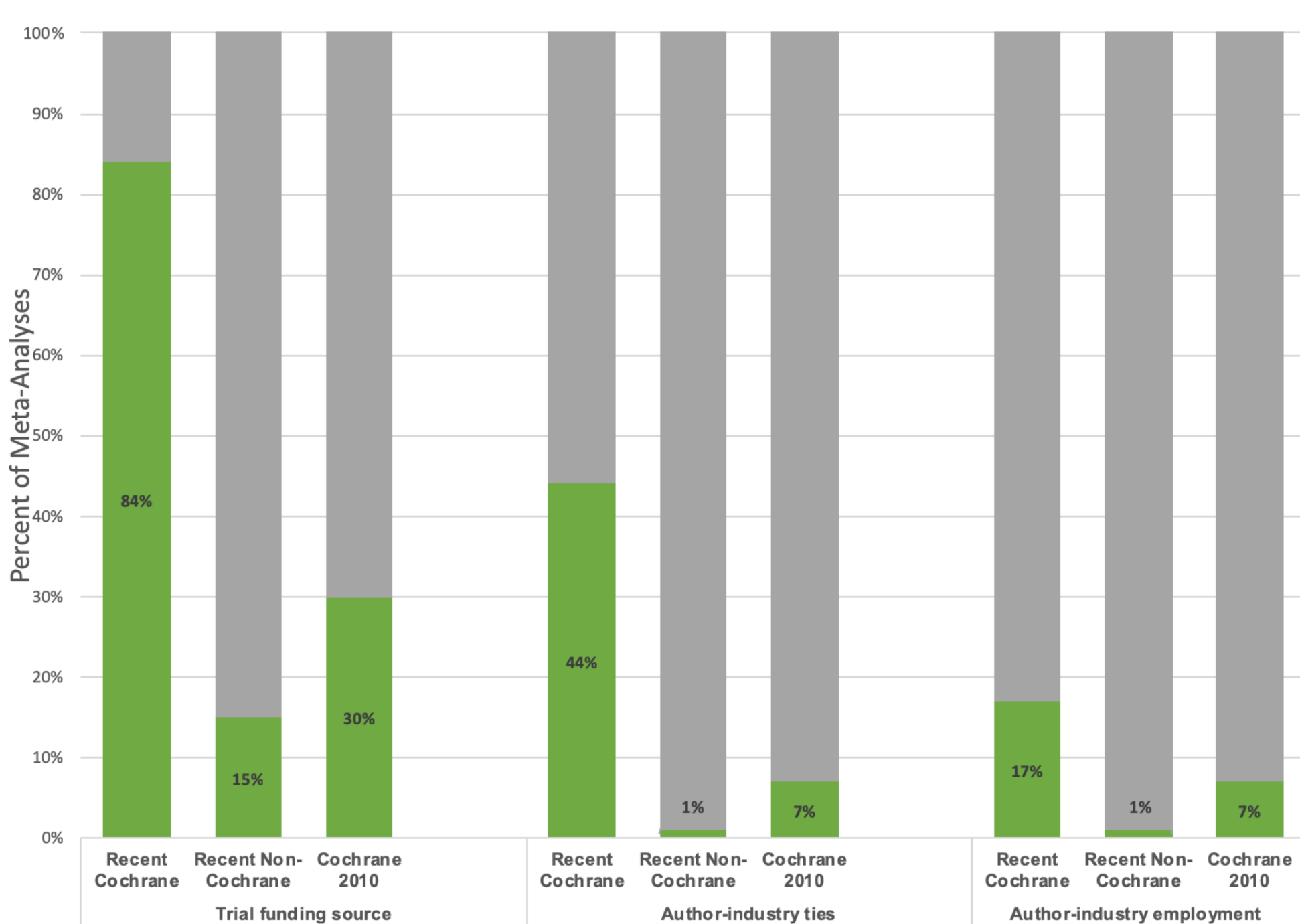
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3 **Supplementary Material**  
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8 **eMethods1.** Search strategy  
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10 **eMethods2.** Data extraction form  
11

12 **eMethods3.** Power analysis  
13

14 **eTable1.** Detailed characteristics of included meta-analyses  
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16 **eTable2.** Detailed reporting of study funding source, author-industry financial ties, and author-  
17 industry employment from included RCTs  
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## eMethods1. Search strategy

To obtain our sample, we searched the MEDLINE database via PubMed on October 19, 2018 using the following search strategy:

```
((("Randomized Controlled Trials as Topic"[Mesh] or randomized control trial [tiab] or randomized controled trial [tiab] OR randomized controlled trial [tiab] or randomized control trials [tiab] OR randomized controled trials [tiab] OR Randomized controlled trials [tiab] or randomised control trial [tiab] or randomised controled trial [tiab] OR randomised controlled trial [tiab] or randomised control trials [tiab] OR randomised controled trials [tiab] OR Randomised controlled trials [tiab]) AND ("Therapeutic Uses"[Mesh] OR "Vaccines"[Mesh]) AND ("Meta-Analysis" [Publication Type] or meta analysis [tiab]) AND (systematic review [tiab] OR search [tiab] or searched [tiab] or MEDLINE [tiab] OR PubMed [tiab])))
```



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3 **eMethods 2. Data extraction form**  
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7

8 **First Author, last name:** Last name of first author of meta-analysis  
9

10  
11 **Year of publication (or in press):** Year of publication of meta-analysis  
12  
13

14 **Journal:** Name of journal in which meta-analysis was published  
15  
16

17  
18 **Journal Impact factor:** Where meta-analysis published (low-high split or continuous based on  
19 data distribution)  
20  
21

22  
23 **Specialty area of Journal:** Where meta-analysis published (per Thomson Reuters Journal  
24 Science Citation Index - Expanded categories)  
25  
26

27  
28 **Cochrane Review (Y/N):** Is the meta-analysis a Cochrane Review? Select "Yes" even if the  
29 Cochrane Review is being published in another journal  
30  
31

32 Response from radio options:

- 33 - Y (Yes)  
34  
35 - N (No)  
36  
37

38  
39 **Journal policies for reporting COI of Included Trials:** Presence or absence of instructions for  
40 reporting in the author instructions  
41

- 42 - Y (Yes)  
43  
44 - N (No)  
45  
46

47 **# of RCTs synthesized in Meta-Analysis** (total RCTs in included meta-analysis related to  
48 drugs)  
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3 **Date Range of Included Trials:** Date range in years of publication of studies (RCTs) included  
4 related to drugs in the meta-analysis (XXXX - XXXX). Use "In press" for end date if there are in  
5 press trials. Use "Unpublished" if a trial is in progress or has never been published.  
6  
7  
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9

10 **Study population:** Characteristics of study population of included trials (e.g. condition/disorder,  
11 adult/child)  
12  
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14  
15 **Pharmacological agent:** Pharmacologic treatment evaluated in the meta-analysis

- 16 - Name(s) of treatment if specific drug(s) investigated
- 17 - Class of treatment if broader category of drugs investigated, and number of drugs  
18 evaluated (e.g. SSRIs – 5 included)  
19  
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24 **Control/comparison arms:** Other treatment arms (control/comparison) included in the meta-  
25 analysis (e.g. placebo, name of comparison pharmacologic treatment, name of behavioral  
26 intervention)  
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30  
31 **Meta-Analysis Author Financial Ties / Funding Sources Reported:** Does the meta-analysis  
32 report meta-analysis author financial ties (including former and current industry employment)  
33 and/or the funding source? Note that reporting "no funding" is different from not reporting.  
34  
35

36 Response from radio options:

- 37 - Meta-analysis author financial ties
- 38 - Meta-analysis funding sources
- 39 - Both financial ties and funding sources
- 40 - Neither reported  
41  
42  
43  
44  
45

46 **Funding Source of Meta-Analysis (if applicable – only shown if above item indicates meta-  
47 analysis funding sources reported or both financial ties and meta-analysis funding sources  
48 reported)** Source of financial support for the meta-analysis:  
49  
50

51 Response from radio options:

- 52 - Industry
- 53 - Combined industry and non-industry  
54  
55  
56  
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- Non-industry (e.g. public granting agency, private not-for-profit granting agency)
- No study funding

**Type of Industry Funding (if applicable – only shown if above item indicates industry funding or combined industry and non-industry present):** If the meta-analysis is industry funded, what is the type of support provided by industry? Response from radio options:

- Financial support
- Resources (e.g. statistical analyses)
- Both financial support and resources

**# of Meta-Analysis Authors:** Number of authors of the meta-analysis (count authors named in byline or in an author group)

**# of Meta-Analysis Authors with Financial Ties to Industry (if applicable – only shown if meta-analysis author financial ties or both financial ties and meta-analysis funding sources are reported):** Number of authors of the meta-analysis who have financial ties such as industry board member, consultant, investments, patents, research funding, royalties (including former, and excluding current industry employment):

- Numbers 0 -  $\geq 10$

**# Meta-Analysis Authors with Current Industry Employment (if applicable – only shown if meta-analysis author financial ties or both financial ties and meta-analysis funding sources are reported):** Number of authors of the meta-analysis who are current industry employees.

Response from radio options:

Numbers 0 -  $\geq 10$

**Quality or Risk Assessment of Included RCTs (Y/N):** Was quality or risk assessment of included RCTs, by methods from Cochrane, Jadad, etc., reported in the meta-analysis.

Response from radio options:

- Y (Yes)
- N (No)

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5 **Quality or Risk Assessment Method of Included RCTs (if applicable – only shown if**  
6 **answer to previous item is yes- quality or risk assessment of included RCTs is reported):** If  
7 the meta-analysis authors report a quality or risk assessment method of included RCTs, what is  
8 the reported method of quality assessment?  
9  
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12

13 **Meta-analysis Authors Report Funding Sources of Included Studies:** Response from radio  
14 options:  
15

- 16 - Reported for each included study
  - 17 - Reported in summary statement or for some, but not all, trials
  - 18 - Included study funding sources not reported
- 19  
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24 **Placement in publication of Included RCTs' Funding Source** (if applicable – only shown if  
25 the response to Meta-analysis Authors Report Funding Sources of Included Studies is (1)  
26 Reported for Each included Study or (2) Reported in summary statement or for some, but not all,  
27 trials):  
28  
29

- 30 - Abstract
  - 31 - Main text, other than risk of bias or quality section
  - 32 - In risk of bias or quality assessment
  - 33 - Other in main document (e.g., a characteristics of studies table, other table, in a  
34 footnote of a table
  - 35 - Online appendix
  - 36 - Lay Summary
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44 **Placement in risk of bias or quality assessment of Included RCTs' Funding Source** (if  
45 applicable – only shown if placement in publication of included RCT's Funding Source is risk of  
46 bias or quality assessment):  
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48

- 49 - Text
  - 50 - Figure/table
  - 51 - Both text and figure/table
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3 **Meta-analysis Authors Report Author Financial Ties of Included Studies:** Response from  
4 radio options:

- 5  
6  
7 - Reported for each included study  
8  
9 - Reported in summary statement or for some, but not all, trials  
10  
11 - Included study author financial ties not reported  
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13 **Placement in publication of Included RCTs' Author Financial Ties** (if applicable – only  
14 shown if the response Meta-analysis Authors Report Author Financial Ties of Included Studies is  
15 (1) Reported for Each included Study or (2) Reported in summary statement or for some, but not  
16 all, trials):  
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20 - Abstract  
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22 - Main text, other than risk of bias or quality section  
23  
24 - In risk of bias or quality assessment  
25  
26 - Other in main document (e.g., a characteristics of studies table, other table, in a  
27 footnote of a table  
28  
29 - Online appendix  
30  
31 - Lay Summary  
32  
33

34 **Placement in risk of bias or quality assessment of Included RCTs' Author Financial Ties** (if  
35 applicable – only shown if placement in publication of included RCT's Author Financial ties is  
36 risk of bias or quality assessment):  
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38

- 39 - Text  
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41 - Figure/table  
42  
43 - Both text and figure/table  
44  
45

46 **Meta-analysis Authors Report Author Industry Employment of Included Studies:** Do the  
47 authors of the meta-analysis report current author industry affiliation (employment) for the  
48 included studies? Response from radio options:  
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- 50  
51 - Reported for each included study  
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53 - Reported in summary statement or for some, but not all, trials  
54  
55 - Included study author industry employment not reported  
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5 **Placement in publication of Included RCTs' Author Industry Employment** (if applicable –  
6 only shown if the response to Meta-analysis Authors Report Author Industry Affiliation  
7 (Employment) of Included Studies is (1) Reported for Each included Study or (2) Reported in  
8 summary statement or for some, but not all, trials):  
9

- 10 - Abstract
- 11 - Main text, other than risk of bias or quality section
- 12 - In risk of bias or quality assessment
- 13 - Other in main document (e.g., a characteristics of studies table, other table, in a  
14 footnote of a table)
- 15 - Online appendix
- 16 - Lay Summary

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26 **Placement in risk of bias or quality assessment of Included RCTs' Author Industry**  
27 **Employment** (only shown if placement in publication of included RCT's Author Industry  
28 Affiliation is risk of bias or quality assessment):  
29

- 30 - Text
- 31 - Figure/table
- 32 - Both text and figure/table

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38 **Do the authors report a PROSPERO registration number in the text?**

- 39 - Yes
- 40 - No

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43 **What is the registration number (e.g., CRD42017062454)?** (if applicable – only shown if the  
44 response to Do the authors report a PROSPERO registration number in the text? Is yes)  
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48 **What stages were completed (ignore started) at the time of registration. Make sure to select**  
49 **the earliest registration version at the bottom of the page. Please check all stages that were**  
50 **completed.** (if applicable – only shown if the response to Do the authors report a PROSPERO  
51 registration number in the text? Is yes)  
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- 53 - Preliminary searches

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- 3 - Piloting of the study selection process
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- 5 - Formal screening of search results against eligibility criteria
- 6
- 7 - Data extraction
- 8
- 9 - Risk of bias (quality) assessment
- 10
- 11 - Data analysis
- 12
- 13 - None completed
- 14

15 **Was a registration found in PROSPERO?** (if applicable – only shown if the response to Do  
16 the authors report a PROSPERO registration number in the text? Is no)

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20 **What is the registration number (e.g., CRD42017062454)?** (if applicable – only shown if the  
21 response to Was a registration found in PROSPERO? Is yes)

22  
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25 **What stages were completed (ignore started) at the time of registration. Make sure to select  
26 the earliest registration version at the bottom of the page. Please check all stages that were  
27 completed.** (if applicable – only shown if the response to Was a registration found in  
28 PROSPERO? Is yes)

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- 32 - Preliminary searches
- 33
- 34 - Piloting of the study selection process
- 35
- 36 - Formal screening of search results against eligibility criteria
- 37
- 38 - Data extraction
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- 40 - Risk of bias (quality) assessment
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- 42 - Data analysis
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- 44 - None completed
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3 **eMethods3. Power analysis**  
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7 **Allocation ratio: 50% and 50% (1:1)**

8 20% difference

9 Proportion reporting COI		10 Sample size group 1	11 Sample size group 2	12 Sample size total	13 Actual power	14 Actual alpha
15 Low impact	16 High impact					
17 10%	18 30%	19 69	20 69	21 138	22 .807	23 .033
24 20%	25 40%	26 90	27 90	28 180	29 .802	30 .037
31 30%	32 50%	33 102	34 102	35 204	36 .806	37 .042
38 40%	39 60%	40 102	41 102	42 204	43 .801	44 .038
45 50%	46 70%	47 102	48 102	49 204	50 .806	51 .036
52 60%	53 80%	54 90	55 90	56 180	57 .802	58 .032
59 70%	60 90%	61 69	62 69	63 138	64 .807	65 .025

66 **Allocation ratio: 30% and 70% (3:7)**

67 20% difference

68 Proportion reporting COI		69 Sample size group 1	70 Sample size group 2	71 Sample size total	72 Actual power	73 Actual alpha
74 Low impact	75 High impact					
76 10%	77 30%	78 105	79 44	80 149	81 .815	82 .038
83 20%	84 40%	85 141	86 59	87 200	88 .807	89 .040
90 30%	91 50%	92 165	93 69	94 234	95 .801	96 .045
97 40%	98 60%	99 168	100 71	101 239	102 .805	103 .043
104 50%	105 70%	106 166	107 70	108 236	109 .864	110 .042
111 60%	112 80%	113 148	114 62	115 210	116 .802	117 .040
118 70%	119 90%	120 133	121 47	122 160	123 .802	124 .035

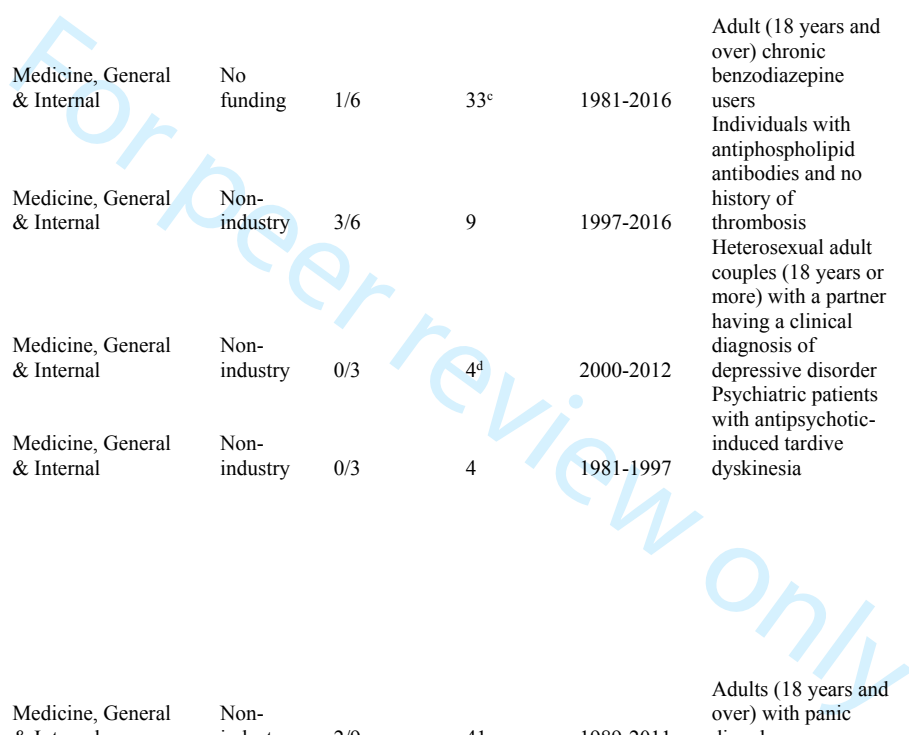


eTable1. Detailed characteristics of included meta-analyses

eTable1. Detailed characteristics of included meta-analyses

First Author	Year	Journal	2017 Impact Factor	Specialty Area	Meta-analysis Funding source(s)	Number of Meta-analysis Authors with Industry Financial Ties / Number of Meta-analysis Authors <sup>a</sup>	Number of drug RCTs Included	Publication Dates of included drug RCTs	Population	Drug Intervention(s)	Comparison Arm(s)
<b>Cochrane Reviews (n = 107)</b>											
Abdel-Rahman <sup>1</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	7	2004-2016	Adults (19 years and over) with advanced biliary tract carcinomas	Gemcitabine, vandetanib, S-1 (tegafur + gimeracil + oteracil), gemcitabine + oxaliplatin, 5-fluorouracil + folinic acid, capecitabine	Best supportive care, 5-fluorouracil + cisplatin + radiotherapy
Adams <sup>2</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	36	1994-2012	Participants with or without evidence of cardiovascular disease	Fluvastatin	Placebo
Agabio <sup>3</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	27	1969-2015	People with co-occurring depression and alcohol dependence	Antidepressants - 16 types, diazepam, memantine	Placebo, psychotherapy
Al-Shahi Salman <sup>4</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Not reported	0/5	11 <sup>b</sup>	1999-2015	Adults (16 years and over) with acute spontaneous intracerebral haemorrhage	Blood clotting factors, antifibrinolytic drugs	Placebo, open control, fresh frozen plasma
Alabed <sup>5</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	11	1976-2008	Patients with antipsychotic-induced tardive dyskinesia (TD)	Gamma-aminobutyric acid agonists - 6 types	Placebo
Allegretti <sup>6</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	3/8	8	1998-2016	Patients with hepatorenal syndrome	Terlipressin, terlipressin + albumin	Placebo, no intervention, albumin
Arechabala <sup>7</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/7	37	1998-2017	Patients undergoing haemodialysis using a central venous catheter	Antibiotic antimicrobial lock solutions - 11 types, non-antibiotic antimicrobial lock	Heparin, saline

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										solutions - 10 types, antibiotic + non-antibiotic antimicrobial lock solutions - 3 types	
										Valproate, carbamazepine, lithium, pregabalin, captodiame, paroxetine, tricyclic antidepressants - 4 types, alpidem, buspirone, flumazenil, propranolol, progesterone, magnesium aspartate, bromazepam, cyamemazine, zopiclone, flunitrazepam	Placebo, no intervention
Baandrup <sup>8</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	1/6	33 <sup>c</sup>	1981-2016	Adult (18 years and over) chronic benzodiazepine users		
Bala <sup>9</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	3/6	9	1997-2016	Individuals with antiphospholipid antibodies and no history of thrombosis	Aspirin + anticoagulants, aspirin, aspirin + low molecular weight heparin	Placebo, immunoglobulin, unfractionated heparin
Barbato <sup>10</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	4 <sup>d</sup>	2000-2012	Heterosexual adult couples (18 years or more) with a partner having a clinical diagnosis of depressive disorder	Antidepressants - 9 types	Couples therapy
Bergman <sup>11</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	4	1981-1997	Psychiatric patients with antipsychotic-induced tardive dyskinesia	Benzodiazepines - 3 types Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), norepinephrine reuptake inhibitors (NRIs), nefazodone, ritanserin	Placebo, usual care
Bighelli <sup>12</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	2/9	41	1989-2011	Adults (18 years and over) with panic disorder		Placebo
Birks <sup>13</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/2	30	1996-2017	People with Alzheimer's disease	Donepezil	Placebo
Boyapati <sup>14</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	3/8	6	1978-2017	Adults (18 years and over) with quiescent Crohn's disease	Azathioprine, infliximab	No treatment, usual care (azathioprine + infliximab)

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3			Cochrane									
4			Database of						Women of			
5	Brown <sup>15</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	5	1993-2017	reproductive age	Combined oral contraceptive	Placebo, leuprolide,
6			Reviews		& Internal	industry				with endometriosis	pill - 3 types	goserelin
7			Cochrane									
8	Bruins Slot <sup>16</sup>	2018	Database of	6.8	Medicine, General	Non-	1/2 <sup>e</sup>	13	2008-2014	Adults with atrial	Factor Xa inhibitors - 7	Warfarin
9			Systematic		& Internal	industry				fibrillation	types	
10			Reviews							People with		
11										schizophrenia and		
12										schizophrenia-like		
13										disorders such as		
14			Cochrane							schizophreniform		
15	Bryan <sup>17</sup>	2017	Database of	6.8	Medicine, General	No	0/3	20	1968-2007	disorder, or	Zuclophenthixol	Placebo, other drugs -
16			Systematic		& Internal	funding				schizoaffective	dihydrochloride	11 types
17			Reviews							disorder	Antifibrinolytic agents - 2	
18											types, non-steroidal anti-	Placebo, herbal
19	Bryant-Smith <sup>18</sup>	2018	Database of	6.8	Medicine, General	No	1/4	13	1970-2016	Women of	inflammatory drugs	medicines,
20			Systematic		& Internal	funding				reproductive age	(NSAIDs), progestogens,	levonorgestrel
21			Reviews							with heavy	ethamsylate	intrauterine system
22										menstrual bleeding		
23	Burry <sup>19</sup>	2018	Database of	6.8	Medicine, General	Non-	0/9	9	1996-2016	Adults (17 years and	Antipsychotics - 5 types	Nonantipsychotics,
24			Systematic		& Internal	industry				over) in non-ICU		placebo
25			Reviews							acute care settings		
26	Campschroer <sup>20</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	67	2002-2017	diagnosed with	Alpha-blockers - 6 types	Placebo, usual care
27			Systematic		& Internal	industry				delirium		
28			Reviews							Adult patients (18		
29										years and older)		
30	Candy <sup>21</sup>	2018	Database of	6.8	Medicine, General	Non-	0/5	8	1996-2017	with ureteral stone	Mu-opioid antagonists - 3	Placebo
31			Systematic		& Internal	industry				disease	types	
32			Reviews							Adults with cancer		
33	Chiew <sup>22</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	9 <sup>f</sup>	1976-2014	and adults receiving	Methionine, cysteamine,	Placebo, no treatment
34			Systematic		& Internal	industry				palliative care with	dimercaprol, acetylcysteine	
35			Reviews							opioid-induced		
36										bowel dysfunction		
37	Das <sup>23</sup>	2018	Database of	6.8	Medicine, General	Not	0/3	7	2010-2017	Patients with	Vitamin D	Placebo, antibiotics
38			Systematic		& Internal	reported				paracetamol		alone
39			Reviews							(acetaminophen)		
40	Demicheli <sup>24</sup>	2018	Database of	6.8	Medicine, General	Non-	1/5	71 <sup>g</sup>	1969-2014	overdose	Inactivated parenteral	Placebo, no treatment
41			Systematic		& Internal	industry				Children aged up to	influenza vaccine	
42			Reviews							five years with a		
43										clinical diagnosis of		
44										community-acquired		
45										pneumonia (CAP)		
46										Healthy individuals		
47										(16 to 65 years) and		
										pregnant women and		
										their newborns		

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3			Cochrane									
4			Database of									
5	Demicheli <sup>25</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/7	8	1969-2004	Elderly participants	Influenza vaccines	Placebo
6			Reviews		& Internal	industry				(65 years and over)	Fondaparinux,	
7											rivaroxaban, low molecular	
8											weight heparin, non-	
9											steroidal anti-inflammatory	
10											drugs, vasotonin,	
11											sulodexide,	
12			Cochrane								heparansulphate, vitamin K	
13			Database of								antagonists, enzyme	
14	Di Nisio <sup>26</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/3	32	1970-2017	Patients with	heparin, heparin calcium,	Placebo, elastic
15			Reviews		& Internal	industry				superficial	defibrotide	stockings
16			Cochrane									
17	El-Sayeh <sup>27</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	10	1973-2010	antipsychotic-	Noradrenergic drugs - 2	Placebo
18			Systematic		& Internal	industry				induced tardive	types, dopaminergic drugs	
19			Reviews							dyskinesia	- 7 types	
20										People of all ages on		
21										continuous vitamin		
22			Cochrane							K antagonist (VKA)		
23	Engelen <sup>28</sup>	2018	Database of	6.8	Medicine, General	Non-	0/5	3	1989-2015	or direct oral		Usual care (surgical
24			Systematic		& Internal	industry				anticoagulant	Antifibrinolytic agents - 2	treatment), usual care
25			Reviews							(DOAC) treatment	types	(surgical treatment) +
26										undergoing an oral	Selective serotonin	placebo
27	Eshun-Wilson <sup>29</sup>	2018	Database of	6.8	Medicine, General	Non-	1/6	10	1994-2014	or dental procedure	reuptake inhibitors (SSRIs)	
28			Systematic		& Internal	industry					- 4 types, tricyclic	Placebo, mirtazapine
29			Reviews							Adults (18 years and	antidepressants (TCAs) - 2	
30	Essali <sup>30</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/4	3	1992-1997	over) living with	types	
31			Database of		& Internal	industry				HIV and depression		
32			Systematic							People with	Calcium channel blockers -	Placebo
33			Reviews							antipsychotic-	3 types	
34	Everitt <sup>31</sup>	2018	Database of	6.8	Medicine, General	Non-	3/8	23	1978-2013	induced tardive	Selective serotonin	Placebo, insomnia
35			Systematic		& Internal	industry				dyskinesia	reuptake inhibitors - 4	medication - 2 types
36			Reviews							People (18 years and	types; tricyclic	
37	Fanshawe <sup>32</sup>	2017	Cochrane	6.8	Medicine, General	Non-	0/6	4	2004-2014	over) with insomnia	antidepressants - 3 types;	
38			Database of		& Internal	industry				Regular tobacco	other antidepressants - 6	Placebo
39			Systematic							smokers (20 years	types	Placebo, selective
40	Franik <sup>33</sup>	2018	Reviews	6.8	Medicine, General	Non-	0/5	42	2004-2017	and under)	Nicotine replacement	estrogen receptor
41			Cochrane		& Internal	industry				Subfertile women of	therapy, bupropion	modulators,
42			Database of							reproductive age		clomiphene citrate
43			Systematic							with polycystic		
44			Reviews							ovary syndrome	Letrozole	
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											followed by intrauterine insemination, laparoscopic ovarian drilling, follicle-stimulating hormone, anastrozole
González <sup>34</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/6	6	1994-2014	Pregnant women living in malaria-endemic areas	Mefloquine	Sulfadoxine-pyrimethamine, cotrimoxazole, placebo
Grabosch <sup>35</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	3	2006-2017	Adult women with moderate or severe cervical intraepithelial neoplasia (CIN)	Non-steroidal anti-inflammatory agents (NSAIDs) - 2 types	Placebo
Graves <sup>36</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	24 <sup>b</sup>	1981-2017	Adults and children being treated for falciparum malaria	Primaquine	Usual treatment, bulaquine
Haas <sup>37</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	11	1997-2017	Pregnant women who were about to receive a cesarean delivery	Antiseptic solutions - 3 types	Placebo, no treatment
Hakoum <sup>38</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/10	15	1991-2009	People with cancer and venous thromboembolism	Low molecular weight heparin, unfractionated heparin	Fondaparinux Placebo, no treatment, alternative therapies - 7 types, other drug comparators - 6 types, other non-drug comparators - 4 types
Heras-Mosteiro <sup>39</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/10	89	1990-2015	Immunocompetent patients with localised Old World cutaneous leishmaniasis	Antimonials – 2 types, non-antimonials – 22 types	Chemotherapy, targeted therapy, EGFR-targeting agents, cetuximab, ramucirumab
Janmaat <sup>40</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/8	41	1980-2015	People with esophageal or gastroesophageal junction cancer		Best supportive care, unspecified control
Jefferson <sup>41</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	1/4	41	1971-2016	Healthy children (15 years and under)	Influenza vaccine - 2 types	Placebo, no intervention
Jung <sup>42</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/6	19	2006- Unpublished	Middle-aged and older men (40 or over) with lower urinary tract symptoms as a result of benign prostatic hyperplasia	Sildenafil, tamsulosin, naftopidil, and alfuzosin	Placebo

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3			Cochrane									
4			Database of									
5	Kaempfen <sup>43</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	3	2013-2017	Preterm infants	Propranolol	Placebo, no treatment
6			Reviews		& Internal	industry						
7			Cochrane									
8			Database of									
9	Kahale <sup>44</sup>	2017	Systematic	6.8	Medicine, General	Non-	0/10	7	1979-2012	Ambulatory people	Warfarin, apixaban	Placebo, no treatment
10			Reviews		& Internal	industry				with cancer		
11			Cochrane									
12			Database of							People with cancer		
13			Systematic	6.8	Medicine, General	Non-	0/10	13	1990-2013	and central venous	Anticoagulant - 6 types	Placebo, no treatment
14			Reviews		& Internal	industry				catheters	Vitamin K antagonist - 2	
15			Cochrane								types, direct oral	
16	Kahale <sup>46</sup>	2018	Database of	6.8	Medicine, General	Non-	0/11	16	2001-2018	People with cancer	anticoagulant - 4 types;	
17			Systematic		& Internal	industry				and venous	low molecular weight	
18			Reviews							thromboembolism	heparin - 4 types	Anticoagulants
19			Cochrane									
20			Database of									
21	Kapur <sup>47</sup>	2018	Systematic	6.8	Medicine, General	Non-	3/5	7	1992-2012	Children and adults	Corticosteroids - 3 types	Placebo, no treatment
22			Reviews		& Internal	industry				with bronchiectasis		
23			Cochrane									
24			Database of									
25			Systematic									
26			Reviews									
27			Cochrane									
28			Database of									
29			Systematic									
30			Reviews									
31			Cochrane									
32			Database of									
33			Systematic									
34			Reviews									
35	Lawrie <sup>51</sup>	2018	Database of	6.8	Medicine, General	Non-	0/9	38	1978-2016	Adults (18 years and	Inactivated influenza	Placebo
36			Systematic		& Internal	industry				over) undergoing	vaccine	
37			Reviews							radiotherapy for	Aminosaliculates - 4 types,	
38			Cochrane							pelvic cancers	corticosteroids, superoxide	
39			Database of								dismutase, amifostine, bile	
40			Systematic								acid sequestrants,	
41			Reviews								magnesium oxide,	
42			Cochrane								misoprostol, octreotide,	
43			Database of								selenium, sodium butyrate,	
44			Systematic								sucralfate, ibuprofen,	
45			Reviews								famotidine, smectite,	
46			Cochrane								simethicone, tropisetron	Placebo, no treatment
47			Database of									

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3			Systematic								selective progesterone-	
4			Reviews								receptor modulators	
5			Cochrane									
6			Database of									0.9% sodium chloride
7	López-Briz <sup>54</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/6	11	2002-2015	Adults with central	Heparin	(normal saline
8			Reviews		& Internal	industry				venous catheters		solution)
9			Cochrane							Children (18 years		
10			Database of							and under) with		
11	Marchant <sup>55</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/4	3	1993-2012	prolonged wet	Antibiotics - 2 types	Placebo, no treatment
12			Reviews		& Internal	industry				cough (longer than		
13			Cochrane							10 days)		
14	Matar <sup>56</sup>	2018	Database of	6.8	Medicine, General	Non-	0/3	7	1963-1999	Patients with	Fluphenazine	Placebo
15			Systematic		& Internal	industry				schizophrenia		
16			Reviews									
17	Matar <sup>57</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/11	20	1986-2018	People with solid or	Low-molecular weight	Unfractionated heparin
18			Database of		& Internal	industry				hematologic cancer	heparin (LMWH) - 10	(UFH), fondaparinux
19			Systematic							undergoing surgery	types	
20	McNicol <sup>58</sup>	2018	Reviews	6.8	Medicine, General	Non-	1/3	13	1992-2016	Postoperative	Ketorolac	Placebo, opioid
21			Cochrane		& Internal	industry				paediatric patients		
22			Database of							(17 years and under)		
23			Systematic							Children (16 years		
24			Reviews							and under)		
25	McTague <sup>59</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/3	18	1995-2014	presenting to a	Lorazepam	Diazepam +
26			Database of		& Internal	industry				hospital or		phenytoin, diazepam,
27			Systematic							emergency		paraldehyde,
28			Reviews							department in an		midazolam
29	Mhaskar <sup>60</sup>	2017	Cochrane	6.8	Medicine, General	Non-	0/4	24	1982-2015	acute tonic-clonic		
30			Database of		& Internal	industry				convulsion		
31			Systematic									
32	Milligan <sup>61</sup>	2018	Reviews	6.8	Medicine, General	Non-	0/4	18	1980-2016	Patients with	Bisphosphonates - 5 types	Placebo, no treatment -
33			Cochrane		& Internal	industry				multiple myeloma		Network meta-analysis
34			Database of							(MM)		
35			Systematic							Adults and children	Typhoid fever vaccines - 4	No treatment, placebo,
36	Monk <sup>62</sup>	2017	Reviews	6.8	Medicine, General	Non-	0/4	32	1993-2016		types	typhoid-inactive
37			Cochrane		& Internal	industry				People undergoing	Tramadol, non-steroidal	agents
38			Database of							orthodontic	anti-inflammatory drugs,	
39			Systematic							treatment	paracetamol, local	
40	Montero <sup>63</sup>	2018	Reviews	6.8	Medicine, General	No	1/7	10	1991-2012	Patients with	anaesthetic	Placebo, no treatment
41			Cochrane		& Internal	funding <sup>1</sup>				hepatitis C virus-	Rituximab, interferon,	Usual care,
42			Database of							associated mixed	immunosuppressive drug	immunoadsorption
43			Systematic							cryoglobulinaemia	therapy	apheresis
44			Reviews							Adults (18 years and		
45	Mücke <sup>64</sup>	2018	Database of	6.8	Medicine, General	Non-	2/5	16	2004-2017	over) with chronic	Cannabis-based medicines	Placebo,
46			Systematic		& Internal	industry				neuropathic pain	- 5 types	dihydrocodeine
47			Reviews									

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3			Systematic									
4			Reviews									
5			Cochrane									
6			Database of									
7	Narula <sup>65</sup>	2018	Systematic	6.8	Medicine, General	Non-	3/7	10 <sup>i</sup>	1990-2014	Adults and children	Corticosteroids - 5 types	Enteral nutrition
8			Reviews		& Internal	industry				Adults or children		
9			Cochrane							with partial onset		
10			Database of							seizures or		
11	Nevitt <sup>66</sup>	2017	Systematic	6.8	Medicine, General	Non-	1/5	76	1981-2015	generalised onset	Antiepileptic drugs - 10	Network meta-analysis
12			Reviews		& Internal	industry				tonic-clonic seizures	types	
13			Cochrane							Adults and children		
14	Nevitt <sup>67</sup>	2018	Database of	6.8	Medicine, General	Non-	1/4	14	1995-2015	with focal onset or	Lamotrigine	Carbamazepine
15			Systematic		& Internal	industry				generalised onset		
16			Reviews							seizures		
17	Norman <sup>68</sup>	2018	Cochrane	6.8	Medicine, General	Non-	1/6	78	1985-2016	Adults (18 years and	Topical agents - 10 types	Dressings - 12 types;
18			Database of		& Internal	industry				over) with venous		Network meta-analysis
19			Systematic							leg ulcers		
20	Normansell <sup>69</sup>	2018	Reviews	6.8	Medicine, General	Non-	0/6	6	1974-2016	Children and adults	Antibiotics - 4 types	Placebo
21			Cochrane		& Internal	industry				with acute asthma	Propranolol, timolol	
22			Database of							exacerbation	maleate, bleomycin,	
23			Systematic								atenolol, prednisolone,	
24			Reviews		Medicine, General	Non-	1/7	24	1977-2016	Children (17 years	captopril, ibuprofen +	Placebo, radiation,
25	Novoa <sup>70</sup>	2018	Cochrane	6.8	& Internal	industry				and under) with	paracetamol, methylene	lasers
26			Database of							single or multiple	blue, triamcinolone,	
27			Systematic							haemangiomas	methylprednisolone	
28			Reviews							located on the skin		
29			Cochrane							Preterm (< 37		
30	Ohlsson <sup>71</sup>	2017	Database of	6.8	Medicine, General	No	0/2	34	1991-2017	weeks' gestation)	Erythropoiesis-stimulating	Placebo, no treatment
31			Systematic		& Internal	funding				and low birth weight	agents (ESAs) - 2 types	
32			Reviews							(< 2500 grams)		
33	Ostinelli <sup>72</sup>	2018	Cochrane	6.8	Medicine, General	No	1/5	3	2005-2016	infants less than	Aripiprazole	Placebo, other anti-
34			Database of		& Internal	funding				eight days of age		psychotic medications
35			Systematic							Adults exhibiting		- 2 types
36	Ostinelli <sup>73</sup>	2018	Reviews	6.8	Medicine, General	No	0/6	9	2010-2014	aggression or	Risperidone	Haloperidol,
37			Cochrane		& Internal	Non-				aggression or		olanzapine, quetiapine,
38			Database of			industry				agitation		oxcarbazepine,
39	Ostuzzi <sup>74</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/5	7	1985-	Adults (18 years and	Antidepressants - 6 types	Placebo
40			Reviews		& Internal	industry			Unpublishe	over) with cancer		
41			Cochrane						d	and depression		
42			Database of									
43			Systematic									
44			Reviews									
45			Cochrane									
46			Database of									
47			Systematic									



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3			Cochrane									
4			Database of						Children and adults			
5	Parker <sup>75</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/5	2	2011-2013	with active Crohn's	Naltrexone	Placebo
6			Reviews		& Internal	industry				disease		Tamoxifen, interferon-
7												alpha, interleukin-2,
8												interferon-alpha +
9												interleukin-2, Bacille
10											Single agent	Calmette-Guérin
11											chemotherapy,	(BCG),
12											polychemotherapy,	corynebacterium
13			Cochrane								temozolomide,	parvum, anti-PD1
14	Pasquali <sup>76</sup>	2018	Database of	6.8	Medicine, General	Non-	0/5	122	1972-2015	Patients with	dacarbazine, anti-CTLA4	monoclonal
15			Systematic		& Internal	industry				unresectable lymph	monoclonal antibodies,	antibodies, sorafenib,
16			Reviews							node metastasis and	other immunostimulating	elesclomol, anti-
17			Cochrane							distant metastatic	agents, MEK inhibitors	angiogenic drugs
18	Pike <sup>77</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	4	2007-2017	Children (18 years	Omalizumab, leukotriene	Placebo
19			Systematic		& Internal	industry				and under) with	receptor antagonists - 2	
20			Reviews							asthma	types, corticosteroids	
21	Rirash <sup>78</sup>	2017	Cochrane	6.8	Medicine, General	Not	Not	38	1982-2000	Patients with		Placebo
22			Database of		& Internal	reported	reported/8			Raynaud's	Calcium channel blockers	
23			Systematic							phenomenon		
24	Robertson <sup>79</sup>	2017	Reviews	6.8	Medicine, General	Non-	0/3	6	1995-2016	Adults (18 years and	Warfarin, aspirin,	Placebo
25			Cochrane		& Internal	industry				over) with	rivaroxaban	
26			Database of							unprovoked venous		
27			Systematic							thromboembolism		
28	Romero <sup>80</sup>	2017	Reviews	6.8	Medicine, General	Non-	0/3	7	1983-1999	Sexually active	Macrolide antibiotics - 3	Other antibiotics - 4
29			Cochrane		& Internal	industry				adults (16 years and	types	types
30			Database of							over) with genital		
31	Rosomeck <sup>81</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/3	15	1996-2016	ulcers compatible	Ivermectin	Permethrin
32			Reviews		& Internal	industry				with chancroid		
33			Cochrane							People with scabies		
34	Rüschén <sup>82</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	7	1995-2012	of all ages and either	Hyaluronidase	Local anaesthetic
35			Systematic		& Internal	industry				sex	Methylphenidate,	mixture (standard
36			Reviews							Adults (18 years and	modafinil, cholinesterase	treatment)
37			Cochrane							over) undergoing	inhibitors (ChEIs), atypical	
38			Database of							intraocular surgery	antipsychotics,	
39	Ruthirakuhan <sup>83</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/5	21	1998-2017	People with	mibampator, valproate,	Placebo
40			Reviews		& Internal	industry				Alzheimer's Disease	semagacestat	
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3			Cochrane								
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5	Sankar <sup>84</sup>	2018	Systematic	6.8	Medicine, General	No	0/3	6	2011-2016	Preterm infants with	Anti-vascular endothelial
6			Reviews		& Internal	funding				retinopathy	growth factor agents - 2
7											Cryo/laser therapy
8											
9			Cochrane								
10			Database of								
11	Schumann <sup>85</sup>	2018	Systematic	6.8	Medicine, General	Non-	3/9	13	1990-2013	Adults (18 years and	epinephrine,
12			Reviews		& Internal	industry				over) with	norepinephrine-
13										cardiogenic shock or	dobutamine, amrinone,
14	Simancas-									acute low cardiac	dopexamine, dopamine,
15	Racines <sup>86</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/6	13 <sup>k</sup>	1992-1994	output syndrome	nitric oxid
16			Reviews		& Internal	industry				People suffering	Acetazolamide, ibuprofen,
17										from high altitude	dexamethasone, oxygen,
18										illness	nitric oxide, gabapentin,
19			Cochrane								magnesium sulphate,
20			Database of								sumatriptan
21			Systematic								Placebo, normal air,
22			Reviews								unspecified control,
23											paracetamol
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4												mepivacaine, prilocaine, prilocaine + felypressin, prilocaine + epinephrine
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6			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/6	17	1972-2015	Adults and children with pneumonia	Corticosteroids - 7 types	Placebo, usual care
7	Stern <sup>92</sup>	2017										
8												
9												
10												
11			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	0/3	4	1995-2013	Children and adolescents (18 years or under) with autism spectrum disorder (ASD) or pervasive developmental disorder (PDD)	Methylphenidate	Placebo
12	Sturman <sup>93</sup>	2017										
13												
14			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/4	14	1976-2014	Psychiatric patients with antipsychotic- induced tardive dyskinesia	Cholinergic drugs - 6 types	Placebo
15	Tammenmaa- Aho <sup>94</sup>	2018										
16												
17												
18												
19			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	2/4	8	2006-2014	Adults (17 years and over) with severe mental illness and co-occurring substance use disorder	Risperidone	Other antipsychotics - 5 types
20	Temmingh <sup>95</sup>	2018										
21												
22			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	1/7	13	1997-2018	Adults with HIV- associated cryptococcal meningitis	Antifungal induction therapies - 6 types	Network meta-analysis H2 receptor antagonists, proton pump inhibitors, prostaglandin analogues, anticholinergics, antacids, sucralfate, teprenone, naloxone, bioflavonoids, placebo, no treatment, other medication (not defined)
23	Tenforde <sup>96</sup>	2018										
24												
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31												
32			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/7	103 <sup>n</sup>	1977-2016	People admitted to intensive care units	H2 receptor antagonists, proton pump inhibitors, prostaglandin analogues, anticholinergics, antacids, sucralfate, teprenone, naloxone, bioflavonoids	
33	Toews <sup>97</sup>	2018										
34												
35			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	1/4	3 <sup>o</sup>	1992-1996	Children (16 years and under) with recurrent acute otitis media	Antibiotics - 3 types	Grommets
36	Venekamp <sup>98</sup>	2018										
37												
38												
39			Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/6	8	1998-2016	Individuals who had an ischemic or hemorrhagic stroke	Preventive antibiotics	Placebo, standard care
40	Vermeij <sup>99</sup>	2018										
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4			Cochrane						Patients with critical			
5			Database of					1983-	limb ischaemia			
6	Vietto <sup>100</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/6	33	Unpublishe	or reconstructive	Prostanoids - 7 types	Placebo, other active
7			Reviews		& Internal	industry			d	intervention		drugs - 4 types
8			Cochrane									
9			Database of									
10	Wall <sup>101</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/5	5	1995-2014	Patients with acute	Glycerol	Treatment as usual
11			Reviews		& Internal	industry				bacterial meningitis		
12										Adult patients (over		
13			Cochrane							18 years)		
14			Database of							undergoing any		
15	Weibel <sup>102</sup>	2018	Systematic	6.8	Medicine, General	Non-	3/10	68	1985-2017	elective or urgent	Lidocaine	Placebo, no treatment,
16			Reviews		& Internal	industry				surgical procedure	Thiazides, beta-blockers,	thoracic epidural
17			Cochrane							under general	angiotensin-converting-	analgesia - 3 types
18			Database of							anaesthesia	enzyme inhibitors, calcium	
19			Systematic							Adult patients with	channel blockers	Placebo
20			Reviews							primary		
21										hypertension		
22	Xiao <sup>104</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/4	2	2001-2003	Patients with focal		
23			Database of		& Internal	industry				epilepsy that failed	Losigamone	Placebo
24			Systematic							to respond to one or		
25			Reviews							more antiepileptic		
26	Zhang <sup>105</sup>	2017	Systematic	6.8	Medicine, General	No	0/5	3	2009-2015	drugs	Thrombopoietin receptor	Placebo
27			Reviews		& Internal	funding				Adult and elder	agonists (TPO-RAs)	
28			Cochrane							patients with solid		
29			Database of							tumours		
30			Systematic							Adults (18 years and		
31			Reviews							over) with	Oxcarbazepine	Placebo
32	Zonneveld <sup>107</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/6	5	2004-2014	neuropathic pain		
33			Database of		& Internal	industry				Adult patients with		
34			Systematic							an ischaemic stroke,	Blood pressure-lowering	Placebo, no treatment
35			Reviews			Not	0/7	11	1970-2017	haemorrhagic stroke	drugs (BPLDs) - 5 types	
36						reported				or transient		
37										ischaemic attack		
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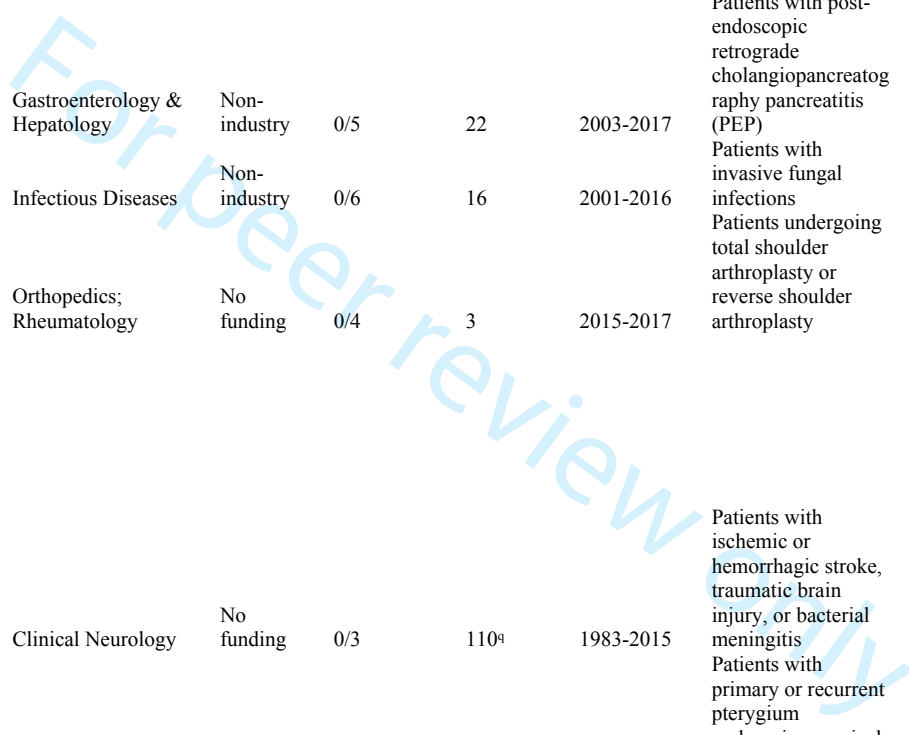
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4	Chen <sup>111</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/3	9	2009-2017	Patients with sepsis	Statins - 3 types	Placebo
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9	Ding <sup>112</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/6	6	2014-2017	Patients with hormone receptor-positive or human epidermal growth factor receptor 2 negative advanced breast cancer	Cyclin-dependent kinases 4/6 inhibitors - 3 types	Placebo
10												
11	Guo <sup>113</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/8	5	2004-2017	Adults undergoing total knee arthroplasty (TKA)	Tranexamic acid (TXA)	Placebo, no treatment
12												
13	Han <sup>114</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/7	18	2007-2016	Patients with myocardial infarction	Statins - 3 types	Placebo
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21	Hu <sup>115</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/5	4	2010-2016	Patients with acute coronary syndrome, percutaneous coronary intervention, or coronary stents given combination therapy with aspirin and clopidogrel	Proton pump inhibitors	Placebo
22												
23	Huang <sup>116</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/5	18	2010-2015	Patients with pterygium or glaucoma	Antivascular endothelial growth factor agents - 3 included	Placebo, sham
24												
25	Jiang <sup>117</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/5	13	2010-2017	Patients with diabetic peripheral neuropathy	Fasudil + methylcobalamin or lipoic acid	Methylcobalamin or lipoic acid alone
26												
27												
28	Jiang <sup>118</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/4	15	2011-2016	Adult women with pathologically confirmed epithelial ovarian cancer	Antiangiogenic therapy (7 included) alone or combined with chemotherapy	Placebo or chemotherapy alone
29												
30	Khan <sup>119</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/8	7	2015-2017	Patients with advanced non-small cell lung cancer	Immune checkpoint inhibitors: anti-PD1/PD-L1 therapies - 3 types	Chemotherapy - 6 regimens
31												
32												
33	Liang <sup>120</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/4	3	2016-2017	Patients undergoing total knee or hip arthroplasty	Acetaminophen	Normal saline or placebo
34												
35	Liu <sup>121</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/7	5	1999-2007	Adults with social anxiety disorder	Fluvoxamine	Placebo
36												
37												
38	Lor <sup>122</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/8	10	1999-2015	Children and adults requiring nasogastric intubation	Lidocaine	Normal saline, K-Y lubricant gel, or no treatment
39												
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41	Wang <sup>123</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/2	4	2015-2017	Adults with intertrochanteric fractures preparing for internal fixation	Tranexamic acid	Placebo, no treatment
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										(dynamic hip screws, proximal femoral nail antirotations)		
												Placebo, octreotide, norepinephrine, dopamine + furosemide, octreotide + midodrine
Wang <sup>124</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/5	18	2001-2016	Patients with hepatorenal syndrome	Terlipressin		
Wang <sup>125</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/3	4	1993-2011	Patients undergoing bronchoscopy	Propofol		Midazolam Chemotherapy, everolimus, ipilimumab
Wei <sup>126</sup>	2017	Medicine	2.0	Medicine, General & Internal	Not reported	0/2	14	2015-2017	Cancer patients Women of reproductive age with primary dysmenorrhea	PD-1 inhibitors - 2 types Non-steroidal anti-inflammatory drugs, analgesics, oral contraceptives		
Woo <sup>127</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/7	34 <sup>P</sup>	1998-2017	Patients who were administered xenon versus propofol as a general anesthetic	Xenon		Acupuncture
Xia <sup>128</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/6	13	2004-2012	Patients prepared for primary total hip arthroplasty (THA)			Propofol
Yang <sup>129</sup>	2017	Medicine	2.0	Medicine, General & Internal	Not reported	0/4	7	2008-2016	Patients undergoing laparoscopic cholecystectomy	Glucocorticoids - 3 types		Placebo, no treatment
Ye <sup>130</sup>	2017	Medicine	2.0	Medicine, General & Internal	Not reported	0/3	5	2004-2016	Adults with acute heart failure	Ketamine		Placebo
Yu <sup>131</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/6	8	2009-2017	Patients with locoregionally advanced nasopharyngeal carcinoma	Serelaxin		Placebo
Yuan <sup>132</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/9	31	1995-2016		Neoadjuvant chemotherapy regimens - 16 included Aspirin, aspirin + dipyridamole, aspirin + clopidogrel, aspirin + warfarin, cilostazol, warfarin, and ticlopidine		Network meta-analysis
Zhang <sup>133</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/2	13	2001-2014	Adults with cerebral infarction			Network meta-analysis
Zhang <sup>134</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/8	10	1989-2006	Healthy volunteers and people with congestive heart failure	Histamine H2 antagonists - 5 types		Placebo, other conventional therapy medicines - 3 types
Zhao <sup>135</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/7	5	2008-2017	Adult patients prepared to undergo laparoscopic cholecystectomy	Lidocaine		Placebo, saline
Zhao <sup>136</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/3	4	2013-2017	Patients with a diagnosis of	Nefopam		Saline or usual care

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11	Zhou <sup>137</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/4	6	2013-2017	symptomatic cholelithiasis and acute cholecystitis who prepared for laparoscopic cholecystectomy Adults with end-staged knee osteoarthritis undergoing total knee arthroplasty	Dexamethasone	Placebo, no treatment
12												
13												
14	Zhu <sup>138</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/3	8	2002-2016	Patients who underwent total hip arthroplasty	Selective non-steroidal anti-inflammatory drugs (selective COX-2 inhibitors) - 4 types	Non-selective non-steroidal anti-inflammatory drugs (non-selective COX-2 inhibitors) - 4 types
15			Postgraduate									
16	Zhou <sup>139</sup>	2018	Medicine	2.1	Medicine, General & Internal	No funding	0/5	10	2007-2017	Patients with dyslipidemia	Anacetrapib	Placebo, placebo + usual care
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18												
19			Revista da Associação Médica Brasileira									
20												
21	Zhang <sup>140</sup>	2018	Medicine	0.7	Medicine, General & Internal	Non-industry	Not reported/6	6	2012-2016	Patients with complicated intra-abdominal infections and complicated urinary tract infections	Ceftazidime-avibactam	Other antibiotics - 3 types, usual care
22	<b>Specialty medicine (n = 100)</b>											
23												
24			Acta Ophthalmologica									
25	Li <sup>141</sup>	2018		3.3	Ophthalmology	Non-industry	Not reported/3	72	1995-2015	Patients with primary open-angle glaucoma or ocular hypertension	Prostaglandin analogues, alpha-2 adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors, miotics	Placebo - Network meta-analysis
26												
27			American Heart Journal									
28	Tarantini <sup>142</sup>	2018		4.2	Cardiovascular Systems	No funding	0/7	5	2007-2016	Patients with acute coronary syndrome	P2Y12 receptor inhibitors - 2 types	Clopidogrel
29												
30			American Journal of Cardiovascular Drugs									
31	Wang <sup>143</sup>	2018		2.7	Cardiovascular Systems; Pharmacology & Pharmacy	Non-industry	0/3	5	2014-2017	Adults aged 18–65 years with hyperlipidemia	Inclisiran	Placebo, other lipid-lowering agents - Network meta-analysis
32												
33												
34			Anaesthesia and Intensive Care									
35	Aman <sup>144</sup>	2018		1.7	Anesthesiology; Critical Care Medicine	Non-industry	Not reported/5	10	1995-2015	Patients undergoing caesarean section under general anaesthesia	Opioid analgesics - 3 types, non-opioid analgesics - 5 types	Placebo
36												
37	Li <sup>145</sup>	2018	Autoimmunity Reviews	8.7	Immunology	Non-industry	0/7	15	2004-2017	Patients with rheumatoid arthritis	Statins - 2 types	Conventional treatment, placebo + conventional treatment
38												
39			Biomed Research International									
40												
41	Wang <sup>146</sup>	2018		2.6	Biotechnology & Applied Microbiology; Medicine, Research & Experimental	Non-industry	0/4	15	2006-2017	Patients with left ventricular dysfunction undergoing cardiac surgery	Levosimendan	Placebo, milrinone, dopamine, intra-aortic balloon pump (IABP), and standard inotropic agents
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Veettil <sup>147</sup>	2017	BMC Cancer	3.3	Oncology	No funding	0/6	8	2003-2014	Adults with history of colorectal cancer or adenoma	Aspirin, non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs)	Placebo, no treatment
Bredemeier <sup>148</sup>	2018	BMC Cardiovascular Disorders	1.8	Cardiac & Cardiovascular Systems	No funding	0/9	91	1973-2017	Adults under treatment for any clinical condition Patients with post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP)	Purine-like xanthine oxidase inhibitors - 2 types, non-purine-like xanthine oxidase inhibitors - 2 types	Placebo, no treatment
Lyu <sup>149</sup>	2018	BMC Gastroenterology	2.7	Gastroenterology & Hepatology	Non-industry	0/5	22	2003-2017	Patients with invasive fungal infections	Nonsteroidal anti-inflammatory drugs (NSAIDs) - 6 types	Placebo
Xing <sup>150</sup>	2017	BMC Infectious Diseases	2.6	Infectious Diseases	Non-industry	0/6	16	2001-2016	Patients undergoing total shoulder arthroplasty or reverse shoulder arthroplasty	Voriconazole	Other antifungal agents - 7 types
Kuo <sup>151</sup>	2018	BMC Musculoskeletal Disorders	2.0	Orthopedics; Rheumatology	No funding	0/4	3	2015-2017	Patients with ischemic or hemorrhagic stroke, traumatic brain injury, or bacterial meningitis	Tranexamic acid Pharmacological agents for traumatic brain injury – 14 types, pharmacological agents for stroke – 23 types, pharmacological agents for bacterial meningitis – 1 type, pharmacological agents for intracerebral haemorrhage – 6 types, pharmacological agents for aneurysmal subarachnoid hemorrhage – 19 types	Placebo
Beez <sup>152</sup>	2017	BMC Neurology	2.2	Clinical Neurology	No funding	0/3	110 <sup>a</sup>	1983-2015	Patients with primary or recurrent pterygium undergoing surgical removal combined with toxic agents	Anti-fibrotic and anti-VEGF (vascular endothelial growth factor) medications - 3 types	Unspecified control
Zeng <sup>153</sup>	2017	BMC Ophthalmology	1.8	Ophthalmology	No funding	0/7	32	1990-2016	Patients with acute coronary syndrome and patients who underwent percutaneous coronary intervention		Placebo - Network meta-analysis
Bundhun <sup>154</sup>	2017	BMC Pharmacology & Toxicology	1.9	Pharmacology & Pharmacy; Toxicology	Non-industry	0/3	4	2013-2016		Prasugrel	Ticagrelor



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4										People with schizophrenia or related disorders that had a duration of treatment that was no more than 1 year		
5										Patients with acute exacerbations of chronic obstructive pulmonary disease (COPD)		
6			BMC Psychiatry	2.4	Psychiatry	No funding	0/11	47	2003-2015		Antipsychotic drugs - 12 types	Placebo - Network meta-analysis
7	Zhang <sup>155</sup>	2017										
8												
9			BMC Pulmonary Medicine	2.7	Respiratory System	No funding	0/5	19	1996-2016		Antibiotics - 17 types	Placebo - Network meta-analysis
10	Zhang <sup>156</sup>	2017										
11			BMC Pulmonary Medicine	2.7	Respiratory System	Non-industry	0/4	25	1993-2016	Preterm infants	Corticosteroids	Placebo
12	Zhang <sup>157</sup>	2017b								Post-menopausal women with metastatic HR-positive, HER2-negative breast cancer	Cyclin-dependent kinase 4/6 inhibitors - 3 types + aromatase inhibitor - 2 types	
13					Oncology; Obstetrics & Gynecology	No funding	0/4	3	2016-2017	Patients with osteoarthritis in any joint	Non-steroidal anti-inflammatory drugs - 9 types	Aromatase inhibitors - 2 types
14												
15												
16	Ramos-Esquivel <sup>158</sup>	2018	Breast Cancer British Journal of Sports Medicine	1.8		Non-industry	0/12	36	1979-2016			Network meta-analysis FOLFOX (leucovorin + fluorouracil + oxaliplatin) + bevacizumab, FOLFIRI (leucovorin + fluorouracil + irinotecan) + bevacizumab
17												
18	Zeng <sup>159</sup>	2018		7.9	Sport Sciences							Miltefosine, paromomycin, antimonial compounds - 2 types, pentamidine, sitamaquine
19												Placebo, nonsteroidal anti-inflammatory drugs (NSAIDs), disease modifying antirheumatic drugs (DMARDs)
20			Cellular Physiology and Biochemistry	5.5	Cell Biology; Physiology	Not reported	0/6	4	2015-2017	Patients with metastatic colorectal cancer	FOLFOXIRI (leucovorin + fluorouracil + oxaliplatin + irinotecan) + bevacizumab	
21	Shui <sup>160</sup>	2018										
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26	Rodrigo <sup>161</sup>	2018	Clinical Microbiology and Infection	5.4	Infectious Diseases; Microbiology	No funding	0/4	28	1996-2017	Patients with visceral leishmaniasis	Amphotericin B	
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34	Wang <sup>162</sup>	2018	Clinical Rheumatology	2.1	Rheumatology	Non-industry	0/3	25	2002-2014	Patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis	Tumor necrosis factor (TNF) inhibitors - 5 types, non-tumor necrosis factor (TNF) inhibitors - 2 types	
35											Low molecular-weight heparin (LMWH) - 5 types, enoxaparin + vitamin K antagonists (VKA)	
36												
37			Critical Reviews in Oncology / Hematology	4.5	Oncology; Hematology	No funding	1/5	13	1996-2015	Adults with acute venous thromboembolism	Proprotein convertase subtilisin/kexin type 9 gene inhibitors (PCSK9i)	Rivaroxaban, unfractionated heparin (UFH)
38	Hong <sup>163</sup>	2018										Placebo, placebo + other lipid-lowering therapy
39												
40	de Carvalho <sup>164</sup>	2018	Diabetes Care	13.4	Endocrinology & Metabolism	Not reported <sup>f</sup>	0/3	20	2012-2017	Patients with familial or nonfamilial		
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Jaafar <sup>165</sup>	2018	Digestive Diseases and Sciences	2.8	Gastroenterology & Hepatology	Not reported	0/5	17	2000-2016	Adults (18 and over) with organic or functional dyspepsia	Rebamipide	Placebo, standard treatment, no treatment
Liu <sup>166</sup>	2018	Drug Delivery	3.1	Pharmacology & Pharmacy	Not reported	0/2	9	2002-2015	Patients with neurodegenerative movement disorders	Riluzole	Placebo
Liu <sup>167</sup>	2018	Drug Design, Development and Therapy	2.9	Chemistry, Medicinal; Pharmacology & Pharmacy	Not reported	0/5	9	2010-2016	Patients undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI)	Atorvastatin	Placebo
Sun <sup>168</sup>	2017	Drug Design, Development and Therapy	2.9	Chemistry, Medicinal; Pharmacology & Pharmacy	Not reported	0/5	9	2009-2016	Adults (≥ 18 years) undergoing spinal anesthesia	Dexmedetomidine	Fentanyl
Paraschakis <sup>169</sup>	2017	East Asian Archives of Psychiatry	None	Not applicable	Not reported	0/2	4	2005-2010	Adults with traumatic brain injuries and depressive disorders	Antidepressants - 2 types	Placebo
D'Souza <sup>170</sup>	2018	Emergency Medicine Journal	2.0	Emergency Medicine	No funding	0/8	4	2001-2016	Patients taking acute antiemetic drugs	Diphenhydramine	Placebo
Mei <sup>171</sup>	2016	European Journal of Gynecological Oncology	0.6	Oncology; Obstetrics & Gynecology	Not reported	Not reported/4	4	2004-2013	Adult women with epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer who have achieved complete clinical remission after debulking surgery and first-line chemotherapy	CA125-targeted antibody – 2 types	Placebo
Verberkt <sup>172</sup>	2017	European Respiratory Journal	12.2	Respiratory System	Non-industry	3/9*	35	1982-2015	Patients with chronic breathlessness	Opioids - 8 types	Placebo
Sridharan <sup>173</sup>	2018	Expert Opinion on Pharmacotherapy	3.5	Pharmacology & Pharmacy	No funding	0/3	51	1980-2016	Critically ill patients receiving stress ulcer prophylaxis (SUP)	Antacids, proton pump inhibitors (PPI), histamine-2 receptor antagonists (H2RA), and sucralfate	Placebo - Network meta-analysis
Habibi <sup>174</sup>	2018	Expert Review of Clinical Pharmacology	2.8	Pharmacology & Pharmacy	No funding	0/4	5	1999-2012	Patients undergoing coronary artery bypass surgery	Lidocaine	Placebo
Li <sup>175</sup>	2018	Expert Review of Clinical Pharmacology	2.8	Pharmacology & Pharmacy	Non-industry	0/4	14	2002-2017	Patients with stable angina pectoris requiring elective percutaneous	Nicorandil	Placebo (saline, isosorbide dinitrate), no treatment

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5			Expert Review							intervention (PCI)		
6	Sangroongruang	2018	of Clinical	2.8	Pharmacology &	Non-	0/5	11	2010-2017	Patients diagnosed	Anti-vascular endothelial	Sham injection -
7	sri <sup>176</sup>		Pharmacology		Pharmacy	industry				with retinal vein	growth factor (VEGF)	Network meta-analysis
8										occlusion	drugs - 3 types	
9										Adult patients with		
10	Hickey <sup>177</sup>	2018	Foot and Ankle	1.5	Orthopedics	Not	0/7	7	1993-2015	foot or ankle trauma	Low molecular weight	Placebo, no treatment
11			Surgery		Oncology;	reported				treated with below	heparin - 5 types	
12	Zhao <sup>178</sup>	2018	Gastric Cancer	5.0	Gastroenterology &	Non-	0/9	16	2002-2017	immobilization	Targeted agents - 11 types,	Placebo - Network
13					Hepatology	industry				Patients with	targeted agents +	meta-analysis
14										advanced gastric	chemotherapy	
15	Khera <sup>179</sup>	2018	Gastroenterolog	20.8	Gastroenterology &	No	0/9	29	1998-2015	cancer	Orlistat, loracaserin,	Placebo - Network
16			y		Hepatology	funding				Obese and	naltrexone-bupropion,	meta-analysis
17										overweight adults	phentermine-topiramate,	
18										(18 years and over)	liraglutide	
19	Li <sup>180</sup>	2018	Gynecologic	4.5	Oncology;	Non-	0/6	7	2005-2016	Patients with low-	Methotrexate (MEX) based	Network meta-analysis
20			Oncology		Obstetrics &	industry				risk gestational	chemotherapy regimens,	
21	Zhuge <sup>181</sup>	2018	Helicobacter	4.1	Gynecology	Non-	0/6	18	1999-2016	trophoblastic	actinomycin-d (Act-D)	Other antibiotics - 7
22			Indian Journal		Gastroenterology &	industry				neoplasia (LRGTN)	based chemotherapy	types
23	Kim <sup>182</sup>	2017	of Cancer	0.7	Hepatology;	No	0/4	21	1993-2011	Patients with	regimens	Placebo
24					Microbiology	funding				helicobacter pylori		
25			Indian Journal		Oncology					infection	Furazolidone	
26	Garg <sup>183</sup>	2018	of Gastroenterolog	None	Not applicable	Not	0/4	6	2007-2016	Adults at risk of	Statins - 7 types	Placebo
27			y			reported				developing cancer		
28										Patients undergoing		
29	Rosanova <sup>184</sup>	2017	Infectious	1.9	Infectious Diseases	Not	0/5	7	2002-2011	endoscopic	Indomethacin	Placebo
30			Diseases			reported				retrograde		
31	Yu <sup>185</sup>	2018	Inflammopharm	3.3	Immunology;	Non-	0/6	3	2007-2016	cholangiopancreatog	Immunosuppressed	Other antifungal
32			acology		Toxicology	industry				raphy	haematology-	agents or placebo
33										Adults (17 years and	oncology patients	Non-steroidal anti-
34	Kakkos <sup>186</sup>	2018	International	1.2	Peripheral Vascular	Not	2/2	7	1982-2015	over) diagnosed	Voriconazole	inflammatory drugs
35			Angiology		Disease	reported				with acute gout	Prednisolone	(NSAIDs) - 2 types
36	Ou <sup>187</sup>	2018	International	3.1	Immunology;	No	Not	8	2014-2017	Patients with		
37			Immunopharma		Pharmacology &	funding	reported/5			chronic venous	Micronized purified	Placebo
38			cology		Pharmacy					disorders (CVD) or	flavonoid faction (Daflon)	
39										venous edema		
40	Yin <sup>188</sup>	2018	International	3.1	Immunology;	No	0/4	53	1984-2017	Adults with	Dupilumab	Placebo
41			Immunopharma		Pharmacology &	funding				moderate-to-severe		
42			cology		Pharmacy					atopic dermatitis	Broncho-Vaxom	Placebo, routine
43										Children diagnosed		therapies
44										with recurrent		
45										respiratory tract		
46										infections (RRTIs)		
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Zhu <sup>189</sup>	2018	International Journal of Clinical Oncology	2.6	Oncology	Non-industry	0/7	35	2005-2016	Cancer patients	Anti-EGFR monoclonal antibodies (EGFR-MoAbs)	Placebo, usual care
Liu <sup>190</sup>	2018	International Journal of Neuroscience	1.8	Neurosciences	Not reported	0/2	4	2007-2016	Patients with seizures	Lacosamide	Placebo
Coccolini <sup>191</sup>	2018	International Journal of Surgery	2.7	Surgery	No funding	0/12	15	1993-2014	Patients with advanced gastric and esophago-gastric cancer	Neoadjuvant chemotherapy (with surgery)	No neoadjuvant chemotherapy (only surgery)
Fan <sup>192</sup>	2018	International Journal of Surgery	2.7	Surgery	Non-industry	0/8	7	2005-2016	Patients with scheduled total knee arthroplasty	Dexamethasone	Placebo, no treatment ("nothing controlled multimodal analgesia method")
Li <sup>193</sup>	2018	International Journal of Surgery	2.7	Surgery	No funding	0/5	6	2008-2017	Patients with a diagnosis of symptomatic cholelithiasis and acute cholecystitis who prepared for laparoscopic cholecystectomy	Lidocaine	Placebo, saline
Li <sup>194</sup>	2018	International Journal of Surgery	2.7	Surgery	No funding	0/4	17	1998-2017	Patients undergoing retrograde cholangiopancreatography	Anaesthetic medications - 12 types	No drug - Network meta-analysis
Liu <sup>195</sup>	2018	International Journal of Surgery	2.7	Surgery	Non-industry	0/5	3 <sup>†</sup>	2005-2017	Patients undergoing total knee arthroplasty or total hip arthroplasty	Tranexamic acid	Aminocaproic acid
Ran <sup>196</sup>	2018	International Journal of Surgery	2.7	Surgery	No funding	0/5	5	2002-2016	Patients with symptomatic knee osteoarthritis	Hyaluronic acid	Methylprednisolone
Zhao <sup>197</sup>	2018	International Journal of Surgery	2.7	Surgery	No funding	0/3	4 <sup>†</sup>	2010-2017	Patients with hepatocellular carcinoma	Anthracyclines	Platinum
Zhu <sup>198</sup>	2018	International Journal of Surgery	2.7	Surgery	Non-industry	0/5	6	2004-2017	Adult patients prepared for laparoscopic cholecystectomy	Ketamine	Saline
Wagner <sup>199</sup>	2018	Journal of Affective Disorders	3.8	Clinical Neurology; Psychiatry	Non-industry	Not reported/6	119	1990- Unpublished	Adults with major depressive disorder	Second generation antidepressants - 16 types	Placebo - Network meta-analysis
Hickman <sup>200</sup>	2018	Journal of Assisted Reproduction and Genetics	2.8	Genetics & Heredity; Obstetrics & Gynecology;	Not reported	0/5	10	2007-2016	Women with lymphoma, ovarian cancer, or breast	Gonadotropin-releasing hormone agonists (GnRH <sub>a</sub> ) - 7 types	Standard treatment (chemotherapy only)

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Reproductive  
Biology  
cancer undergoing  
chemotherapy  
Programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1) inhibitors - 3 types  
Chemotherapy - 2 types  
Patients with non-small-cell lung carcinoma  
Patients with metastatic castration-resistant prostate cancer  
Targeted agents - 16 types  
Placebo - Network meta-analysis  
Cancer patients with moderate to severe pain  
Adults (18 years and over) undergoing any type of cardiac surgery  
Fentanyl  
Morphine  
Placebo, discontinuation of aspirin greater than 7 days before surgery  
Aspirin  
Patients undergoing isolated coronary artery bypass graft (CABG) surgery  
Statins - 3 types  
Antiandrogens, insulin sensitizers, estrogen-progestin oral contraceptives pills (OCPs), OCPs + antiandrogen, OCPs + insulin sensitizer, antiandrogen + insulin sensitizer  
No preoperative statin  
Women with hirsutism  
Placebo - Network meta-analysis  
Patients with type 2 diabetes  
Adults with moderate-to-severe chronic plaque-type psoriasis  
Patients with onset of atrial fibrillation (AF) within 48 h, who were hemodynamically stable and without evidence of acute coronary syndrome,  
Flecainide  
Placebo - Network meta-analysis  
Placebo - Network meta-analysis  
Placebo - Network meta-analysis  
Placebo, verapamil, and other active anti-dysrhythmics

		Journal of Cancer Research and Clinical Oncology	3.3	Oncology	Non-industry	0/4	8	2015-2017	Patients with non-small-cell lung carcinoma	Programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1) inhibitors - 3 types	Chemotherapy - 2 types
Luo <sup>201</sup>	2018	Journal of Cancer Research and Clinical Oncology	3.3	Oncology	Non-industry	0/5	26	2010-2017	Patients with metastatic castration-resistant prostate cancer	Targeted agents - 16 types	Placebo - Network meta-analysis
Wang <sup>202</sup>	2018	Journal of Cancer Research and Therapeutics	0.8	Oncology	No funding	0/4	35	1997-2011	Cancer patients with moderate to severe pain Adults (18 years and over) undergoing any type of cardiac surgery	Fentanyl	Morphine Placebo, discontinuation of aspirin greater than 7 days before surgery
Aboul-Hassan <sup>204</sup>	2017	Journal of Cardiac Surgery	1.2	Cardiac & Cardiovascular Systems; Surgery	No funding	0/8	12	1985-2016	Patients undergoing isolated coronary artery bypass graft (CABG) surgery	Aspirin	No preoperative statin
Wang <sup>205</sup>	2018	Journal of Cardiovascular Surgery	1.2	Cardiac & Cardiovascular Systems; Surgery; Peripheral Vascular Disease	Not reported	0/6	5	1999-2010	Women with hirsutism	Statins - 3 types Antiandrogens, insulin sensitizers, estrogen-progestin oral contraceptives pills (OCPs), OCPs + antiandrogen, OCPs + insulin sensitizer, antiandrogen + insulin sensitizer	Placebo - Network meta-analysis
Barrionuevo <sup>206</sup>	2018	Journal of Clinical Endocrinology and Metabolism	5.8	Endocrinology & Metabolism	Non-industry	0/8	32	1989-2016	Patients with type 2 diabetes Adults with moderate-to-severe chronic plaque-type psoriasis	Statin - 6 types	Placebo - Network meta-analysis
Cui <sup>207</sup>	2018	Journal of Clinical Pharmacy and Therapeutics	1.7	Pharmacology & Pharmacy	Not reported	0/6	23	1993-2014	Patients with onset of atrial fibrillation (AF) within 48 h, who were hemodynamically stable and without evidence of acute coronary syndrome,	Apremilast, biological therapies - 7 types	Placebo - Network meta-analysis
Sawyer <sup>208</sup>	2018	Journal of Dermatological Treatment	2.1	Dermatology	Industry	6/6 <sup>y</sup>	54	2001-2016	Patients with onset of atrial fibrillation (AF) within 48 h, who were hemodynamically stable and without evidence of acute coronary syndrome,	Flecainide	Placebo, verapamil, and other active anti-dysrhythmics
Markey <sup>209</sup>	2018	Journal of Emergency Medicine	1.2	Emergency Medicine	Not reported	Not reported/3	11	1989-2004			

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		Journal of Gastrointestinal and Liver Diseases	2.0	Gastroenterology & Hepatology	Not reported	0/15	10 <sup>w</sup>	2009-2016	congestive heart failure, or structural heart disease Adult patients (18 years and over) taking low-dose aspirin for a minimum of 2 weeks Patients with histologically confirmed solid cancer	Proton-pump inhibitors (PPIs) - 5 types	Histamine-2 receptor antagonists (H2RAs) - 2 types
Szabó <sup>210</sup>	2017										
		Journal of Immunology	3.3	Immunology	Non-industry	0/6	15	2011-2017		Immune checkpoint inhibitors (ICIs) - 5 types	Placebo or chemotherapy
Su <sup>211</sup>	2018										
		Journal of Interventional Cardiac Electrophysiology	1.5	Cardiac & Cardiovascular Systems	Non-industry	0/9	8	2006-2017	Patients with persistent atrial fibrillation	Antiarrhythmic drugs	Catheter ablation
Chen <sup>212</sup>	2018										
		Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	No funding	0/4	6	2008-2014	Patients undergoing knee arthroscopy	Midazolam	Placebo
Chen <sup>213</sup>	2017										
		Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	Not reported	0/5	3 <sup>x</sup>	2002-2017	Patients undergoing a primary total hip or knee arthroplasty	Aminocaproic acid	Placebo or no treatment
Li <sup>214</sup>	2018										
		Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	Not reported	0/4	3 <sup>y</sup>	2002-2017	Patients treated with spine surgery	Tranexamic acid	Control (not specified)
Luo <sup>215</sup>	2018										
		Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	No funding	0/4	4	1991-2015	Patients who underwent hip surgery Patients with a primary diagnosis of major depressive disorder (MDD)	Naproxen Vortioxetine, levomilnacipran, vilazodone	Placebo
Ma <sup>216</sup>	2018										
		Journal of Psychiatric Research	4.0	Psychiatry	Non-industry	0/8	22	2009-2015			Placebo
He <sup>217</sup>	2018										
		Journal of Stroke & Cerebrovascular Diseases	1.6	Neurosciences; Peripheral Vascular Disease	Non-industry	4/8	6	2003-2013	Asian patients with non-valvular atrial fibrillation (AF)	Warfarin, direct oral anticoagulants (DOACs) - 5 types	Network meta-analysis
Wang <sup>218</sup>	2018										
		Journal of the American Academy of Dermatology	6.9	Dermatology	No funding	0/6	15	2000-2016	People with scabies	Permethrin Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors - 2 types	Ivermectin
Dhana <sup>219</sup>	2018										
		Journal of the American Heart Association	4.5	Cardiac & Cardiovascular Systems	Not reported	3/12 <sup>z</sup>	35	2012-2017	Adults with hypercholesterolemia		Placebo, ezetimibe, standard therapy
Karatasakis <sup>220</sup>	2017										

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3			Journal of the									
4			European									
5			Academy of							Adult patients ( $\geq 18$ )		
6			Dermatology and							with moderate-to-severe plaque		
7	Kuo <sup>221</sup>	2018	Venereology	4.3	Dermatology	Non- industry	2/4	4	2012-2016	psoriasis	Tofacitinib	Placebo
8			Journal of									
9			Traditional									
10	Liu <sup>222</sup>	2016	Chinese	0.9	Integrative & Complementary Medicine	Non- industry	Not reported/6	16	2005-2015	Patients with	Methotrexate	Sinomenine
11			Medicine									
12					Biochemistry & Molecular Biology; Biotechnology & Applied Microbiology; Medicine, Research & Experimental							
13			Journal of							Adult patients		
14			Zhejiang							undergoing cardiac		
15	Zheng <sup>223</sup>	2017	University- SCIENCE B	1.8		Not reported	0/7	8	1990-2014	aortic cross-clamp	Amiodarone, lidocaine	Placebo
16										Patients with		
17										isoniazid-resistant, rifampicin- susceptible tuberculosis		Usual care (REZ = rifampicin, ethambutol, pyrazinamide)
18	Fregonese <sup>224</sup>	2018	Lancet Respiratory Medicine	21.5	Critical Care Medicine; Respiratory System	Non- industry	0/57	2	2010-2014		Fluoroquinolone, streptomycin	
19												
20			Neurological							Patients during early		
21	Bornstein <sup>225</sup>	2018	Sciences	2.3	Clinical Neurology; Neurosciences	Not reported	Not reported/10	9	2010- Unpublishe d	post-stroke period	Cerebrolysin	Placebo
22										Patients arranged for	Bevacizumab, bevacizumab + antimetabolite - 2 types	Placebo, antimetabolite - 2 types
23	Chen <sup>226</sup>	2018	Ophthalmic Research	1.8	Ophthalmology		0/4	3	2013-2015	primary trabeculectomy		
24										Patients undergoing		
25	Han <sup>227</sup>	2017	Pain Physician	2.6	Anesthesiology; Clinical Neurology	No funding	0/4	10	2004-2016	spinal surgery	Gabapentin	Placebo
26										Adult patients		
27	Peng <sup>228</sup>	2017	Pain Physician	2.6	Anesthesiology; Clinical Neurology	No funding	0/5	18	2004-2016	undergoing surgical procedures	Dexmedetomidine + opioids	Opioids
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29					Chemistry, Medicinal; Chemistry, Multidisciplinary; Pharmacology & Pharmacy							
30												
31										Patients with		Usual care (chemotherapy), usual care + placebo
32	Feng <sup>229</sup>	2016	Pharmazie	1.0		Not reported	0/7	2 <sup>aa</sup>	2011-2012	tuberculosis	V-5 immunitor	
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36										Patients with non- cystic fibrosis bronchiectasis		Placebo, symptomatic treatment only
37	Xu <sup>230</sup>	2016	Pharmazie PLOS Neglected Tropical Diseases	1.0		Not reported	Not reported/8	12	1999-2014		Antibiotics - 7 types	
38												
39										Patients infected with soil transmitted helminths		Albendazole, ivermectin
40	Palmeirim <sup>231</sup>	2018		4.4	Parasitology; Tropical Medicine	Non- industry	0/9	14 <sup>bb</sup>	1997-2015		Albendazole + ivermectin	
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									Adults with persistent depressive disorder (DSM-5), chronic major depression, recurrent major depression with incomplete interepisode recovery or dysthymia (DSM-IV), or any corresponding conditions	Antidepressants - 6 types, cognitive-behavioral analysis system of psychotherapy, combination of antidepressants and cognitive-behavioral analysis system of psychotherapy	Network meta-analysis
Furukawa <sup>232</sup>	2018	Psychotherapy and Psychosomatics	13.1	Psychiatry; Psychology	Non-industry	2/11	3	2000-2015	Adult patients with chronic kidney disease	Uric acid-lowering therapy - 2 types	Placebo, usual therapy, no treatment
Liu <sup>233</sup>	2018	Renal Failure	1.4	Urology & Nephrology	Not reported	0/6	12	2006-2015	Adults with a history of chronic obstructive pulmonary disease (COPD)	Tiotropium + olodaterol	Tiotropium or olodaterol as monotherapy, salmeterol + fluticasone
Miravittles <sup>234</sup>	2017	Respiratory Research	3.8	Respiratory System	Industry	3/4	10	2014-2016	Patients with intermittent or mild persistent asthma	Corticosteroids, fast-onset-acting $\beta$ 2-agonists	Corticosteroid + fast-onset-acting $\beta$ 2-agonist
Wang <sup>235</sup>	2017	Respiratory Research	3.8	Respiratory System	Non-industry	1/7	6	2006-2016	Adults (18 years and over) with moderate to severe psoriatic arthritis (PsA)	Tumor necrosis factor (antiTNF)- $\alpha$ inhibitors - 4 types	Placebo - Network meta-analysis
Kawalec <sup>236</sup>	2018	Rheumatology International	2.0	Rheumatology	No funding	0/4	8	2011-2016	Adult patients (18 years and over) treated for the secondary prevention of cardiovascular, peripheral vascular, and cerebrovascular disease	Proton pump inhibitors (PPI) + thienopyridines	Thienopyridines - 2 types
Malhotra <sup>237</sup>	2018	Stroke Surgical Laparoscopy Endoscopy & Percutaneous Techniques	6.2	Clinical Neurology; Peripheral Vascular Disease	Not reported	0/6	12	2009-2016	Adults (18 and over) undergoing gastrointestinal endoscopy	Midazolam	Propofol
Zhang <sup>238</sup>	2018	Thrombosis Research	2.8	Hematology; Peripheral Vascular Disease	No funding	3/7	6	2009-2014	Asian and non-Asian adults (18 years and older) with acute venous thromboembolism	Direct oral anticoagulants (DOACs) - 4 types	Vitamin K antagonists (VKAs), heparin
Yamashita <sup>239</sup>	2018	Vaccine	3.3	Immunology; Medicine, Research & Experimental	No funding	1/6	13	1999-2014	HIV-positive people	Influenza vaccine, Placebo	Network meta-analysis
Zhang <sup>240</sup>	2018										



**Multidisciplinary sciences (n = 10)**

Author	Year	Journal	Score	Field	Funding	Studies	Patients	Interventions	Outcomes	
Chen <sup>241</sup>	2018	Medical Science Monitor	1.9	Medicine, Research & Experimental	Non-industry	0/5	20 <sup>cc</sup>	2000-2016	Patients with essential hypertension Adult patients (over 18 years old) that underwent the extraction of any tooth Adults with osteoarthritis or rheumatoid arthritis of the knee or hip Pediatric surgical patients Adults (18 years and over) diagnosed with generalized anxiety disorder (GAD) Patients with hypertension and chronic kidney disease stage 3 to 5 and dialysis Adults (19 years and over) undergoing cardiac surgery Cancer patients	Anti-hypertensive drugs - 8 types Acupuncture Chlorhexidine Etoricoxib Magnesium Duloxetine Calcium channel blockers Dexmedetomidine Erythropoiesis-stimulating agents Digoxin mTOR-inhibitors - 2 types
Arteagoitia <sup>242</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/3	8	1989-2015	Placebo, standard treatment Placebo, other non-steroidal anti-inflammatory drugs (NSAIDs) - 2 included	
Feng <sup>243</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/4	9	2002-2009		
Kawakami <sup>244</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/5	6	2007-2017	Placebo, no treatment	
Li <sup>245</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/7	8	2007-2014	Placebo	
Lin <sup>246</sup>	2017	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/6	21	1992-2012	Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers	
Ling <sup>247</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	Not reported/6	9	2003-2017	Propofol, morphine, placebo	
Rohner <sup>248</sup>	2017	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	2/7	94	1993-2014	Usual care Placebo, no intervention, beta blockers, calcium antagonists, amiodarone	
Sethi <sup>249</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/6	28	1986-2017		
Wolf <sup>250</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Industry	1/9	13	2002-2016	Calcineurin-inhibitors	

<sup>a</sup>Only 3 studies reported that authors were employed by industry and therefore we included them as ties for the purposes of this table; <sup>b</sup>11/12 included RCTs had a drug arm; <sup>c</sup>33/38 included RCTs had a drug arm; <sup>d</sup>4/14 included RCTs had a drug arm; <sup>e</sup>One author reported pharmaceutical company employment; <sup>f</sup>9/11 included RCTs had a drug arm; <sup>g</sup>71/120 included studies were RCTs; <sup>h</sup>24/25 included studies were RCTs; <sup>i</sup>Meta-analysis funding sources reported as 'None, Other' we coded as no study funding; <sup>j</sup>10/27 included RCTs had a drug arm; <sup>k</sup>Flow chart indicates that 0 RCTs were included in the quantitative synthesis, but 2 RCTs were quantitatively synthesized and 13 were included; <sup>l</sup>Declarations of interest were provided for only 3 out of 5 meta-analysis authors; <sup>m</sup>24/31 included RCTs had a drug arm; <sup>n</sup>103/106 included RCTs had a drug arm; <sup>o</sup>3/5 included RCTs had a drug arm; <sup>p</sup>34/60 included RCTs had a drug arm; <sup>q</sup>110/123 included RCTs had an eligible drug arm; <sup>r</sup>Salary was reported under 'funding' but they did not specify whether there was any funding for the study itself; <sup>s</sup>ICMJE forms only provided for 5/9 authors; <sup>t</sup>3/4 included studies were RCTs; <sup>u</sup>4/11 included studies were RCTs; <sup>v</sup>Four authors reported financial ties with a pharmaceutical company and employment by Symmetron, a company that provides health economic research services to pharmaceutical companies, and two authors reported employment by a pharmaceutical company; <sup>w</sup>10/12 included studies were RCTs; <sup>x</sup>3/7 included studies were RCTs; <sup>y</sup>3/4 included studies were RCTs; <sup>z</sup>Of the 3 authors that reported financial ties, one also reported industry employment; <sup>aa</sup>2/4 included studies were RCTs; <sup>bb</sup>14/30 included studies were RCTs; <sup>cc</sup>20/30 included studies were RCTs with a drug arm

eTable2. – Detailed reporting of study funding sources (F), author-industry financial ties (T), and author-industry employment (E) form included RCTs

First Author	Year	Journal	Funding Sources of Included Trials Reported in Meta-analysis?	Author-Industry Financial Ties of Included Trials Reported in Meta-analysis?	Author-Industry Employment of Included Trials Reported in Meta-analysis?	Location Reported					Abstract	Lay summary	Online appendix
						Risk of Bias Text	Risk of Bias Figure or Table	Main Text, Other than Risk of Bias	Other in Main Document (Characteristics of Included Studies Table, other table, footnote)				
<b>Cochrane Reviews (n = 107)</b>													
Abdel-Rahman <sup>1</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F	F		F		F	F	
Adams <sup>2</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F		F	F				
Agabio <sup>3</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No			F, T	F, T			F	
Al-Shahi Salman <sup>4</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	No			F	F				
Alabed <sup>5</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	Partial				F, E				
Allegretti <sup>6</sup>	2017	Cochrane Database of Systematic Reviews	Full	No	No	F	F				F	F	
Arechabala <sup>7</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	Partial	F	F, E	F, T	F, T, E			F	
Baandrup <sup>8</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	Partial	F	F	F	F, T, E			F	
Bala <sup>9</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F			F				
Barbato <sup>10</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No								
Bergman <sup>11</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No				F, T				
Bighelli <sup>12</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	Partial	F	F, T, E	F	F, T, E	F	F	F	
Birks <sup>13</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No			F	F, T	F			
Boyapati <sup>14</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No								
Brown <sup>15</sup>	2018	Cochrane Database of Systematic Reviews	Partial	Partial	No	F	F	F	F, T	F	F	F	
Bruins Slot <sup>16</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F				
Bryan <sup>17</sup>	2017	Cochrane Database of Systematic Reviews	Partial	No	No				F				

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3			Cochrane Database of							
4	Bryant-Smith <sup>18</sup>	2018	Systematic Reviews	Full	No	No				F
5	Burry <sup>19</sup>	2018	Cochrane Database of	Full	No	No	F	F		F
6			Systematic Reviews							
7	Campschroer <sup>20</sup>	2018	Cochrane Database of	Full	Full	No				F, T
8			Systematic Reviews							
9	Candy <sup>21</sup>	2018	Cochrane Database of	Full	No	No		F		F
10			Systematic Reviews							
11	Chiew <sup>22</sup>	2018	Cochrane Database of	No	No	No				
12			Systematic Reviews							
13	Das <sup>23</sup>	2018	Cochrane Database of	Full	No	No		F		F
14			Systematic Reviews							
15	Demicheli <sup>24</sup>	2018	Cochrane Database of	Full <sup>a</sup>	Partial	Partial				F, T, E
16			Systematic Reviews							
17	Demicheli <sup>25</sup>	2018	Cochrane Database of	No	No	No				
18			Systematic Reviews							
19	Di Nisio <sup>26</sup>	2018	Cochrane Database of	Partial	Partial	No				F, T
20			Systematic Reviews							
21	El-Sayeh <sup>27</sup>	2018	Cochrane Database of	Full	No	No	F			F
22			Systematic Reviews							
23	Engelen <sup>28</sup>	2018	Cochrane Database of	No	No	No				
24			Systematic Reviews							
25	Eshun-Wilson <sup>29</sup>	2018	Cochrane Database of	Full	Full	No				F, T
26			Systematic Reviews							
27	Essali <sup>30</sup>	2018	Cochrane Database of	Full	No	No				F
28			Systematic Reviews							
29	Everitt <sup>31</sup>	2018	Cochrane Database of	Partial	Partial	No	F, T	F, T	F	F, T
30			Systematic Reviews							
31	Fanshawe <sup>32</sup>	2017	Cochrane Database of	No	No	No				
32			Systematic Reviews							
33	Franik <sup>33</sup>	2018	Cochrane Database of	Full	Partial	No				F, T
34			Systematic Reviews							
35	González <sup>34</sup>	2018	Cochrane Database of	Full	No	No				F
36			Systematic Reviews							
37	Grabosch <sup>35</sup>	2018	Cochrane Database of	No	No	No				
38			Systematic Reviews							
39	Graves <sup>36</sup>	2018	Cochrane Database of	Partial <sup>b</sup>	No	No				F
40			Systematic Reviews							
41	Haas <sup>37</sup>	2018	Cochrane Database of	Full	Full	No		F, T		F, T
42			Systematic Reviews							
43	Hakoum <sup>38</sup>	2018	Cochrane Database of	Full	Full	No				F, T
44			Systematic Reviews							
45	Heras-Mosteiro <sup>39</sup>	2017	Cochrane Database of	Partial <sup>c</sup>	Partial <sup>d</sup>	Partial				F, T, E
46			Systematic Reviews							
47	Janmaat <sup>40</sup>	2017	Cochrane Database of	No	No	No				
48			Systematic Reviews							
49	Jefferson <sup>41</sup>	2018	Cochrane Database of	Full	No	No				F
50			Systematic Reviews							
51	Jung <sup>42</sup>	2017	Cochrane Database of	Full	Full	Partial		F, T		F, T, E
52			Systematic Reviews							

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Kaempfen <sup>43</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No					
Kahale <sup>44</sup>	2017	Cochrane Database of Systematic Reviews	Full	Full	Partial <sup>e</sup>				F, T, E	
Kahale <sup>45</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No				F, T	
Kahale <sup>46</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No				F, T	
Kapur <sup>47</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F	
Kelly <sup>48</sup>	2018	Cochrane Database of Systematic Reviews	Partial <sup>f</sup>	Partial	No		F		F, T	
Knightly <sup>49</sup>	2017	Cochrane Database of Systematic Reviews	Full	No	No				F	
Kopsaftis <sup>50</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No					
Lawrie <sup>51</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	Partial				F, T, E	
Leathersich <sup>52</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No	F, T	F, T	F, T	F, T	
Lethaby <sup>53</sup>	2017	Cochrane Database of Systematic Reviews	Full	No	No			F	F	F
López-Briz <sup>54</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F	
Marchant <sup>55</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	No				F	
Matar <sup>56</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No		F			
Matar <sup>57</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No				F, T	
McNicol <sup>58</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F	
McTague <sup>59</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No					
Mhaskar <sup>60</sup>	2017	Cochrane Database of Systematic Reviews	Full	Full	Partial				F, T, E	
Milligan <sup>61</sup>	2018	Cochrane Database of Systematic Reviews	Partial <sup>g</sup>	No	No	F	F			
Monk <sup>62</sup>	2017	Cochrane Database of Systematic Reviews	Full	Full	No			F, T	F, T	
Montero <sup>63</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	No		F			
Mücke <sup>64</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	Partial			F, T	F, T, E	
Narula <sup>65</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No					
Nevitt <sup>66</sup>	2017	Cochrane Database of Systematic Reviews	Partial	No	No			F	F	
Nevitt <sup>67</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F	



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3			Cochrane Database of									
4	Sturman <sup>93</sup>	2017	Systematic Reviews	Full	Full	No	F, T	F, T	F, T			
5	Tammenmaa-		Cochrane Database of									
6	Aho <sup>94</sup>	2018	Systematic Reviews	Partial	No	No				F		
7	Temmingh <sup>95</sup>	2018	Cochrane Database of									
8			Systematic Reviews	Full	Partial	Partial	F, T	F, T, E	F, T, E	F, T		
9	Tenforde <sup>96</sup>	2018	Cochrane Database of									
10			Systematic Reviews	Full	Full	No	F, T	F, T		F, T		
11	Toews <sup>97</sup>	2018	Cochrane Database of						F, E	F	F, T	
12	Venekamp <sup>98</sup>	2018	Systematic Reviews	Full	Full	No			F		F, T	
13	Vermeij <sup>99</sup>	2018	Cochrane Database of									
14			Systematic Reviews	No	No	No						
15	Vietto <sup>100</sup>	2018	Cochrane Database of							F	F	
16			Systematic Reviews	Full	No	No						
17	Wall <sup>101</sup>	2018	Cochrane Database of				F, T	F	F	F		
18	Weibel <sup>102</sup>	2018	Systematic Reviews	Full	No	No			F	F		
19			Cochrane Database of									
20	Wright <sup>103</sup>	2018	Systematic Reviews	Partial	Partial	No	F	F, T				
21	Xiao <sup>104</sup>	2018	Cochrane Database of							F		
22			Systematic Reviews	Full	No	No						
23	Zhang <sup>105</sup>	2017	Cochrane Database of				F	F	F	F	F	
24			Systematic Reviews	Full	No	No						
25	Zhou <sup>106</sup>	2017	Cochrane Database of						F	F, T	F	
26			Systematic Reviews	Partial <sup>l</sup>	No	No		F				
27	Zonneveld <sup>107</sup>	2018	Systematic Reviews	Partial <sup>l</sup>	No	No		F				
28	<b>General Medicine (n = 33)</b>											
29	López-López <sup>108</sup>	2017	BMJ	Full	No	No			F		F	
30	Wang <sup>109</sup>	2018	BMJ Open	No	No	No						
31	Cipriani <sup>110</sup>	2018	Lancet	Full <sup>k</sup>	No	No			F		F	
32	Chen <sup>111</sup>	2018	Medicine	No	No	No						
33	Ding <sup>112</sup>	2018	Medicine	No	No	No						
34	Guo <sup>113</sup>	2018	Medicine	No	No	No						
35	Han <sup>114</sup>	2018	Medicine	No	No	No						
36	Hu <sup>115</sup>	2018	Medicine	No	No	No						
37	Huang <sup>116</sup>	2018	Medicine	Full	Partial	No	F, T					
38	Jiang <sup>117</sup>	2018	Medicine	No	No	No						
39	Jiang <sup>118</sup>	2018	Medicine	No	No	No						
40	Khan <sup>119</sup>	2018	Medicine	No	No	No						
41	Liang <sup>120</sup>	2017	Medicine	No	No	No						
42	Liu <sup>121</sup>	2018	Medicine	Partial <sup>l</sup>	No	No			F			
43	Lor <sup>122</sup>	2017	Medicine	No	No	No						
44	Wang <sup>123</sup>	2017	Medicine	No	No	No						
45	Wang <sup>124</sup>	2018	Medicine	No	No	No						
46	Wang <sup>125</sup>	2018	Medicine	No	No	No						
47	Wei <sup>126</sup>	2017	Medicine	No	No	No						

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3	Woo <sup>127</sup>	2018	Medicine	No	No	No		
4	Xia <sup>128</sup>	2018	Medicine	No	No	No		
5	Yang <sup>129</sup>	2017	Medicine	No	No	No		
6	Ye <sup>130</sup>	2017	Medicine	No	No	No		
7	Yu <sup>131</sup>	2018	Medicine	No	No	No		
8	Yuan <sup>132</sup>	2018	Medicine	No	No	No		
9	Zhang <sup>133</sup>	2018	Medicine	No	No	No		
10	Zhang <sup>134</sup>	2018	Medicine	No	No	No		
11	Zhao <sup>135</sup>	2018	Medicine	No	No	No		
12	Zhao <sup>136</sup>	2018	Medicine	No	No	No		
13	Zhou <sup>137</sup>	2018	Medicine	No	No	No		
14	Zhu <sup>138</sup>	2018	Medicine	No	No	No		
15	Zhou <sup>139</sup>	2018	Postgraduate Medicine Revista da Associação Médica Brasileira	No	No	No		
16	Zhang <sup>140</sup>	2018	Full	Full <sup>m</sup>	No		F, T	
17	<b>Specialty medicine (n = 100)</b>							
18	Li <sup>141</sup>	2018	Acta Ophthalmologica American Heart Journal	Full <sup>n</sup>	No	No	F	F
19	Tarantini <sup>142</sup>	2018	American Journal of Cardiovascular Drugs	No	No	No		
20	Wang <sup>143</sup>	2018	Anaesthesia and Intensive Care	No	No	No		
21	Aman <sup>144</sup>	2018	Autoimmunity Reviews	No	No	No		
22	Li <sup>145</sup>	2018	Biomed Research International	No	No	No		
23	Wang <sup>146</sup>	2018	BMC Cancer	No	No	No		
24	Veetil <sup>147</sup>	2017	BMC Cardiovascular Disorders	Full	No	No		F
25	Bredemeier <sup>148</sup>	2018	BMC Gastroenterology	No	No	No		
26	Lyu <sup>149</sup>	2018	BMC Infectious Diseases	No	No	No		
27	Xing <sup>150</sup>	2017	BMC Musculoskeletal Disorders	No	No	No		
28	Kuo <sup>151</sup>	2018	BMC Neurology	No	No	No		
29	Beez <sup>152</sup>	2017	BMC Ophthalmology	No	No	No		
30	Zeng <sup>153</sup>	2017	BMC Pharmacology & Toxicology	No	No	No		
31	Bundhun <sup>154</sup>	2017	BMC Psychiatry	No	No	No		
32	Zhang <sup>155</sup>	2017	BMC Pulmonary Medicine	No	No	No		
33	Zhang <sup>156</sup>	2017	BMC Pulmonary Medicine	Full	No	No		
34	Zhang <sup>157</sup>	2017	Breast Cancer	No	No	No		
35	Ramos-Esquivel <sup>158</sup>	2018	British Journal of Sports Medicine	Partial <sup>o</sup>	No	No	F	F
36	Zeng <sup>159</sup>	2018						
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3			Cellular Physiology					
4	Shui <sup>160</sup>	2018	and Biochemistry	No	No	No		
5	Rodrigo <sup>161</sup>	2018	Clinical Microbiology	Partial	No	No		F
6			and Infection					
7	Wang <sup>162</sup>	2018	Clinical	No	No	No		
8			Rheumatology					
9			Critical Reviews in					
10	Hong <sup>163</sup>	2018	Oncology /	No	No	No		
11	de Carvalho <sup>164</sup>	2018	Hematology	No	No	No		
12			Diabetes Care	No	No	No		
13	Jaafar <sup>165</sup>	2018	Digestive Diseases and	No	No	No		
14	Liu <sup>166</sup>	2018	Sciences	No	No	No		
15			Drug Delivery	No	No	No		
16			Drug Design,					
17	Liu <sup>167</sup>	2018	Development and	No	No	No		
18			Therapy					
19	Sun <sup>168</sup>	2017	Drug Design,	No	No	No		
20			Development and					
21	Paraschakis <sup>169</sup>	2017	Therapy	No	No	No		
22			East Asian Archives of					
23	D'Souza <sup>170</sup>	2018	Psychiatry	No	No	No		
24			Emergency Medicine					
25			Journal	No	No	No		
26			European Journal of					
27	Mei <sup>171</sup>	2016	Gynecological	No	No	No		
28			Oncology					
29	Verberkt <sup>172</sup>	2017	European Respiratory	No	No	No		
30			Journal					
31	Sridharan <sup>173</sup>	2018	Expert Opinion on	No	No	No		
32			Pharmacotherapy					
33	Habibi <sup>174</sup>	2018	Expert Review of	No	No	No		
34			Clinical Pharmacology					
35	Lj <sup>175</sup>	2018	Expert Review of	No	No	No		
36	Sangroongruangsr	2018	Clinical Pharmacology	No	No	No		
37	i <sup>176</sup>		Expert Review of	Full	No	No	F	
38			Clinical Pharmacology					
39	Hickey <sup>177</sup>	2018	Foot and Ankle	No	No	No		
40	Zhao <sup>178</sup>	2018	Surgery	No	No	No		
41	Khera <sup>179</sup>	2018	Gastric Cancer	Partial <sup>p</sup>	No	No	F	F
42			Gastroenterology					
43			Gynecologic	No	No	No		
44	Lj <sup>180</sup>	2018	Oncology	No	No	No		
45	Zhuge <sup>181</sup>	2018	Helicobacter	No	No	No		
46			Indian Journal of					
47	Kim <sup>182</sup>	2017	Cancer	No	No	No		
			Indian Journal of					
	Garg <sup>183</sup>	2018	Gastroenterology	No	No	No		
	Rosanova <sup>184</sup>	2017	Infectious Diseases	No	No	No		
			Inflammopharmacolog					
	Yu <sup>185</sup>	2018	y	No	No	No		



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3			International					
4	Kakkos <sup>186</sup>	2018	Angiology	No	No	No		
5	Ou <sup>187</sup>	2018	International	Full	No	No	F	
6			Immunopharmacology					
7	Yin <sup>188</sup>	2018	International	No	No	No		
8			Immunopharmacology					
9	Zhu <sup>189</sup>	2018	International Journal	No	No	No		
10			of Clinical Oncology					
11	Liu <sup>190</sup>	2018	International Journal	No	No	No		
12			of Neuroscience					
13	Coccolini <sup>191</sup>	2018	International Journal	No	No	No		
14			of Surgery					
15	Fan <sup>192</sup>	2018	International Journal	No	No	No		
16			of Surgery					
17	Li <sup>193</sup>	2018	International Journal	No	No	No		
18			of Surgery					
19	Li <sup>194</sup>	2018	International Journal	No	No	No		
20			of Surgery					
21	Liu <sup>195</sup>	2018	International Journal	No	No	No		
22			of Surgery					
23	Ran <sup>196</sup>	2018	International Journal	No <sup>†</sup>	No	No		
24			of Surgery					
25	Zhao <sup>197</sup>	2018	International Journal	No	No	No		
26			of Surgery					
27	Zhu <sup>198</sup>	2018	International Journal	No	No	No		
28			Journal of Affective					
29	Wagner <sup>199</sup>	2018	Disorders	Partial	No	No	F	
30			Journal of Assisted					
31	Hickman <sup>200</sup>	2018	Reproduction and	No	No	No		
32			Genetics					
33	Luo <sup>201</sup>	2018	Journal of Cancer	No	No	No		
34			Research and Clinical					
35			Oncology					
36	Wang <sup>202</sup>	2018	Journal of Cancer	Partial <sup>†</sup>	No	No	F	F
37			Research and					
38	Wang <sup>203</sup>	2018	Therapeutics	No	No	No		
39			Journal of Cardiac					
40	Aboul-Hassan <sup>204</sup>	2017	Surgery	No	No	No		
41			Journal of					
42			Cardiovascular					
43	Wang <sup>205</sup>	2018	Surgery	No	No	No		
44			Journal of Clinical					
45			Endocrinology and					F
46	Barrionuevo <sup>206</sup>	2018	Metabolism	Full	No	No	F	
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Cui <sup>207</sup>	2018	Journal of Clinical Pharmacy and Therapeutics	Full <sup>s</sup>	No	No	F
Sawyer <sup>208</sup>	2018	Journal of Dermatological Treatment	No	No	No	
Markey <sup>209</sup>	2018	Journal of Emergency Medicine	No	No	No	
Szabó <sup>210</sup>	2017	Journal of Gastrointestinal and Liver Diseases	No	No	No	
Su <sup>211</sup>	2018	Journal of Immunology Research	No	No	No	
Chen <sup>212</sup>	2018	Journal of Interventional Cardiac Electrophysiology	No	No	No	
Chen <sup>213</sup>	2017	Journal of Orthopaedic Surgery and Research	No	No	No	
Li <sup>214</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
Luo <sup>215</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
Ma <sup>216</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
He <sup>217</sup>	2018	Journal of Psychiatric Research	Full	No	No	F
Wang <sup>218</sup>	2018	Journal of Stroke & Cerebrovascular Diseases	No	No	No	
Dhana <sup>219</sup>	2018	Journal of the American Academy of Dermatology	No	No	No	
Karatasakis <sup>220</sup>	2017	Journal of the American Heart Association	No	No	No	
Kuo <sup>221</sup>	2018	Journal of the European Academy of Dermatology and Venereology	Full	No	No	
Liu <sup>222</sup>	2016	Journal of Traditional Chinese Medicine	No	No	No	
Zheng <sup>223</sup>	2017	Journal of Zhejiang University-SCIENCE B	No	No	No	
Fregonese <sup>224</sup>	2018	Lancet Respiratory Medicine	No	No	No	
Bornstein <sup>225</sup>	2018	Neurological Sciences	No	No	No	
Chen <sup>226</sup>	2018	Ophthalmic Research	No	No	No	
Han <sup>227</sup>	2017	Pain Physician	No	No	No	
Peng <sup>228</sup>	2017	Pain Physician	No	No	No	

3	Feng <sup>229</sup>	2016	Pharmazie	No	No	No	
4	Xu <sup>230</sup>	2016	Pharmazie	No	No	No	
5	Palmeirim <sup>231</sup>	2018	PLOS Neglected Tropical Diseases	No	No	No	
6			Psychotherapy and				
7	Furukawa <sup>232</sup>	2018	Psychosomatics	No	No	No	
8	Liu <sup>233</sup>	2018	Renal Failure	No	No	No	
9	Miravittles <sup>234</sup>	2017	Respiratory Research	Full	No	No	F
10	Wang <sup>235</sup>	2017	Respiratory Research	No	No	No	
11			Rheumatology				
12	Kawalec <sup>236</sup>	2018	International	No	No	No	
13	Malhotra <sup>237</sup>	2018	Stroke	No	No	No	
14			Surgical Laparoscopy				
15			Endoscopy & Percutaneous				
16	Zhang <sup>238</sup>	2018	Techniques	No	No	No	
17	Yamashita <sup>239</sup>	2018	Thrombosis Research	No	No	Partial	E
18	Zhang <sup>240</sup>	2018	Vaccine	No	No	No	
19	<b>Other (n = 10)</b>						
20			Medical Science				
21	Chen <sup>241</sup>	2018	Monitor	No	No	No	
22	Arteagoitia <sup>242</sup>	2018	PLOS ONE	No	No	No	
23	Feng <sup>243</sup>	2018	PLOS ONE	No	No	No	
24	Kawakami <sup>244</sup>	2018	PLOS ONE	No	No	No	
25	Lj <sup>245</sup>	2018	PLOS ONE	No	No	No	
26	Lin <sup>246</sup>	2017	PLOS ONE	No	No	No	
27	Ling <sup>247</sup>	2018	PLOS ONE	No	No	No	
28	Rohner <sup>248</sup>	2017	PLOS ONE	No	No	No	
29	Sethi <sup>249</sup>	2018	PLOS ONE	Partial	No	No	F
30	Wolf <sup>250</sup>	2018	PLOS ONE	No	No	No	

<sup>a</sup>Funding sources categorized as government funded, industry funded, or mixed for most trials. Specific details about funding were reported for 2 trials and details on author ties and employment were reported for a single trial; <sup>b</sup>Authors reported extracting funding sources from included RCTs but funding sources are only reported for a single study; <sup>c</sup>Reported funding sources for all included studies except for one; <sup>d</sup>Reported author financial ties for all included studies except for 2; <sup>e</sup>Non-industry author employment reported for some included RCTs; <sup>f</sup>Funding sources and author ties reported for all included RCTs except one that was a conference abstract; <sup>g</sup>Funding sources only reported for a single RCT; <sup>h</sup>Authors reported whether or not included RCTs had declared COI (yes, no) and, if yes, indicated the page of the original study the declaration could be found on. This was coded as partially reporting because the nature of these COI was not reported within the meta-analysis publication itself and it was unclear whether these were financial ties and whether they were with industry; <sup>i</sup>Non-industry author financial ties reported for some included RCTs; <sup>j</sup>A single RCT was reported as 'industry sponsored' with no specifics about the sponsor; <sup>k</sup>Authors coded studies as sponsored by industry or not, and any of author industry affiliation, industry funding, or data obtained from pharmaceutical company qualified an RCT as 'sponsored'; <sup>l</sup>Authors report that 'some trials had a high risk of reporting bias because they were sponsored by pharmaceutical companies' but do not specify which or even how many trials; <sup>m</sup>Authors reported that all included RCTs had authors with financial ties to industry but provided no further information; <sup>n</sup>Reported whether each included RCT was industry funded (yes or no) but provided no further information; <sup>o</sup>For some analyses the authors reported how many included RCTs were non-commercially funded and present results including only non-commercially funded trials, but do not provide further information on which trials were commercially funded; <sup>p</sup>Authors state 14 trials were industry-sponsored and reference figure 1 in the supplementary material where 14 studies were marked as high risk for other bias, but it is not explicitly specified what was considered as 'other bias'; <sup>q</sup>Authors considered RCT funding sources within 'other bias'. In their risk of bias assessment but did not report any specific information; <sup>r</sup>Authors report that most studies were funded by the pharmaceutical industry and refer readers to figure 2 (risk of bias figure), but the figure does not give any information about which RCTs; <sup>s</sup>Included RCTs were coded as having company funding (Yes/No).

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# PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	N/A
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3,4
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6,7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eMethods1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-12
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3, 10,11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	10,11



# PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	11
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12, 13, 26, 27 (Table 1)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	28 (Table 2)
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-17
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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# BMJ Open

## Reporting of Drug Trial Funding Sources and Author Financial Conflicts of Interest in Cochrane and non-Cochrane Meta-analyses: A Cross-sectional Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-035633.R1
Article Type:	Original research
Date Submitted by the Author:	07-Feb-2020
Complete List of Authors:	Turner, Kimberly; Jewish General Hospital and McGill University Carboni-Jiménez, Andrea; McGill University Benea, Carla; Jewish General Hospital Elder, Katharine; Jewish General Hospital Levis, Brooke; McGill University, Epidemiology, Biostatistics and Occupational Health Boruff, Jill; McGill University, Schulich Library of Physical Sciences, Life Sciences, and Engineering Roseman, Michelle; McGill University Bero, Lisa; University of Sydney, Charles Perkins Centre / Pharmacy Lexchin, Joel; York University, School of Health Policy and Management Turner, Erick; Portland VA Medical Center, ; Oregon Health & Science University, Psychiatry Benedetti, Andrea; McGill University Thombs, Brett; Jewish General Hospital and McGill University
<b>Primary Subject Heading</b>:	Research methods
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, STATISTICS & RESEARCH METHODS, MEDICAL ETHICS

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3 **1 Reporting of Drug Trial Funding Sources and Author Financial Conflicts of Interest in**  
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5 **2 Cochrane and non-Cochrane Meta-analyses: A Cross-sectional Study**  
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10 4 Kimberly A Turner, Andrea Carboni-Jiménez, Carla Benea, Katharine Elder, Brooke Levis,  
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13 5 Jill Boruff, Michelle Roseman, Lisa A Bero, Joel Lexchin, Erick H Turner, Andrea Benedetti,  
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52 44  
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54 45 **Word count:** 4,277  
55

1  
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3 46 **ABSTRACT**  
4

5 47 **Objective:** To (1) investigate the extent to which recently published meta-analyses report trial  
6  
7 48 funding, author-industry financial ties, and author-industry employment from included RCTs,  
8  
9 49 comparing Cochrane and non-Cochrane meta-analyses; (2) examine characteristics of meta-  
10  
11 50 analyses independently associated with reporting funding sources of included RCTs; and (3)  
12  
13 51 compare reporting among recently published Cochrane meta-analyses to Cochrane reviews  
14  
15 52 published in 2010.

16  
17 53 **Design:** Review of consecutive sample of recently published meta-analyses.  
18

19  
20 54 **Data sources:** MEDLINE database via PubMed searched on October 19, 2018.  
21

22  
23 55 **Eligibility criteria for selecting articles:** We selected the 250 most recent meta-analyses listed  
24  
25 56 in PubMed that included a documented search of at least one database, statistically combined  
26  
27 57 results from  $\geq 2$  RCTs, and evaluated the effects of a drug or class of drugs.  
28

29  
30 58 **Results:** 90 of 107 (84%) Cochrane meta-analyses reported funding sources for some or all  
31  
32 59 included trials compared with 21 of 143 (15%) non-Cochrane meta-analyses, a difference of 69%  
33  
34 60 (95% confidence interval [CI], 59% to 77%). Percent reporting was also higher for Cochrane  
35  
36 61 meta-analyses compared with non-Cochrane meta-analyses for trial author-industry financial ties  
37  
38 62 (44% versus 1%; 95% CI for difference, 33% to 52%) and employment (17% versus 1%; 95%  
39  
40 63 CI for difference, 9% to 24%). In multivariable analysis, compared with Cochrane meta-  
41  
42 64 analyses, the odds ratio for reporting trial funding was  $\leq 0.11$  for all other journal category and  
43  
44 65 impact factor combinations. Compared with Cochrane reviews from 2010, reporting of funding  
45  
46 66 sources of included RCTs among recently published Cochrane meta-analyses improved by 54%  
47  
48 67 (95% CI, 42% to 63%), and reporting of trial author-industry financial ties and employment  
49  
50 68 improved by 37% (95% CI, 26% to 47%) and 10% (95% CI, 2% to 19%).  
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69 **Conclusions:** Reporting of trial funding sources, trial author-industry financial ties, and trial  
70 author-industry employment in Cochrane meta-analyses has improved since 2010 and is higher  
71 than in non-Cochrane meta-analyses.

For peer review only

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2  
3 72 **Strengths and limitations of this study**  
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- 5 73       • The meta-analyses selected for inclusion in our study was a consecutive sample of  
6  
7  
8 74       meta-analyses of drug interventions published in 2016-2018.  
9  
10 75       • We compared reporting of funding and financial conflicts of interest among trials  
11  
12 76       included in recent Cochrane and non-Cochrane meta-analyses.  
13  
14  
15 77       • We compared reporting of funding and financial conflicts of interest among trials  
16  
17 78       included in recent Cochrane meta-analyses with Cochrane systematic reviews  
18  
19 79       from 2010.  
20  
21  
22 80       • We were unable to examine whether meta-analyses published in different types of  
23  
24 81       journals or journals with different impact factors are more or less likely to report  
25  
26 82       on financial conflicts of interest from included trials because most meta-analyses  
27  
28 83       of drug trials are published as Cochrane reviews or in relatively low-impact  
29  
30 84       specialty medicine journals.  
31  
32  
33 85       • Our study examined only disclosed financial conflicts of interest and did not  
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35 86       attempt to identify non-disclosed conflicts.  
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## 87 INTRODUCTION

88 Financial conflicts of interest (FCOIs) can introduce bias in drug trials by influencing  
89 how a trial is designed, inclusion and exclusion criteria, choice of drug dosages and comparators,  
90 selection of trial outcomes, how analyses are conducted, interpretation of findings, which  
91 outcomes are reported, and whether trial results are published.<sup>1-10</sup> Drug trials funded by industry  
92 are approximately 30% more likely to report favourable efficacy findings than non-industry  
93 trials,<sup>8</sup> and drug trials with principal investigators with FCOIs have higher odds of reporting  
94 favourable outcomes than those led by principal investigators without FCOIs, even after  
95 controlling for trial funding sources.<sup>7</sup>

96 Previous studies that have examined meta-analyses of drug trials published in high-  
97 impact journals and Cochrane systematic reviews of drug trials have found that funding sources  
98 and author FCOIs of included randomized controlled trials (RCTs) were rarely reported.<sup>11, 12</sup> A  
99 2011 study found that only 2 of a sample of 29 (7%) meta-analyses on the effects of drug  
100 interventions published in high-impact journals in 2009 reported the funding sources of included  
101 drug trials and that none reported trial author-industry financial ties or author-industry  
102 employment.<sup>11</sup> A second study, published in 2012, examined Cochrane systematic reviews of  
103 drug trials and found that only 46 of 151 (30%) eligible reviews published in 2010 reported  
104 information on the funding source of some or all included trials, 11 (7%) provided any  
105 information on author-industry financial ties, and 10 (7%) provided any information on author-  
106 industry employment from included trials.<sup>12</sup>

107 In 2012, the Cochrane Collaboration began to require that Cochrane reviews report trial  
108 funding sources and FCOIs of the primary researchers of all included trials in the characteristics  
109 of included studies table (Methodological Expectations of Cochrane Intervention Reviews

1  
2  
3 110 (MECIR), standards R69 and R70).<sup>13, 14</sup> The Preferred Reporting Items for Systematic Reviews  
4  
5 111 and Meta-analyses (PRISMA) statement, however, has not been updated since its publication in  
6  
7 112 2009<sup>15, 16</sup> and does not address the reporting of trial funding or author FCOIs of trials included in  
8  
9 113 systematic reviews and meta-analyses.

10  
11  
12 114 We do not know of any studies that have compared reporting among Cochrane meta-  
13  
14 115 analyses with meta-analyses published in other journals or examined whether reporting in  
15  
16 116 Cochrane reviews has improved since Cochrane implemented its reporting policy. The objectives  
17  
18 117 of the present study were to (1) investigate the extent to which Cochrane and non-Cochrane  
19  
20 118 meta-analyses of drug trials report trial funding sources, author-industry financial ties, and  
21  
22 119 author-industry employment; (2) examine characteristics of meta-analyses that are independently  
23  
24 120 associated with reporting funding sources of included RCTs; and (3) compare reporting among  
25  
26 121 recently published Cochrane meta-analyses to reporting from Cochrane systematic reviews  
27  
28 122 published in 2010,<sup>11</sup> prior to implementation of Cochrane's reporting policy.

## 32 123 **METHODS**

33  
34  
35 124 The methods for the present study were based on our previous study of reporting of  
36  
37 125 funding sources, author-industry financial ties, and author-industry employment from trials  
38  
39 126 included in Cochrane systematic reviews published in 2010; however in the present study, we  
40  
41 127 included only Cochrane reviews that contained a meta-analysis, whereas in the previous study all  
42  
43 128 Cochrane reviews that included results from at least one RCT were eligible.<sup>12</sup> Because of this  
44  
45 129 difference, in our comparison, in addition to main analyses, we conducted sensitivity analyses  
46  
47 130 that only included systematic reviews with meta-analyses from the previous study. A study  
48  
49 131 protocol was developed prior to initiating the present study and was posted on the Open Science  
50  
51 132 Framework (<https://osf.io/njk5w/>).

### 133 **Selection of meta-analyses**

134           Meta-analyses in any language were eligible if they (1) included a documented search for  
135 eligible RCTs using at least one database, (2) statistically combined results from  $\geq 2$  RCTs, and  
136 (3) evaluated the efficacy/effectiveness or harm of a drug or class of drugs against an alternative  
137 treatment (e.g., placebo, alternative drug, non-pharmacological treatment) or no treatment. Meta-  
138 analyses that only assessed different methods of administration, dosages, or dosage schedules of  
139 the same drug were excluded. Drugs were defined broadly to include biologics and vaccines, but  
140 not nutritional supplements or medical devices without a drug component. Meta-analyses that  
141 investigated a combination of pharmacological and non-pharmacological interventions or  
142 interventions which may or may not involve a drug (e.g., amnioinfusion) were included if a study  
143 group was exclusively given a drug intervention or if the meta-analysis assessed the addition of a  
144 drug to a treatment received by both intervention and control groups. Interventions were  
145 classified as having a drug component if any form of the active ingredient (e.g., dosage, route,  
146 strength, compound) was listed as an approved or discontinued brand name, generic drug or  
147 therapeutic biological product by the US Food and Drug Administration (FDA) as listed in the  
148 Drugs@FDA database at the time of review.<sup>17</sup> If an agent was not listed in the Drugs@FDA  
149 database and was classified by the FDA as a non-drug (e.g., food additive, supplement), then it  
150 was not considered a drug. If an agent was not regulated as a drug and was not listed as a non-  
151 drug by the FDA, drug status was determined based on consensus among investigators using  
152 publicly available sources that provided information on the agent.

153           We searched the MEDLINE database via PubMed on October 19, 2018 using a search  
154 developed by a medical librarian (see eMethods1 for strategy). Citations were uploaded into the  
155 systematic review software DistillerSR (Evidence Partners, Ottawa, Canada), which was used to



1  
2  
3 156 code and track results. Two investigators independently evaluated titles and abstracts for  
4  
5 157 potential eligibility. Full texts of titles and abstracts deemed potentially eligible by either  
6  
7 158 investigator were then reviewed by two investigators independently. Disagreements at the full-  
8  
9 159 text level were resolved through consensus with a third investigator consulted as necessary.  
10  
11 160 Because we sought to include the most recently published meta-analyses that met eligibility  
12  
13 161 criteria, prior to reviewing, citations were organized by PubMed reference identification numbers  
14  
15 162 with the most recent first. Title and abstract and full-text reviews were conducted sequentially  
16  
17 163 until we obtained our desired number of included meta-analyses based on our power analysis.  
18  
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21

#### 22 164 **Data extraction**

23  
24 165 For each eligible meta-analysis, one reviewer initially extracted all data into a pre-defined  
25  
26 166 form in DistillerSR, and a second reviewer validated all extracted data using the DistillerSR  
27  
28 167 Quality Control function. Discrepancies were resolved by consensus and consultation with a  
29  
30 168 third investigator, if needed. For each included meta-analysis, reviewers extracted first author  
31  
32 169 last name; year of publication; journal name; Clarivate Analytics 2017 journal impact factor;  
33  
34 170 journal speciality area based on Clarivate Analytics classification; whether it was a Cochrane  
35  
36 171 meta-analysis published in the Cochrane Database of Systematic Reviews or elsewhere; funding  
37  
38 172 source for the meta-analysis and author-industry financial ties and employment; reporting in the  
39  
40 173 meta-analysis of trial funding sources, trial author-industry financial ties, and trial author-  
41  
42 174 industry employment; and whether the meta-analysis referenced a published protocol or  
43  
44 175 contained a PROSPERO registration number. If a registration number was not provided, we  
45  
46 176 searched the PROSPERO website (<https://www.crd.york.ac.uk/PROSPERO/>) using key terms  
47  
48 177 from the published article, then attempted to match the principal investigator, funding source,  
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3 178 intervention, non-intervention comparator group, and design from the article to registrations  
4  
5 179 obtained in the search.

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8 180 To extract information on meta-analysis funding source, meta-analysis author-industry  
9  
10 181 financial ties, and meta-analysis author-industry employment and to determine whether or not  
11  
12 182 trial funding sources, trial author-industry financial ties, and trial author-industry employment  
13  
14 183 were reported in the meta-analysis, for each included meta-analysis, reviewers examined all text,  
15  
16 184 tables, figures, appendices, disclosure statements, acknowledgements and any online  
17  
18 185 supplemental material, published with the manuscript or linked to the manuscript. Funding  
19  
20 186 sources for meta-analyses were classified as (1) non-industry (e.g., public granting agency,  
21  
22 187 private not-for-profit granting agency), (2) pharmaceutical industry, (3) combined  
23  
24 188 pharmaceutical industry and non-industry, (4) no funding or (5) not reported. Financial ties of  
25  
26 189 meta-analysis authors to industry were defined per the International Committee of Medical  
27  
28 190 Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest<sup>18</sup> and included  
29  
30 191 current or former board membership, current or former consultancy, current or former industry  
31  
32 192 employment, expert testimony, industry grants (issued or pending), payment for lectures  
33  
34 193 including service on speakers bureaus, payment for manuscript preparation, patents (planned,  
35  
36 194 pending, or issued), royalties, payment for development of educational presentations, stock or  
37  
38 195 stock options, travel reimbursement, or other relationships with industry, as disclosed in the  
39  
40 196 review. Of these, we specifically coded if industry employees were part of the author group. If a  
41  
42 197 meta-analysis did not contain a disclosure statement, meta-analysis author-industry financial ties  
43  
44 198 were coded as not reported.

45  
46 199 For reporting of (1) trial funding sources, (2) trial author-industry financial ties, and (3)  
47  
48 200 trial author-industry employment, meta-analyses were coded as (1) reporting for all included  
49  
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3 201 trials; (2) reporting for some, but not all, included trials (partial reporting); or (3) not reporting.  
4  
5 202 Meta-analyses that included data from a pharmaceutical industry database or noted that trial  
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7 203 drugs were supplied by the manufacturers for certain trials, but that did not make any explicit  
8  
9 204 statement of trial funding sources, were coded as not reporting. For meta-analyses that reported  
10  
11 205 information on funding sources or author FCOIs from included trials, either fully or partially, we  
12  
13 206 recorded where in the meta-analysis the information was reported. Specifically, we recorded  
14  
15 207 whether the information was reported in the abstract, lay summary, risk of bias material (text,  
16  
17 208 figure or table, both), main text other than risk of bias, elsewhere in the main document (e.g.,  
18  
19 209 characteristics of included studies table, other table, footnote of a table), or in an online  
20  
21 210 appendix. See eMethods2.

## 211 **Power analysis**

212 To determine the number of meta-analyses to target, we first calculated the number of  
213 included meta-analyses that would be needed for 80% power to find a statistically significant  
214 difference if there were a 20% difference in reporting trial funding sources based on meta-  
215 analysis characteristics, with  $\alpha = 0.05$ . We varied the rates of reporting from 10% versus 30% to  
216 70% versus 90% and considered scenarios where the proportion of reporting meta-analyses with  
217 each characteristic (e.g., high-impact journals versus low-impact journals) was 50% versus 50%  
218 and 30% versus 70%. For a two-tailed binomial test with  $\alpha = 0.05$ , the maximum number of  
219 included meta-analyses needed in any scenario was 239. Because the consequence of  
220 overpowering the study was additional labour and not risk to human participants, we rounded  
221 this number up to 250 meta-analyses. See eMethods3.

## 222 **Statistical analyses**

223 We presented characteristics of included meta-analyses descriptively, including funding  
224 sources and FCOIs. We determined the proportion of meta-analyses that reported trial funding  
225 source, author-industry financial ties, and author-industry employment of included trials for (1)  
226 all included trials, (2) some, but not all, included trials, and (3) no included trials, along with  
227 95% confidence intervals (CIs). We compared the difference between the proportion of recently  
228 published Cochrane meta-analyses that reported study funding, author-industry financial ties, and  
229 author-industry employment from included RCTs with recently published non-Cochrane meta-  
230 analyses and with Cochrane systematic reviews published in 2010. Because the present study  
231 included meta-analyses only, but the previous study of Cochrane reviews included systematic  
232 reviews with or without meta-analyses,<sup>12</sup> we conducted a sensitivity analysis in which we  
233 excluded Cochrane systematic reviews from 2010 that did not include a meta-analysis and would  
234 not have been eligible for inclusion in the present study. We calculated 95% CIs for all  
235 differences.<sup>19</sup>

236 To assess the relationship between meta-analysis characteristics and reporting of funding  
237 sources for some or all included trials, versus not reporting, we fit unadjusted (bivariate) and  
238 adjusted (multivariate) logistic regression models with all predictors using the glm function in R  
239 (R version 3.2.3; RStudio Version 1.0.136).<sup>20, 21</sup> The predictor variables that were considered in  
240 bivariate and adjusted analyses were: (1) combined category (Cochrane, specialty medicine,  
241 general medicine, multidisciplinary) and impact factor of the journal in which the meta-analysis  
242 was published; and (2) whether there was industry funding for the meta-analysis or any FCOI  
243 disclosed by meta-analysis authors. We combined journal category and impact factor because of  
244 the small number of journals in some categories and the small number of journals with impact  
245 factor greater than that of Cochrane. Thus, meta-analyses were categorized as (1) low-impact ( $\leq$

1  
2  
3 246 3.0) specialty medicine journals, (2) low-impact ( $\leq 3.0$ ) general medicine or multidisciplinary  
4  
5 247 journals, (3) medium-impact (3.1 - 6.7) specialty medicine journals, (4) high-impact ( $> 6.8$ )  
6  
7 248 specialty medicine or general medicine journals, and (5) Cochrane meta-analyses (impact factor  
8  
9 249 = 6.8; reference category). Because 28 of 33 meta-analyses in general medicine journals were  
10  
11 250 from a single journal (*Medicine*) and not necessarily representative of general medicine as a  
12  
13 251 category, and because 9 of the 10 meta-analyses published in multidisciplinary science journals  
14  
15 252 were published in a single journal (*PLOS ONE*), we combined general medicine and  
16  
17 253 multidisciplinary journals.

18  
19 254 Our initial protocol indicated that, if possible, we would include in the logistic regression  
20  
21 255 model the year of publication of the meta-analysis and whether there was meta-analysis funding  
22  
23 256 by industry, meta-analysis author-industry financial ties, and meta-analysis author-industry  
24  
25 257 employment, separately. However, 246 of 250 included meta-analyses were published in 2017-  
26  
27 258 2018, and only 3 meta-analyses had industry funding; thus, we did not include year of  
28  
29 259 publication, and we grouped meta-analysis funding source and author FCOIs into a single  
30  
31 260 variable (No FCOIs including funding source versus any FCOI). Additionally, we only  
32  
33 261 conducted a multivariable analysis for the reporting of funding sources of included RCTs and not  
34  
35 262 for reporting of author-industry financial ties and author-industry employment, because there  
36  
37 263 were not enough examples of meta-analyses that reported author-industry financial ties and  
38  
39 264 author-industry employment.

## 265 **Patient and Public Involvement**

266 Patients and members of the public were not involved in the design, conduct,  
267 reporting, or plan for dissemination of our research.

## 268 **RESULTS**

## 269 Selection of eligible meta-analyses

270 Our initial search of PubMed without date restrictions retrieved 9,725 unique citations.  
271 To select 250 eligible meta-analyses, working backwards from the most recent, a total of 401  
272 citations were screened for eligibility; 64 were excluded at the title and abstract level and 76 at  
273 the full-text level. See Figure 1.

274 As shown in Table 1, of the 250 included meta-analyses, 107 (43%) were Cochrane  
275 reviews, all of which were published in the Cochrane Database of Systematic Reviews. Among  
276 the 143 non-Cochrane meta-analyses, 33 (23%) were published in general medicine journals  
277 (including 28 in the journal *Medicine*), 100 (70%) in specialty medicine journals, and 10 (7%) in  
278 multidisciplinary journals (including 9 in *PLOS ONE*). The mean number of included RCTs for  
279 both Cochrane and non-Cochrane meta-analyses was approximately 20. Among the 143 non-  
280 Cochrane meta-analyses, 25 (17%) referenced a published protocol or were registered in  
281 PROSPERO, and 106 (74%) were published in a journal with impact factor  $\leq 3$ .

282 Of the 250 meta-analyses, 3 (1%) reported being funded by industry, 148 (59%) reported  
283 funding from non-industry sources, 56 (22%) reported no funding, and 43 (17%) did not report  
284 funding source; 3 (1%) had at least 1 author who reported current industry employment, 51  
285 (20%) had at least 1 author that reported other financial ties with industry, 187 (75%) reported  
286 that there were no authors with FCOIs, and 12 (5%) did not report any information about author  
287 FCOIs. Characteristics of each of the 250 included meta-analyses are shown in eTable 1.

## 288 Reporting in meta-analyses of funding sources and author FCOIs from included drug trials

289 As shown in Table 2, 111 of the 250 (44%) included meta-analyses reported the funding  
290 sources for some or all included trials, 49 (20%) reported author-industry financial ties for some  
291 or all included trials, and 19 (8%) reported author-industry employment for some or all included

1  
2  
3 292 trials. Of the 107 Cochrane meta-analyses, 90 (84%) reported funding sources for some or all  
4  
5 293 included trials compared with 21 of 143 (15%) non-Cochrane meta-analyses, a difference of 69%  
6  
7  
8 294 (95% CI, 59% to 77%); 47 (44%) Cochrane meta-analyses reported author-industry financial ties  
9  
10 295 for some or all included trials compared with 2 (1%) non-Cochrane meta-analyses, a difference  
11  
12 296 of 43% (95% CI, 33% to 52%); 18 (17%) Cochrane meta-analyses reported, fully or partially  
13  
14 297 (for some but not all trials), author-industry employment compared with 1 (1%) non-Cochrane  
15  
16 298 meta-analysis, a difference of 16% (95% CI, 9% to 24%).

19 299 Among the 90 Cochrane meta-analyses that reported funding sources for some or all  
20  
21 300 included trials, 77 (86%) provided this information in the characteristics of included studies  
22  
23 301 table, including 23 (26%) that also included it in the assessment of risk of bias of included trials;  
24  
25 302 7 (8%) included it in the risk of bias assessment and at least one other place, but not the  
26  
27 303 characteristics of included studies table, and 6 (7%) reported only as part of the risk of bias  
28  
29 304 assessment. In total, 36 (40%) reported in the context of the risk of bias assessment. See eTable2  
30  
31 305 for reporting for all 250 included meta-analyses.

### 306 **Factors associated with reporting FCOIs from included trials in multivariable analysis**

37 307 As shown in Table 3, the odds ratio for reporting funding sources for some or all included  
38  
39 308 RCTs among non-Cochrane meta-analyses was  $\leq 0.11$  compared with Cochrane meta-analyses  
40  
41 309 for all journal category and impact factor combinations. Meta-analyses with any declared FCOI  
42  
43 310 (OR 1.29, 95% CI 0.53 to 3.19) and meta-analyses for which the presence of FCOIs was not  
44  
45 311 reported (OR 1.18, 95% CI 0.40 to 3.44) did not differ significantly in reporting compared with  
46  
47 312 those with no declared FCOIs.

### 313 **Comparison of recent Cochrane meta-analyses versus Cochrane reviews published in 2010**

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3 314 Reporting of funding sources for some or all included trials improved from 30% in  
4  
5 315 Cochrane reviews of drug trials published in 2010 to 84% in recently published Cochrane meta-  
6  
7 316 analyses, an improvement of 54% (95% CI, 42% to 63%). Reporting of author-industry financial  
8  
9 317 ties for some or all included trials improved from 7% in 2010 to 44% in recent meta-analyses, a  
10  
11 318 37% change (95% CI, 26% to 47%). Reporting of author-industry employment for some or all  
12  
13 319 included trials improved from 7% in 2010 to 17% in recent meta-analyses (10%; 95% CI, 2% to  
14  
15 320 19%). Results did not change when the comparison was restricted to Cochrane reviews published  
16  
17 321 in 2010 that included a meta-analysis. See Table 2. Figure 2 summarizes reporting among  
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19 322 recently published Cochrane and non-Cochrane meta-analyses and Cochrane reviews from 2010.  
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## 24 323 **DISCUSSION**

### 25 26 324 **Principal findings**

27  
28 325 We reviewed the 250 most recent meta-analyses of drug treatments listed in PubMed at  
29  
30 326 the time of our search. Of these, 107 (43%) were Cochrane reviews, 100 (40%) were published  
31  
32 327 in specialty medicine journals, and 43 (17%) were published in general medicine or  
33  
34 328 multidisciplinary journals, including 28 in *Medicine* and 9 in *PLOS ONE*. Of the 143 non-  
35  
36 329 Cochrane meta-analyses, 106 (74%) were published in journals with impact factor  $\leq 3$ .

37  
38 330 Among Cochrane meta-analyses, 84% reported funding sources for some or all included  
39  
40 331 RCTs compared with 15% of non-Cochrane meta-analyses. Cochrane meta-analyses were also  
41  
42 332 more likely than non-Cochrane meta-analyses to report author-industry financial ties (44%  
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44 333 versus 1%) and author-industry employment (17% versus 1%).

45  
46 334 In 2010, only 30% of 151 Cochrane systematic reviews of drug treatments reported trial  
47  
48 335 funding sources.<sup>12</sup> This improved to 84% among recent Cochrane meta-analyses. Cochrane  
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50 336 reviews also improved reporting of author-industry financial ties and author-industry  
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3 337 employment of included RCTs from 7% to 44% and from 7% to 17%. It is possible that the  
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5 338 reason that few meta-analyses reported author-industry employment is because some may have  
6  
7 339 assumed that author-industry employment would be considered a type of author-industry  
8  
9 340 financial tie and did not report employment separately, whereas we considered author-industry  
10  
11 341 financial ties and employment separately.

12  
13  
14 342 Among the 90 Cochrane meta-analyses that reported funding sources of included trials in  
15  
16 343 the present study, 86% included the information in the characteristics of included studies table,  
17  
18 344 as required by Cochrane, and 40% included the information in the risk of bias assessment.

### 21 345 **Findings in context**

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24 346 In 2012, soon after our previous results showed that few Cochrane systematic reviews of  
25  
26 347 drug trials reported funding sources and author FCOIs of included trials,<sup>12</sup> the Cochrane  
27  
28 348 Collaboration began to require that trial funding sources and FCOIs be reported for every  
29  
30 349 included RCT in the characteristics of included studies table.<sup>13, 14</sup> Reporting of trial funding  
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32 350 sources among recent Cochrane meta-analyses has not reached 100%, and work is needed to  
33  
34 351 improve the reporting of other types of author FCOIs, which was under 50% despite being  
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36 352 required by Cochrane. Nonetheless, the improvements documented in the present study are  
37  
38 353 substantial, both compared with previous Cochrane reviews and with contemporary non-  
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40 354 Cochrane meta-analyses. Cochrane is a global organization consisting of a large number of  
41  
42 355 different review and methods groups that span numerous fields of health research. This diversity  
43  
44 356 suggests that changes that have occurred likely resulted from change in the mandatory reporting  
45  
46 357 requirements for Cochrane reviews and widespread adoption by the organization. We did not  
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48 358 examine whether performance differed by review groups or whether updated reviews based on  
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50 359 initial protocols that pre-dated Cochrane's reporting policy may have been less likely to fully  
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3 360 report. It is possible that reporting in Cochrane reviews could be improved even further by  
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5 361 ensuring that all review groups are fully compliant and that even reviews with older initial  
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7 362 protocols report per Cochrane's current MECIR standards, as required by Cochrane.<sup>14</sup>  
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10 363 The improved performance in reporting in Cochrane reviews suggests the possibility that  
11  
12 364 other journals could improve the transparency of reporting of trial funding and trial author FCOI  
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14 365 in evidence syntheses by adopting similar reporting requirements. Most journals that specify  
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16 366 reporting requirements stipulate that authors follow reporting standards for meta-  
17  
18 367 analyses articulated in the PRISMA statement. The current version of the PRISMA  
19  
20 368 statement does not address reporting of trial funding sources and FCOIs of trial authors by  
21  
22 369 investigators who publish systematic reviews and meta-analyses.<sup>16, 17</sup> The forthcoming updated  
23  
24 370 PRISMA statement, however, will require that trial funding, although not trial author FCOIs, be  
25  
26 371 reported (personal communication, David Moher, May 22, 2019). Adoption and enforcement of  
27  
28 372 the updated PRISMA reporting standards by journals could result in authors being better  
29  
30 373 informed about the need for reporting funding sources and FCOI and in peer reviewers and  
31  
32 374 journals being more likely to require transparent reporting.  
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39 375 Members of our research team have previously recommended that risk of bias from trial  
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41 376 funding and trial author FCOIs be included in the Cochrane Risk of Bias Tool based on evidence  
42  
43 377 that links trial sponsorship and trial author FCOIs to outcomes.<sup>11</sup> This recommendation was  
44  
45 378 debated at a Cochrane Methods Symposium in 2013, but consensus was not reached for  
46  
47 379 inclusion.<sup>13, 22</sup> The present study found that 40% of Cochrane meta-analyses that  
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49 380 reported on FCOIs from included trials included this as part of a risk of bias assessment,  
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51 381 even though this has not been recommended by Cochrane. Currently, a new tool, the  
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3 382 Tool for Addressing Conflicts of Interest in Trials (TACIT),<sup>23</sup> which specifically addresses risk  
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5 383 of bias from industry sponsorship of trials and author-industry financial ties and employment, is  
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7 384 being developed for inclusion in Cochrane reviews. Once the TACIT tool is completed, risk of  
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9 385 bias from trial funding and trial author FCOIs will be explicitly considered in Cochrane reviews  
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11 386 and, potentially, in non-Cochrane reviews, as well. Meanwhile, authors should, at a minimum,  
12  
13 387 describe FCOIs and discuss the degree to which they may influence confidence in findings.  
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### 16 17 388 **Strengths and limitations**

18  
19 389 A strength of the present study is that we assessed reporting in a large number of recently  
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21 390 published meta-analyses, including 107 Cochrane meta-analyses, which allowed us to compare  
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23 391 reporting practices among Cochrane and non-Cochrane meta-analyses and recent Cochrane  
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25 392 meta-analyses with Cochrane systematic reviews from 2010. However, there are limitations that  
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27 393 should be considered. First, we used impact factor as a rough proxy of the quality of the meta-  
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29 394 analyses included, but journal impact factor is very much an imperfect proxy; it does not  
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31 395 necessarily reflect the quality of the methods of the included meta-analyses. Rating meta-  
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33 396 analysis quality in all included meta-analyses was beyond the scope of our study, given the  
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35 397 resources that would have been required. Second, since most meta-analyses of drug trials are  
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37 398 published as Cochrane reviews or in relatively low-impact specialty medicine journals, we were  
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39 399 not able to conduct robust assessments of whether meta-analyses published in different types of  
40  
41 400 journals or journals with different impact factors are more or less likely to report on trial funding  
42  
43 401 and trial author FCOIs for included drug trials. The vast majority of meta-analyses published in  
44  
45 402 general medicine journals were from a single journal (*Medicine*), which further limited our  
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47 403 ability to examine this factor. However, the meta-analyses included in our study constituted a  
48  
49 404 consecutive sample of the most recent meta-analyses listed in PubMed and, thus, represented all  
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3 405 meta-analyses of drug interventions listed in PubMed during the study period. Third, our study  
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5 406 examined only disclosed FCOIs. A surprising finding was that a higher proportion of Cochrane  
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7 407 meta-analysis authors indicated that they had FCOIs compared with non-Cochrane authors; it is  
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9 408 not known if this reflects greater industry involvement among Cochrane authors or a higher  
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11 409 propensity to report transparently and completely among this group of authors. Fourth,  
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13 410 information about FCOIs from included RCTs was not extracted from the RCT publications.  
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15 411 Fifth, our previous study of Cochrane reviews from 2010 included all systematic reviews,  
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17 412 whereas the present study was restricted to reviews with meta-analyses. However, a sensitivity  
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19 413 analysis showed that results did not change when we compared recent results to those from 2010  
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21 414 that were restricted to reviews with a meta-analysis.  
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## 25 415 **Conclusions and policy implications**

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28 416 In summary, the percentage of recent Cochrane meta-analyses on the effects of  
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30 417 drug interventions that transparently reported funding sources and trial author-industry  
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32 418 financial ties and employment for included trials far exceeds reporting in other journals.  
33  
34 419 It also far exceeds reporting in Cochrane systematic reviews published in 2010, before  
35  
36 420 the implementation by Cochrane of its policy requiring the reporting of trial funding sources and  
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38 421 author-industry FCOIs. These results suggest that it is possible to achieve more transparent  
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40 422 reporting of FCOIs from trials included in meta-analyses. We encourage the uptake and  
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42 423 enforcement of reporting requirements in the forthcoming updated PRISMA statement.<sup>24</sup> We  
43  
44 424 also encourage the adoption of Cochrane's new TACIT tool<sup>23</sup> by journals and authors in order to  
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46 425 assess trial funding sources and author FCOIs as risks of bias. Continued non-disclosure of  
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48 426 FCOIs when evidence is synthesized in meta-analyses misleads readers of medical journals into  
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3 427 believing that there is not risk of bias from FCOIs to be considered, even though an increasingly  
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5 428 robust evidence base tells us that this is often not the case.<sup>7, 8</sup>  
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For peer review only

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3 429 **Acknowledgement:** The authors thank Drs. Ian Shrier and Jonathan Kimmelman for providing  
4  
5 430 helpful comments on an earlier version of the manuscript. They were not compensated for their  
6  
7  
8 431 contribution. Ms. Turner was supported by a Fonds de Recherche Québec - Santé (FRQ-S)  
9  
10 432 masters training award, Ms. Levis was supported by a Canadian Institutes of Health Research  
11  
12 433 doctoral research award, and Drs. Benedetti and Thombs were supported by FRQ-S researcher  
13  
14 434 awards, all outside of the submitted work.

15  
16  
17 435 **Contributors:** KAT, MR, JB, LAB, JL, EHT, AB, and BDT were responsible for the study  
18  
19 436 conception and design. KAT, ACJ, CB, and KE were responsible for title and abstract and full-  
20  
21 437 text review. KAT and ACJ were responsible for data extraction and validation. KAT, BL, AB,  
22  
23 438 and BDT analysed and interpreted results. KAT and BDT drafted the manuscript. All  
24  
25 439 authors provided a critical review and approved the final manuscript. BDT is the  
26  
27 440 guarantor.

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28  
29  
30 460 **Funding:** There was no funding for the study.

31  
32 461 **Declaration of Competing Interests:** All authors have completed the ICMJE uniform  
33  
34 462 disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf). Dr. Bero disclosed that she is Senior  
35  
36  
37 463 Editor, Cochrane Public Health and Health Systems, for which the University of Sydney  
38  
39  
40 464 receives remuneration. Dr. Thombs disclosed that he is a content editor with the  
41  
42  
43 465 Cochrane Common Mental Disorders review group (no remuneration received). All other  
44  
45  
46 466 authors declared: no support from any organisation for the submitted work; no financial  
47  
48 467 relationships with any organisations that might have an interest in the submitted work in the  
49  
50 468 previous three years; no other relationships or activities that could appear to have influenced the  
51  
52  
53 469 submitted work.

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3 470 **Ethics Statement:** As this study involved only the review of published articles, research ethics  
4  
5 471 approval was not required.

7 472 **Transparency Declaration:** The manuscript's guarantor affirms that this manuscript is an  
8  
9 473 honest, accurate, and transparent account of the study being reported; that no important aspects  
10  
11 474 of the study have been omitted; and that any discrepancies from the study as planned (and, if  
12  
13 475 relevant, registered) have been explained.

16 476 **Data Sharing:** All extracted data are available in the main tables or in online supplementary  
17  
18 477 material. No additional data were extracted.



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3 537 **FIGURES**  
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6 538 **Figure 1.** Flow diagram of selection of eligible meta-analyses.  
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10 539 **Figure 2.** Percentage of recently published Cochrane and non-Cochrane meta-analyses and 2010  
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12 540 Cochrane systematic reviews that reported included trial funding source, author-industry  
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14 541 financial ties, and author-industry employment for some or all included trials.  
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**Table 1. Characteristics of included meta-analyses**

	<b>Cochrane Meta-Analyses (N = 107)</b>	<b>Non-Cochrane Meta-Analyses (N = 143)</b>
<b>Year of publication</b>		
2016, <i>N (%)</i>	0	4 (3%)
2017, <i>N (%)</i>	22 (21%)	31 (22%)
2018, <i>N (%)</i>	85 (79%)	108 (76%)
<b>Number of Included RCTs, mean ± SD</b>	21.4 ± 24.4	19.6 ± 46.4
<b>Registered in PROSPERO or Published Protocol, <i>N (%)</i></b>	107 (100%)	25 (17%) <sup>a</sup>
<b>Impact Factor, mean ± SD</b>		
≤ 3	0	106 (74%)
3.1-6.7	0	27 (19%)
6.8	107 (100%)	0
> 6.8	0	10 (7.0%)
<b>Meta-Analysis Funding Sources</b>		
Not reported	4 (4%) <sup>b</sup>	39 (27%)
Industry	0	3 (2%)
Non-Industry	93 (87%)	55 (38%)
No funding	10 (9%)	46 (32%)
<b>Meta-Analysis Author Financial Ties to Industry (Including Employment)<sup>c</sup></b>		
Not reported, <i>N (%)</i>	1 (1%)	11 (8%)
No authors with reported financial ties, <i>N (%)</i>	70 (65%)	117 (81%)

≥ 1 author with reported financial ties, <i>N (%)</i>	36 (34%)	15 (10%)
Proportion of authors with financial ties, <i>mean ± SD<sup>d</sup></i>	11% ± 17%	4% ± 15%

### Journal Category

Cochrane review, <i>N (%)</i>	107 (100%)	0
Specialty medicine <i>N (%)</i>	0	100 (70%)
General medicine (non-Cochrane), <sup>f</sup> <i>N (%)</i>	0	33 (23%)
Multidisciplinary, <sup>g</sup> <i>N (%)</i>	0	10 (7%)

543 <sup>a</sup>One meta-analysis reported that they registered in PROSPERO but did not provide a registration number and one  
544 could not be found. We contacted the authors and they did not provide us with further information; thus this was  
545 coded as not registered. <sup>b</sup>Only 3 included meta-analyses reported author-industry employment and these were  
546 grouped with author-industry financial ties for this table <sup>c</sup>Cochrane reviews typically have a “Sources of Support”  
547 section with funding information. These reviews did not include that section. <sup>d</sup>Proportion of authors with financial  
548 ties or employment of those that reported. <sup>e</sup>Classifications for specialty medicine journals (note that some journals  
549 had more than one classification): Anesthesiology, N = 3; Biochemistry & Molecular Biology, N = 1; Biotechnology  
550 & Applied Microbiology, N = 2; Cardiac & Cardiovascular Systems, N = 7; Cell Biology, N = 1; Chemistry,  
551 Medicinal, N = 4; Chemistry, Multidisciplinary, N = 2; Clinical Neurology, N = 6; Critical Care Medicine, N = 2;  
552 Dermatology, N = 3; Emergency Medicine, N = 2; Endocrinology & Metabolism, N = 2; Gastroenterology &  
553 Hepatology, N = 6; Genetics & Heredity, N = 1; Hematology, N = 2; Immunology, N = 6; Infectious Diseases, N =  
554 = 3; Integrative & Complementary Medicine, N = 1; Medicine, Research & Experimental, N = 3; Microbiology, N =  
555 2; Neurosciences, N = 3; No classification, N = 2; Obstetrics & Gynecology, N = 4; Oncology, N = 11;  
556 Ophthalmology, N = 3; Orthopedics, N = 6; Parasitology, N = 1; Peripheral Vascular Disease, N = 5; Pharmacology  
557 & Pharmacy, N = 13; Physiology, N = 1; Psychiatry, N = 4; Psychology, N = 1; Reproductive Biology, N = 1;  
558 Respiratory System, N = 6; Rheumatology, N = 3; Sport Sciences, N = 1; Surgery, N = 11; Toxicology, N = 2;  
559 Tropical Medicine, N = 1; Urology & Nephrology, N = 1. <sup>f</sup>Of the 33 included general medicine journals, 28 were  
560 published in the journal “Medicine”. <sup>g</sup>Of the 10 journals classified as multidisciplinary, 9 were published in the  
561 journal “PLOS ONE”.

**Table 2. Summary of reporting patterns of disclosed funding source and author-industry FCOI from included RCTs**

	Number of Meta-analyses Reporting Funding Sources of Included RCTs			Number of Meta-analyses Reporting Author Financial Ties of Included RCTs			Number of Meta-analyses Reporting Author-Industry Employment of Included RCTs		
	Full	Partial	Full or Partial	Full	Partial	Full or Partial	Full	Partial	Full or Partial
	<b>Recently Published Meta-analyses:</b>								
Cochrane (N = 107), N (%)	70 (65%)	20 (19%)	90 (84%)	24 (22%)	23 (21%)	47 (44%)	1 (1%)	17 (16%)	18 (17%)
Non-Cochrane (N = 143), N (%)	14 (10%)	7 (5%)	21 (15%)	1 (1%)	1 (1%)	2 (1%)	0	1 (1%)	1 (1%)
<b>Difference in Reporting Between Cochrane and Non-Cochrane Meta-analyses, % (95% CI)</b>	56% (44% to 65%)	14% (6% to 23%)	69% (59% to 77%)	22% (14% to 31%)	21% (13% to 30%)	43% (33% to 52%)	1% (-2% to 5%)	15% (9% to 23%)	16% (9% to 24%)
<b>2010:</b>									
All Cochrane Systematic Reviews (N = 151), N (%) <sup>a</sup>	30 (20%)	16 (11%)	46 (30%)	2 (1%)	9 (6%)	11 (7%)	0	10 (7%)	10 (7%)
<b>Difference in Reporting Between Recently Published Cochrane Meta-analyses versus Cochrane Systematic Reviews Published in 2010, % (95% CI)</b>	46% (34% to 56%)	8% (-1% to 18%)	54% (42% to 63%)	21% (13% to 30%)	16% (7% to 25%)	37% (26% to 47%)	1% (-2% to 5%)	9% (2% to 18%)	10% (2% to 19%)
<b>2010:</b>									
Cochrane Meta-analyses (N = 119),	21 (19%)	15 (13%)	36 (30%)	0 (0%)	7 (6%)	7 (6%)	0 (0%)	7 (6%)	7 (6%)

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<b>Difference in Reporting Between</b>	48%	6%	54%	22%	16%	38%	1%	10%	11%
<b>Recently Published Cochrane Meta-</b>	(36% to 58%)	(-3% to 16%)	(42% to 63%)	(15% to 31%)	(7% to 25%)	(27% to 48%)	(-2% to 5%0	(2% to 19%)	(3% to 20%)
<b>analyses versus Cochrane Meta-</b>									
<b>analyses Published in 2010, % (95%</b>									
<b>CI)</b>									

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562 <sup>a</sup>Results from Roseman et al., 2012.

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**Table 3. Factors associated with reporting funding sources of included RCTs**

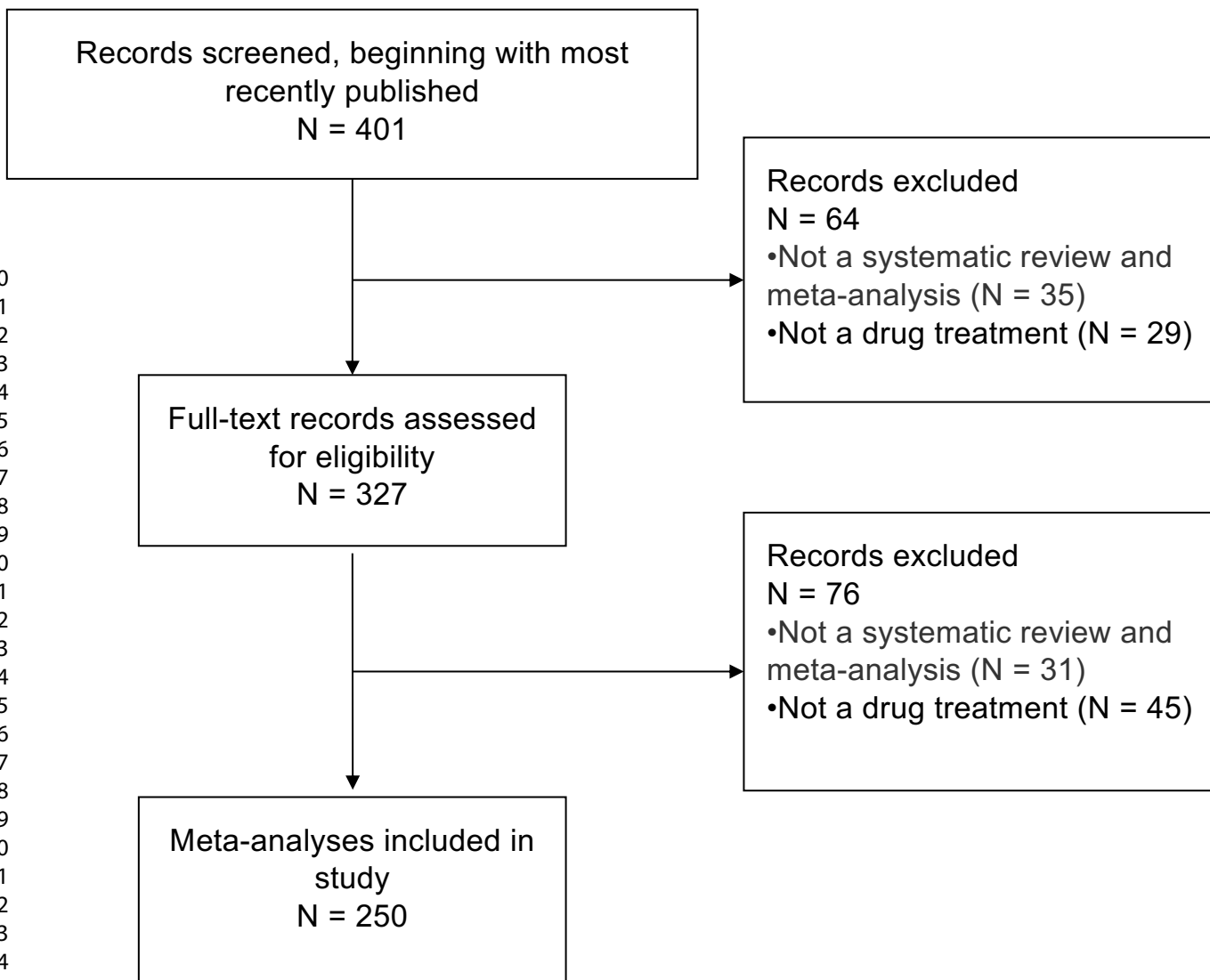
	<b>Proportion that reported some or all declared funding sources from included RCTs</b>	<b>Unadjusted odds ratio (95% CI)</b>	<b>Adjusted odds ratio (95% CI)</b>
<b>FCOI of meta-analysis (including meta-analysis funding)</b>			
reference = no FCOI	67/151 (44%)		
Any disclosed FCOI	35/51 (69%)	2.74 (1.42 to 5.49)	1.29 (0.53 to 3.19)
Not reported	9/48 (19%)	0.29 (0.12 to 0.62)	1.18 (0.40 to 3.44)
<b>Impact Factor and Journal Type</b>			
reference = Cochrane	90/107 (84%)		
Specialty impact factor $\leq 3^b$	4/65 (6%)	0.01 (< 0.01 to 0.03)	0.01 (< 0.01 to 0.04)
General (N=31) or Multidisciplinary (N=10) impact factor $\leq 3$	4/41 (10%)	0.02 (< 0.01 to 0.06)	0.02 (< 0.01 to 0.06)
Specialty impact factor 3.1 - 6.7 <sup>c</sup>	10/27 (37%)	0.11 (0.04 to 0.28)	0.11 (0.04 to 0.28)
Specialty (N=8) or General (N=2) impact factor > 6.8	3/10 (30%)	0.08 (0.02 to 0.32)	0.08 (0.02 to 0.32)

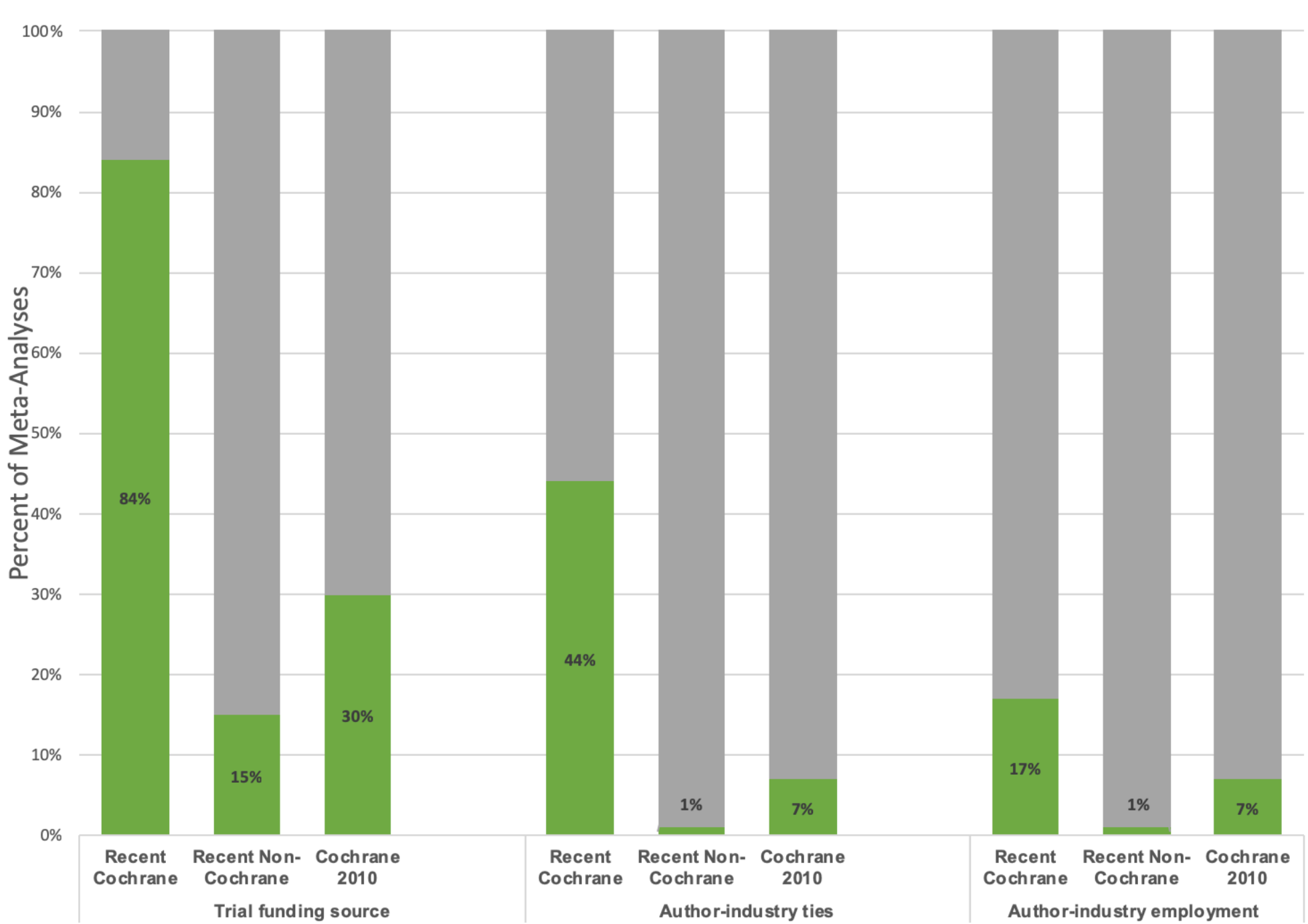
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563 <sup>a</sup>Not reported included meta-analyses for which the presence of FCOI could not be determined  
 564 because either meta-anlaysis funding, meta-analysis author FCOI, or both were not reported.  
 565 <sup>b</sup> Two meta-analyses were from journals that did not have an impact factor, and these were coded as having an impact factor of 0.5 for our  
 566 analyses.  
 567 <sup>c</sup> There were no multidisciplinary or general medicine journals with an impact factor of 3.1-6.7.  
 568 FCOI = financial conflicts of interest

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3 **Supplementary Material**  
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8 **eMethods1.** Search strategy  
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10 **eMethods2.** Data extraction form  
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12 **eMethods3.** Power analysis  
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14 **eTable1.** Detailed characteristics of included meta-analyses  
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16 **eTable2.** Detailed reporting of study funding source, author-industry financial ties, and author-  
17 industry employment from included RCTs  
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3 **eMethods1. Search strategy**  
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5 To obtain our sample, we searched the MEDLINE database via PubMed on October 19,  
6 2018 using the following search strategy:  
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11 (((("Randomized Controlled Trials as Topic"[Mesh] or randomized control trial  
12 [tiab] or randomized controled trial [tiab] OR randomized controlled trial [tiab] or  
13 randomized control trials [tiab] OR randomized controled trials [tiab] OR  
14 Randomized controlled trials [tiab] or randomised control trial [tiab] or randomised  
15 controled trial [tiab] OR randomised controlled trial [tiab] or randomised control  
16 trials [tiab] OR randomised controled trials [tiab] OR Randomised controlled trials  
17 [tiab]) AND ("Therapeutic Uses"[Mesh] OR "Vaccines"[Mesh]) AND ("Meta-  
18 Analysis" [Publication Type] or meta analysis [tiab]) AND (systematic review  
19 [tiab] OR search [tiab] or searched [tiab] or MEDLINE [tiab] OR PubMed [tiab])))  
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3 **eMethods 2.** Data extraction form  
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8 **First Author, last name:** Last name of first author of meta-analysis  
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11 **Year of publication (or in press):** Year of publication of meta-analysis  
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15 **Journal:** Name of journal in which meta-analysis was published  
16  
17

18 **Journal Impact factor:** Where meta-analysis published (low-high split or continuous based on  
19 data distribution)  
20  
21

22  
23 **Specialty area of Journal:** Where meta-analysis published (per Thomson Reuters Journal  
24 Science Citation Index - Expanded categories)  
25  
26

27  
28 **Cochrane Review (Y/N):** Is the meta-analysis a Cochrane Review? Select "Yes" even if the  
29 Cochrane Review is being published in another journal  
30  
31

32 Response from radio options:

- 33  
34 - Y (Yes)  
35 - N (No)  
36  
37

38  
39 **Journal policies for reporting COI of Included Trials:** Presence or absence of instructions for  
40 reporting in the author instructions  
41

- 42 - Y (Yes)  
43 - N (No)  
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47 **# of RCTs synthesized in Meta-Analysis** (total RCTs in included meta-analysis related to  
48 drugs)  
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3 **Date Range of Included Trials:** Date range in years of publication of studies (RCTs) included  
4 related to drugs in the meta-analysis (XXXX - XXXX). Use "In press" for end date if there are in  
5 press trials. Use "Unpublished" if a trial is in progress or has never been published.  
6  
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10 **Study population:** Characteristics of study population of included trials (e.g. condition/disorder,  
11 adult/child)  
12  
13

14  
15 **Pharmacological agent:** Pharmacologic treatment evaluated in the meta-analysis

- 16 - Name(s) of treatment if specific drug(s) investigated
- 17 - Class of treatment if broader category of drugs investigated, and number of drugs  
18 evaluated (e.g. SSRIs – 5 included)  
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24 **Control/comparison arms:** Other treatment arms (control/comparison) included in the meta-  
25 analysis (e.g. placebo, name of comparison pharmacologic treatment, name of behavioral  
26 intervention)  
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31 **Meta-Analysis Author Financial Ties / Funding Sources Reported:** Does the meta-analysis  
32 report meta-analysis author financial ties (including former and current industry employment)  
33 and/or the funding source? Note that reporting "no funding" is different from not reporting.  
34  
35

36 Response from radio options:

- 37 - Meta-analysis author financial ties
- 38 - Meta-analysis funding sources
- 39 - Both financial ties and funding sources
- 40 - Neither reported  
41  
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46 **Funding Source of Meta-Analysis (if applicable – only shown if above item indicates meta-  
47 analysis funding sources reported or both financial ties and meta-analysis funding sources  
48 reported)** Source of financial support for the meta-analysis:  
49  
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51 Response from radio options:

- 52 - Industry
- 53 - Combined industry and non-industry  
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- Non-industry (e.g. public granting agency, private not-for-profit granting agency)
- No study funding

**Type of Industry Funding (if applicable – only shown if above item indicates industry funding or combined industry and non-industry present):** If the meta-analysis is industry funded, what is the type of support provided by industry? Response from radio options:

- Financial support
- Resources (e.g. statistical analyses)
- Both financial support and resources

**# of Meta-Analysis Authors:** Number of authors of the meta-analysis (count authors named in byline or in an author group)

**# of Meta-Analysis Authors with Financial Ties to Industry (if applicable – only shown if meta-analysis author financial ties or both financial ties and meta-analysis funding sources are reported):** Number of authors of the meta-analysis who have financial ties such as industry board member, consultant, investments, patents, research funding, royalties (including former, and excluding current industry employment):

- Numbers 0 -  $\geq 10$

**# Meta-Analysis Authors with Current Industry Employment (if applicable – only shown if meta-analysis author financial ties or both financial ties and meta-analysis funding sources are reported):** Number of authors of the meta-analysis who are current industry employees.

Response from radio options:

Numbers 0 -  $\geq 10$

**Quality or Risk Assessment of Included RCTs (Y/N):** Was quality or risk assessment of included RCTs, by methods from Cochrane, Jadad, etc., reported in the meta-analysis.

Response from radio options:

- Y (Yes)
- N (No)

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5 **Quality or Risk Assessment Method of Included RCTs (if applicable – only shown if**  
6 **answer to previous item is yes- quality or risk assessment of included RCTs is reported):** If  
7 the meta-analysis authors report a quality or risk assessment method of included RCTs, what is  
8 the reported method of quality assessment?  
9  
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13 **Meta-analysis Authors Report Funding Sources of Included Studies:** Response from radio  
14 options:  
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- 16 - Reported for each included study
  - 17 - Reported in summary statement or for some, but not all, trials
  - 18 - Included study funding sources not reported
- 19  
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24 **Placement in publication of Included RCTs' Funding Source** (if applicable – only shown if  
25 the response to Meta-analysis Authors Report Funding Sources of Included Studies is (1)  
26 Reported for Each included Study or (2) Reported in summary statement or for some, but not all,  
27 trials):  
28  
29

- 30 - Abstract
  - 31 - Main text, other than risk of bias or quality section
  - 32 - In risk of bias or quality assessment
  - 33 - Other in main document (e.g., a characteristics of studies table, other table, in a  
34 footnote of a table
  - 35 - Online appendix
  - 36 - Lay Summary
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45 **Placement in risk of bias or quality assessment of Included RCTs' Funding Source** (if  
46 applicable – only shown if placement in publication of included RCT's Funding Source is risk of  
47 bias or quality assessment):  
48  
49

- 50 - Text
  - 51 - Figure/table
  - 52 - Both text and figure/table
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3 **Meta-analysis Authors Report Author Financial Ties of Included Studies:** Response from  
4 radio options:

- 5  
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7 - Reported for each included study  
8 - Reported in summary statement or for some, but not all, trials  
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10 - Included study author financial ties not reported  
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13 **Placement in publication of Included RCTs' Author Financial Ties** (if applicable – only  
14 shown if the response Meta-analysis Authors Report Author Financial Ties of Included Studies is  
15 (1) Reported for Each included Study or (2) Reported in summary statement or for some, but not  
16 all, trials):  
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- 19  
20 - Abstract  
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22 - Main text, other than risk of bias or quality section  
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24 - In risk of bias or quality assessment  
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26 - Other in main document (e.g., a characteristics of studies table, other table, in a  
27 footnote of a table  
28  
29 - Online appendix  
30  
31 - Lay Summary  
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33

34 **Placement in risk of bias or quality assessment of Included RCTs' Author Financial Ties** (if  
35 applicable – only shown if placement in publication of included RCT's Author Financial ties is  
36 risk of bias or quality assessment):  
37  
38

- 39 - Text  
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41 - Figure/table  
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43 - Both text and figure/table  
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46 **Meta-analysis Authors Report Author Industry Employment of Included Studies:** Do the  
47 authors of the meta-analysis report current author industry affiliation (employment) for the  
48 included studies? Response from radio options:  
49

- 50  
51 - Reported for each included study  
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53 - Reported in summary statement or for some, but not all, trials  
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55 - Included study author industry employment not reported  
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5 **Placement in publication of Included RCTs' Author Industry Employment** (if applicable –  
6 only shown if the response to Meta-analysis Authors Report Author Industry Affiliation  
7 (Employment) of Included Studies is (1) Reported for Each included Study or (2) Reported in  
8 summary statement or for some, but not all, trials):  
9

- 10 - Abstract
- 11 - Main text, other than risk of bias or quality section
- 12 - In risk of bias or quality assessment
- 13 - Other in main document (e.g., a characteristics of studies table, other table, in a  
14 footnote of a table)
- 15 - Online appendix
- 16 - Lay Summary

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26 **Placement in risk of bias or quality assessment of Included RCTs' Author Industry**  
27 **Employment** (only shown if placement in publication of included RCT's Author Industry  
28 Affiliation is risk of bias or quality assessment):  
29

- 30 - Text
- 31 - Figure/table
- 32 - Both text and figure/table

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38 **Do the authors report a PROSPERO registration number in the text?**

- 39 - Yes
- 40 - No

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43 **What is the registration number (e.g., CRD42017062454)?** (if applicable – only shown if the  
44 response to Do the authors report a PROSPERO registration number in the text? Is yes)  
45

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48 **What stages were completed (ignore started) at the time of registration. Make sure to select**  
49 **the earliest registration version at the bottom of the page. Please check all stages that were**  
50 **completed.** (if applicable – only shown if the response to Do the authors report a PROSPERO  
51 registration number in the text? Is yes)  
52

- 53 - Preliminary searches

- Piloting of the study selection process
- Formal screening of search results against eligibility criteria
- Data extraction
- Risk of bias (quality) assessment
- Data analysis
- None completed

**Was a registration found in PROSPERO?** (if applicable – only shown if the response to Do the authors report a PROSPERO registration number in the text? Is no)

**What is the registration number (e.g., CRD42017062454)?** (if applicable – only shown if the response to Was a registration found in PROSPERO? Is yes)

**What stages were completed (ignore started) at the time of registration. Make sure to select the earliest registration version at the bottom of the page. Please check all stages that were completed.** (if applicable – only shown if the response to Was a registration found in PROSPERO? Is yes)

- Preliminary searches
- Piloting of the study selection process
- Formal screening of search results against eligibility criteria
- Data extraction
- Risk of bias (quality) assessment
- Data analysis
- None completed

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3 **eMethods3. Power analysis**  
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7 **Allocation ratio: 50% and 50% (1:1)**

8 20% difference

9 Proportion reporting COI		10 Sample size group 1	11 Sample size group 2	12 Sample size total	13 Actual power	14 Actual alpha
15 Low impact	16 High impact					
17 10%	18 30%	19 69	20 69	21 138	22 .807	23 .033
24 20%	25 40%	26 90	27 90	28 180	29 .802	30 .037
31 30%	32 50%	33 102	34 102	35 204	36 .806	37 .042
38 40%	39 60%	40 102	41 102	42 204	43 .801	44 .038
45 50%	46 70%	47 102	48 102	49 204	50 .806	51 .036
52 60%	53 80%	54 90	55 90	56 180	57 .802	58 .032
59 70%	60 90%	61 69	62 69	63 138	64 .807	65 .025

66 **Allocation ratio: 30% and 70% (3:7)**

67 20% difference

68 Proportion reporting COI		69 Sample size group 1	70 Sample size group 2	71 Sample size total	72 Actual power	73 Actual alpha
74 Low impact	75 High impact					
76 10%	77 30%	78 105	79 44	80 149	81 .815	82 .038
83 20%	84 40%	85 141	86 59	87 200	88 .807	89 .040
90 30%	91 50%	92 165	93 69	94 234	95 .801	96 .045
97 40%	98 60%	99 168	100 71	101 239	102 .805	103 .043
104 50%	105 70%	106 166	107 70	108 236	109 .864	110 .042
111 60%	112 80%	113 148	114 62	115 210	116 .802	117 .040
118 70%	119 90%	120 133	121 47	122 160	123 .802	124 .035

**eTable1.** Detailed characteristics of included meta-analyses**eTable1.** Detailed characteristics of included meta-analyses

First Author	Year	Journal	2017 Impact Factor	Specialty Area	Meta-analysis Funding source(s)	Number of Meta-analysis Authors with Industry Financial Ties / Number of Meta-analysis Authors <sup>a</sup>	Number of drug RCTs Included	Publication Dates of included drug RCTs	Population	Drug Intervention(s)	Comparison Arm(s)
<b>Cochrane Reviews (n = 107)</b>											
Abdel-Rahman <sup>1</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	7	2004-2016	Adults (19 years and over) with advanced biliary tract carcinomas	Gemcitabine, vandetanib, S-1 (tegafur + gimeracil + oteracil), gemcitabine + oxaliplatin, 5-fluorouracil + folinic acid, capecitabine	Best supportive care, 5-fluorouracil + cisplatin + radiotherapy
Adams <sup>2</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	36	1994-2012	Participants with or without evidence of cardiovascular disease	Fluvastatin	Placebo
Agabio <sup>3</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	27	1969-2015	People with co-occurring depression and alcohol dependence	Antidepressants - 16 types, diazepam, memantine	Placebo, psychotherapy
Al-Shahi Salman <sup>4</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Not reported	0/5	11 <sup>b</sup>	1999-2015	Adults (16 years and over) with acute spontaneous intracerebral haemorrhage	Blood clotting factors, antifibrinolytic drugs	Placebo, open control, fresh frozen plasma
Alabed <sup>5</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	11	1976-2008	Patients with antipsychotic-induced tardive dyskinesia (TD)	Gamma-aminobutyric acid agonists - 6 types	Placebo
Allegretti <sup>6</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	3/8	8	1998-2016	Patients with hepatorenal syndrome	Terlipressin, terlipressin + albumin	Placebo, no intervention, albumin
Arechabala <sup>7</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/7	37	1998-2017	Patients undergoing haemodialysis using a central venous catheter	Antibiotic antimicrobial lock solutions - 11 types, non-antibiotic antimicrobial lock	Heparin, saline

1													
2													
3													
4												solutions - 10 types,	
5												antibiotic + non-antibiotic	
6												antimicrobial lock	
7												solutions - 3 types	
8												Valproate, carbamazepine,	
9												lithium, pregabalin,	
10												captodiame, paroxetine,	
11												tricyclic antidepressants - 4	
12												types, alpidem, buspirone,	
13	Baandrup <sup>8</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	1/6	33 <sup>c</sup>	1981-2016	Adult (18 years and over) chronic benzodiazepine users		progesterone, magnesium aspartate, bromazepam, cyamemazine, zopiclone, flunitrazepam	Placebo, no intervention
14													
15													
16													
17	Bala <sup>9</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	3/6	9	1997-2016	Individuals with antiphospholipid antibodies and no history of thrombosis		Aspirin + anticoagulants, aspirin, aspirin + low molecular weight heparin	Placebo, immunoglobulin, unfractionated heparin
18													
19													
20													
21													
22	Barbato <sup>10</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	4 <sup>d</sup>	2000-2012	Heterosexual adult couples (18 years or more) with a partner having a clinical diagnosis of depressive disorder		Antidepressants - 9 types	Couples therapy
23													
24													
25	Bergman <sup>11</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/3	4	1981-1997	Psychiatric patients with antipsychotic-induced tardive dyskinesia		Benzodiazepines - 3 types Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), norepinephrine reuptake inhibitors (NRIs), nefazodone, ritanserin	Placebo, usual care
26													
27													
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32													
33	Bighelli <sup>12</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	2/9	41	1989-2011	Adults (18 years and over) with panic disorder			Placebo
34													
35													
36	Birks <sup>13</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/2	30	1996-2017	People with Alzheimer's disease		Donepezil	Placebo
37													
38													
39	Boyapati <sup>14</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	3/8	6	1978-2017	Adults (18 years and over) with quiescent Crohn's disease		Azathioprine, infliximab	No treatment, usual care (azathioprine + infliximab)
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3			Cochrane									
4			Database of						Women of			
5	Brown <sup>15</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	5	1993-2017	reproductive age	Combined oral contraceptive	Placebo, leuprolide,
6			Reviews		& Internal	industry				with endometriosis	pill - 3 types	goserelin
7			Cochrane									
8			Database of									
9	Bruins Slot <sup>16</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/2 <sup>e</sup>	13	2008-2014	Adults with atrial	Factor Xa inhibitors - 7	Warfarin
10			Reviews		& Internal	industry				fibrillation	types	
11										People with		
12										schizophrenia and		
13										schizophrenia-like		
14			Cochrane							disorders such as		
15	Bryan <sup>17</sup>	2017	Systematic	6.8	Medicine, General	No	0/3	20	1968-2007	schizophreniform	Zuclophenthixol	Placebo, other drugs -
16			Reviews		& Internal	funding				disorder	dihydrochloride	11 types
17										schizo-affective	Antifibrinolytic agents - 2	
18			Cochrane							disorder	types, non-steroidal anti-	Placebo, herbal
19	Bryant-Smith <sup>18</sup>	2018	Systematic	6.8	Medicine, General	No	1/4	13	1970-2016	People with	inflammatory drugs	medicines,
20			Reviews		& Internal	funding				heavy	(NSAIDs), progestogens,	levonorgestrel
21										menstrual bleeding	ethamsylate	intrauterine system
22			Cochrane							Adults (17 years and		
23	Burry <sup>19</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/9	9	1996-2016	over) in non-ICU	Antipsychotics - 5 types	Nonantipsychotics,
24			Reviews		& Internal	industry				acute care settings		placebo
25			Cochrane							diagnosed with		
26	Campschroer <sup>20</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	67	2002-2017	delirium	Alpha-blockers - 6 types	Placebo, usual care
27			Reviews		& Internal	industry				Adult patients (18		
28										years and older)		
29			Cochrane							with ureteral stone		
30	Candy <sup>21</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/5	8	1996-2017	disease	Mu-opioid antagonists - 3	Placebo
31			Reviews		& Internal	industry				Adults with cancer	types	
32			Cochrane							and adults receiving		
33	Chiew <sup>22</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	9 <sup>f</sup>	1976-2014	palliative care with		
34			Reviews		& Internal	industry				opioid-induced	Methionine, cysteamine,	Placebo, no treatment
35										bowel dysfunction	dimercaprol, acetylcysteine	
36			Cochrane							Patients with		
37	Das <sup>23</sup>	2018	Systematic	6.8	Medicine, General	Not	0/3	7	2010-2017	paracetamol	Vitamin D	Placebo, antibiotics
38			Reviews		& Internal	reported				(acetaminophen)		alone
39			Cochrane							overdose		
40	Demicheli <sup>24</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/5	71 <sup>g</sup>	1969-2014	Children aged up to	Inactivated parenteral	Placebo, no treatment
41			Reviews		& Internal	industry				five years with a	influenza vaccine	
42										clinical diagnosis of		
43										community-acquired		
44										pneumonia (CAP)		
45										Healthy individuals		
46										(16 to 65 years) and		
47										pregnant women and		
										their newborns		

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3			Cochrane									
4			Database of									
5	Demicheli <sup>25</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/7	8	1969-2004	Elderly participants	Influenza vaccines	Placebo
6			Reviews		& Internal	industry				(65 years and over)	Fondaparinux,	
7											rivaroxaban, low molecular	
8											weight heparin, non-	
9											steroidal anti-inflammatory	
10											drugs, vasotonin,	
11											sulodexide,	
12			Cochrane								heparansulphate, vitamin K	
13			Database of								antagonists, enzyme	
14	Di Nisio <sup>26</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/3	32	1970-2017	Patients with	therapy, unfractionated	Placebo, elastic
15			Reviews		& Internal	industry				superficial	heparin, heparin calcium,	stockings
16			Cochrane							thrombophlebitis of	defibrotide	
17	El-Sayeh <sup>27</sup>	2018	Database of	6.8	Medicine, General	Non-	0/4	10	1973-2010	of a thrombus in a		
18			Systematic		& Internal	industry				superficial vein	Noradrenergic drugs - 2	Placebo
19			Reviews							Patients with	types, dopaminergic drugs	
20										antipsychotic-	- 7 types	
21										induced tardive		
22										dyskinesia		
23										People of all ages on		
24										continuous vitamin		
25										K antagonist (VKA)		
26										or direct oral		
27	Engelen <sup>28</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/5	3	1989-2015	anticoagulant		Usual care (surgical
28			Reviews		& Internal	industry				(DOAC) treatment	Antifibrinolytic agents - 2	treatment), usual care
29										undergoing an oral	types	(surgical treatment) +
30										or dental procedure	Selective serotonin	placebo
31											reuptake inhibitors (SSRIs)	
32											- 4 types, tricyclic	
33											antidepressants (TCAs) - 2	
34	Eshun-Wilson <sup>29</sup>	2018	Systematic	6.8	Medicine, General	Non-	1/6	10	1994-2014	Adults (18 years and		Placebo, mirtazapine
35			Reviews		& Internal	industry				over) living with		
36										HIV and depression		
37										People with		
38										antipsychotic-	Calcium channel blockers -	
39										induced tardive	3 types	
40	Essali <sup>30</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	3	1992-1997	dyskinesia	Selective serotonin	Placebo
41			Reviews		& Internal	industry					reuptake inhibitors - 4	
42											types; tricyclic	
43											antidepressants - 3 types;	
44											other antidepressants - 6	
45											types	Placebo, insomnia
46												medication - 2 types
47												
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50												
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											followed by intrauterine insemination, laparoscopic ovarian drilling, follicle- stimulating hormone, anastrozole Sulfadoxine- pyrimethamine, cotrimoxazole, placebo
González <sup>34</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/6	6	1994-2014	Pregnant women living in malaria- endemic areas Adult women with moderate or severe cervical intraepithelial neoplasia (CIN)	Mefloquine	
Grabosch <sup>35</sup>	2018	Cochrane Database of Systematic Reviews Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/3	3	2006-2017	Adults and children being treated for falciparum malaria Pregnant women who were about to receive a cesarean delivery	Non-steroidal anti- inflammatory agents (NSAIDs) - 2 types	Placebo
Graves <sup>36</sup>	2018	Cochrane Database of Systematic Reviews Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/4	24 <sup>b</sup>	1981-2017	Adults and children being treated for falciparum malaria Pregnant women who were about to receive a cesarean delivery	Primaquine	Usual treatment, bulaquine
Haas <sup>37</sup>	2018	Cochrane Database of Systematic Reviews Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/4	11	1997-2017	Adults and children being treated for falciparum malaria Pregnant women who were about to receive a cesarean delivery	Antiseptic solutions - 3 types	Placebo, no treatment
Hakoum <sup>38</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/10	15	1991-2009	People with cancer and venous thromboembolism	Low molecular weight heparin, unfractioned heparin	Fondaparinux Placebo, no treatment, alternative therapies - 7 types, other drug comparators - 6 types, other non-drug comparators - 4 types
Heras- Mosteiro <sup>39</sup>	2017	Cochrane Database of Systematic Reviews Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/10	89	1990-2015	Immunocompetent patients with localised Old World cutaneous leishmaniasis People with esophageal or gastroesophageal junction cancer	Antimonials – 2 types, non-antimonials – 22 types Chemotherapy, targeted therapy, EGFR-targeting agents, cetuximab, ramucirumab	Best supportive care, unspecified control
Janmaat <sup>40</sup>	2017	Cochrane Database of Systematic Reviews Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/8	41	1980-2015	Healthy children (15 years and under) Middle-aged and older men (40 or over) with lower urinary tract symptoms as a result of benign prostatic hyperplasia	Influenza vaccine - 2 types	Placebo, no intervention
Jefferson <sup>41</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	1/4	41	1971-2016	Healthy children (15 years and under) Middle-aged and older men (40 or over) with lower urinary tract symptoms as a result of benign prostatic hyperplasia	Influenza vaccine - 2 types	Placebo, no intervention
Jung <sup>42</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non- industry	0/6	19	2006- Unpublishe d	Healthy children (15 years and under) Middle-aged and older men (40 or over) with lower urinary tract symptoms as a result of benign prostatic hyperplasia	Silodosin, tamsulosin, naftopidil, and alfuzosin	Placebo

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3			Cochrane									
4			Database of									
5	Kaempfen <sup>43</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	3	2013-2017	Preterm infants	Propranolol	Placebo, no treatment
6			Reviews		& Internal	industry						
7			Cochrane									
8			Database of									
9	Kahale <sup>44</sup>	2017	Systematic	6.8	Medicine, General	Non-	0/10	7	1979-2012	Ambulatory people	Warfarin, apixaban	Placebo, no treatment
10			Reviews		& Internal	industry				with cancer		
11			Cochrane									
12			Database of							People with cancer		
13			Systematic	6.8	Medicine, General	Non-	0/10	13	1990-2013	and central venous	Anticoagulant - 6 types	Placebo, no treatment
14			Reviews		& Internal	industry				catheters	Vitamin K antagonist - 2	
15			Cochrane								types, direct oral	
16			Database of							People with cancer	anticoagulant - 4 types;	
17	Kahale <sup>46</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/11	16	2001-2018	and venous	low molecular weight	Anticoagulants
18			Reviews		& Internal	industry				thromboembolism	heparin - 4 types	
19			Cochrane									
20			Database of									
21			Systematic									
22	Kapur <sup>47</sup>	2018	Reviews	6.8	Medicine, General	Non-	3/5	7	1992-2012	Children and adults	Corticosteroids - 3 types	Placebo, no treatment
23			Cochrane		& Internal	industry				with bronchiectasis		
24			Database of									
25			Systematic									
26			Reviews									
27			Cochrane									
28			Database of									
29			Systematic									
30			Reviews									
31			Cochrane									
32			Database of									
33			Systematic									
34			Reviews									
35			Cochrane									
36			Database of									
37			Systematic									
38			Reviews									
39			Cochrane									
40			Database of									
41			Systematic									
42			Reviews									
43			Cochrane									
44			Database of									
45			Systematic									
46			Reviews									
47			Cochrane									

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3			Systematic								selective progesterone-	
4			Reviews								receptor modulators	
5			Cochrane									
6			Database of									0.9% sodium chloride
7	López-Briz <sup>54</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/6	11	2002-2015	Adults with central	Heparin	(normal saline
8			Reviews		& Internal	industry				venous catheters		solution)
9			Cochrane							Children (18 years		
10			Database of							and under) with		
11	Marchant <sup>55</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/4	3	1993-2012	prolonged wet	Antibiotics - 2 types	Placebo, no treatment
12			Reviews		& Internal	industry				cough (longer than		
13			Cochrane							10 days)		
14	Matar <sup>56</sup>	2018	Database of	6.8	Medicine, General	Non-	0/3	7	1963-1999	Patients with	Fluphenazine	Placebo
15			Systematic		& Internal	industry				schizophrenia		
16			Reviews									
17	Matar <sup>57</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/11	20	1986-2018	People with solid or	Low-molecular weight	Unfractionated heparin
18			Database of		& Internal	industry				hematologic cancer	heparin (LMWH) - 10	(UFH), fondaparinux
19			Systematic							undergoing surgery	types	
20	McNicol <sup>58</sup>	2018	Reviews	6.8	Medicine, General	Non-	1/3	13	1992-2016	Postoperative	Ketorolac	Placebo, opioid
21			Cochrane		& Internal	industry				paediatric patients		
22			Database of							(17 years and under)		
23			Systematic							Children (16 years		
24			Reviews							and under)		
25	McTague <sup>59</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/3	18	1995-2014	presenting to a	Lorazepam	Diazepam +
26			Database of		& Internal	industry				hospital or		phenytoin, diazepam,
27			Systematic							emergency		paraldehyde,
28			Reviews							department in an		midazolam
29	Mhaskar <sup>60</sup>	2017	Database of	6.8	Medicine, General	Non-	0/4	24	1982-2015	acute tonic-clonic		
30			Systematic		& Internal	industry				convulsion		
31			Reviews									
32	Milligan <sup>61</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/4	18	1980-2016	Patients with	Bisphosphonates - 5 types	Placebo, no treatment -
33			Database of		& Internal	industry				multiple myeloma		Network meta-analysis
34			Systematic							(MM)		
35			Reviews									
36	Monk <sup>62</sup>	2017	Cochrane	6.8	Medicine, General	Non-	0/4	32	1993-2016	Adults and children	Typhoid fever vaccines - 4	No treatment, placebo,
37			Database of		& Internal	industry					types	typhoid-inactive
38			Systematic								Tramadol, non-steroidal	agents
39			Reviews								anti-inflammatory drugs,	
40	Montero <sup>63</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/4	10	1991-2012	People undergoing	paracetamol, local	
41			Database of		& Internal	industry				orthodontic	anaesthetic	Placebo, no treatment
42			Systematic							Patients with		
43			Reviews							hepatitis C virus-	Rituximab, interferon,	Usual care,
44			Cochrane							associated mixed	immunosuppressive drug	immunoabsorption
45	Montero <sup>63</sup>	2018	Database of	6.8	Medicine, General	No	1/7	10	1991-2012	cryoglobulinaemia	therapy	apheresis
46			Systematic		& Internal	funding <sup>i</sup>				Adults (18 years and		
47			Reviews							over) with chronic	Cannabis-based medicines	Placebo,
	Mücke <sup>64</sup>	2018	Cochrane	6.8	Medicine, General	Non-	2/5	16	2004-2017	neuropathic pain	- 5 types	dihydrocodeine

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3			Systematic									
4			Reviews									
5			Cochrane									
6			Database of									
7	Narula <sup>65</sup>	2018	Systematic	6.8	Medicine, General	Non-	3/7	10 <sup>j</sup>	1990-2014	Adults and children	Corticosteroids - 5 types	Enteral nutrition
8			Reviews		& Internal	industry				with Crohn's disease		
9			Cochrane							Adults or children		
10			Database of							with partial onset		
11	Nevitt <sup>66</sup>	2017	Systematic	6.8	Medicine, General	Non-	1/5	76	1981-2015	seizures or	Antiepileptic drugs - 10	Network meta-analysis
12			Reviews		& Internal	industry				generalised onset	types	
13			Cochrane							tonic-clonic seizures		
14	Nevitt <sup>67</sup>	2018	Database of	6.8	Medicine, General	Non-	1/4	14	1995-2015	Adults and children	Lamotrigine	Carbamazepine
15			Systematic		& Internal	industry				with focal onset or		
16			Reviews							generalised onset		
17	Norman <sup>68</sup>	2018	Cochrane	6.8	Medicine, General	Non-	1/6	78	1985-2016	seizures	Topical agents - 10 types	Dressings - 12 types; Network meta-analysis
18			Database of							Adults (18 years and		
19			Systematic							over) with venous		
20	Normansell <sup>69</sup>	2018	Reviews	6.8	Medicine, General	Non-	0/6	6	1974-2016	leg ulcers	Antibiotics - 4 types	Placebo
21			Cochrane							Children and adults	Propranolol, timolol	
22			Database of							with acute asthma	maleate, bleomycin,	
23			Systematic							exacerbation	atenolol, prednisolone,	
24			Reviews								captopril, ibuprofen +	
25	Nova <sup>70</sup>	2018	Database of	6.8	Medicine, General	Non-	1/7	24	1977-2016	located on the skin	paracetamol, methylene	Placebo, radiation, lasers
26			Systematic							Preterm (< 37	blue, triamcinolone,	
27			Reviews							weeks' gestation)	methylprednisolone	
28			Cochrane							and low birth weight		
29			Database of							(< 2500 grams)		
30	Ohlsson <sup>71</sup>	2017	Systematic	6.8	Medicine, General	No	0/2	34	1991-2017	infants less than	Erythropoiesis-stimulating	Placebo, no treatment
31			Reviews		& Internal	funding				eight days of age	agents (ESAs) - 2 types	
32			Cochrane							Adults exhibiting		
33	Ostinelli <sup>72</sup>	2018	Database of	6.8	Medicine, General	No	1/5	3	2005-2016	aggression or	Aripiprazole	Placebo, other anti- psychotic medications
34			Systematic		& Internal	funding				agitation (or both)		- 2 types
35			Reviews							due to psychosis		Haloperidol,
36	Ostinelli <sup>73</sup>	2018	Cochrane	6.8	Medicine, General	No	0/6	9	2010-2014	Patients with	Risperidone	olanzapine, quetiapine,
37			Database of			industry				psychosis-induced		oxcarbazepine,
38			Systematic							aggression or		valproic acid
39	Ostuzzi <sup>74</sup>	2018	Reviews	6.8	Medicine, General	Non-	1/5	7	1985- Unpublishe d	Adults (18 years and	Antidepressants - 6 types	Placebo
40			Cochrane							over) with cancer		
41			Database of							and depression		
42			Systematic									
43			Reviews									
44												
45												
46												
47												

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3			Cochrane								
4			Database of								
5	Parker <sup>75</sup>	2018	Systematic	6.8	Medicine, General	Non-	2/5	2	2011-2013	Children and adults	
6			Reviews		& Internal	industry				with active Crohn's	Naltrexone
7										disease	Placebo
8											Tamoxifen, interferon-
9											alpha, interleukin-2,
10											interferon-alpha +
11											interleukin-2, Bacille
12											Calmette-Guérin
13			Cochrane								(BCG),
14			Database of								corynebacterium
15	Pasquali <sup>76</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/5	122	1972-2015	Patients with	parvum, anti-PD1
16			Reviews		& Internal	industry				unresectable lymph	monoclonal
17			Cochrane							node metastasis and	antibodies, sorafenib,
18			Database of							distant metastatic	elesclomo, anti-
19			Systematic							cutaneous	angiogenic drugs
20			Reviews							melanoma	
21	Pike <sup>77</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/4	4	2007-2017	Children (18 years	
22			Reviews		& Internal	industry				and under) with	Omalizumab, leukotriene
23			Cochrane							asthma	receptor antagonists - 2
24			Database of								types, corticosteroids
25			Systematic								Placebo
26			Reviews								
27	Rirash <sup>78</sup>	2017	Systematic	6.8	Medicine, General	Not	Not	38	1982-2000	Patients with	
28			Reviews		& Internal	reported	reported/8			Raynaud's	Calcium channel blockers
29			Cochrane							phenomenon	Placebo
30			Database of							Adults (18 years and	
31			Systematic							over) with	
32	Robertson <sup>79</sup>	2017	Reviews	6.8	Medicine, General	Non-	0/3	6	1995-2016	unprovoked venous	Warfarin, aspirin,
33			Systematic		& Internal	industry				thromboembolism	rivaroxaban
34			Reviews							Sexually active	Placebo
35			Cochrane							adults (16 years and	
36			Database of							over) with genital	
37			Systematic							ulcers compatible	Macrolide antibiotics - 3
38	Romero <sup>80</sup>	2017	Reviews	6.8	Medicine, General	Non-	0/3	7	1983-1999	with chancroid	types
39			Cochrane								Other antibiotics - 4
40			Database of								types
41			Systematic								
42			Reviews								
43	Rosomeck <sup>81</sup>	2018	Systematic	6.8	Medicine, General	Non-	0/3	15	1996-2016	People with scabies	
44			Reviews		& Internal	industry				of all ages and either	Ivermectin
45			Cochrane							sex	Permethrin
46			Database of								
47			Systematic								
48			Reviews								
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5	Sankar <sup>84</sup>	2018	Systematic	6.8	Medicine, General	No	0/3	6	2011-2016	Preterm infants with	Anti-vascular endothelial	
6			Reviews		& Internal	funding				retinopathy	growth factor agents - 2	Cryo/laser therapy
7											types	
8											Levosimendan,	
9			Cochrane							Adults (18 years and	epinephrine,	
10			Database of		Medicine, General	Non-				over) with	norepinephrine-	
11	Schumann <sup>85</sup>	2018	Systematic	6.8	& Internal	industry	3/9	13	1990-2013	cardiogenic shock or	dobutamine, amrinone,	Placebo, no treatment
12			Reviews							acute low cardiac	dopexamine, dopamine,	
13										output syndrome	nitric oxid	
14	Simancas-		Cochrane		Medicine, General	Non-				People suffering	Acetazolamide, ibuprofen,	Placebo, normal air,
15	Racines <sup>86</sup>	2018	Database of	6.8	& Internal	industry	0/6	13 <sup>k</sup>	1992-1994	from high altitude	dexamethasone, oxygen,	unspecified control,
16			Reviews							illness	nitric oxide, gabapentin,	paracetamol
17			Cochrane								sumatriptan	
18	Smith <sup>87</sup>	2017	Database of	6.8	Medicine, General	Non-	0/2	4	1998-2015	Adults and children	Salmeterol, tiotropium	No treatment, placebo
19			Systematic		& Internal	industry				with cystic fibrosis		Placebo, no treatment,
20			Reviews									intramuscular or
21	Smith <sup>88</sup>	2018	Cochrane	6.8	Medicine, General	Non-	0/3	70	1958-2017	Women in labour	Intramuscular or	intravenous opioids -
22			Database of		& Internal	industry					intravenous opioids -	16 types
23			Systematic								16 types	
24			Reviews								Alkaloids - 3 types,	
25											antidepressants - 3 types,	
26											levetiracetam,	
27			Cochrane								cyproheptadin,	
28	Soares-Weiser <sup>89</sup>	2018	Database of	6.8	Medicine, General	Non-	0/5 <sup>l</sup>	24 <sup>m</sup>	1971-2014	Adults with chronic	promethazine, buspiron,	Placebo
29			Systematic		& Internal	industry				psychiatric disorders	cognitive enhancers - 2	
30			Reviews							People with	types, VMAT2 inhibitors,	
31										coronary disease,	ethyleicosapentaenoic acid	
32										ischaemic	(ethyl-EPA), hormones - 3	
33										cerebrovascular	types, lithium, ceruletide	
34			Cochrane							disease, peripheral		
35	Squizzato <sup>90</sup>	2017	Database of	6.8	Medicine, General	Non-	2/5	15	2001-2017	arterial disease, or at	Clopidrogel	Placebo, usual care
36			Systematic		& Internal	industry				high risk of	Articaine, articaine +	(aspirin)
37			Reviews							atherothrombotic	epinephrine, lidocaine +	
38										disease	epinephrine, bupivacaine +	
39			Cochrane								epinephrine, mepivacaine	
40			Database of		Medicine, General	Non-				Individuals	+ epinephrine,	
41	St George <sup>91</sup>	2018	Systematic	6.8	& Internal	industry	1/7	123	1954-2017	undergoing dental	mepivacaine +	Local anaesthetics
42			Reviews							procedures and	levonordefrin,	
43										volunteers who took		
44										part in simulated		
45										scenario studies		
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mepivacaine, prilocaine,  
prilocaine + felypressin,  
prilocaine + epinephrine

Stern <sup>92</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/6	17	1972-2015	Adults and children with pneumonia	Corticosteroids - 7 types	Placebo, usual care
Sturman <sup>93</sup>	2017	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	No funding	0/3	4	1995-2013	Children and adolescents (18 years or under) with autism spectrum disorder (ASD) or pervasive developmental disorder (PDD)	Methylphenidate	Placebo
Tammenmaa-Aho <sup>94</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/4	14	1976-2014	Psychiatric patients with antipsychotic-induced tardive dyskinesia	Cholinergic drugs - 6 types	Placebo
Temmingh <sup>95</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	2/4	8	2006-2014	Adults (17 years and over) with severe mental illness and co-occurring substance use disorder	Risperidone	Other antipsychotics - 5 types
Tenforde <sup>96</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	1/7	13	1997-2018	Adults with HIV-associated cryptococcal meningitis	Antifungal induction therapies - 6 types	Network meta-analysis
Toews <sup>97</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/7	103 <sup>n</sup>	1977-2016	People admitted to intensive care units	H2 receptor antagonists, proton pump inhibitors, prostaglandin analogues, anticholinergics, antacids, sucralfate, teprenone, naloxone, bioflavonoids	H2 receptor antagonists, proton pump inhibitors, prostaglandin analogues, anticholinergics, antacids, sucralfate, teprenone, placebo, no treatment, other medication (not defined)
Venekamp <sup>98</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	1/4	3 <sup>o</sup>	1992-1996	Children (16 years and under) with recurrent acute otitis media	Antibiotics - 3 types	Grommets
Vermeij <sup>99</sup>	2018	Cochrane Database of Systematic Reviews	6.8	Medicine, General & Internal	Non-industry	0/6	8	1998-2016	Individuals who had an ischemic or hemorrhagic stroke	Preventive antibiotics	Placebo, standard care



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4	Chen <sup>111</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/3	9	2009-2017	Patients with sepsis	Statins - 3 types	Placebo
5										Patients with hormone receptor-positive or human epidermal growth factor receptor 2		
6										negative advanced breast cancer	Cyclin-dependent kinases 4/6 inhibitors - 3 types	Placebo
7										Adults undergoing total knee		
8										arthroplasty (TKA)	Tranexamic acid (TXA)	Placebo, no treatment
9	Ding <sup>112</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/6	6	2014-2017	Patients with myocardial infarction		
10										Patients with acute coronary syndrome, percutaneous coronary intervention, or coronary stents given combination therapy with aspirin and clopidogrel		
11	Guo <sup>113</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/8	5	2004-2017	Patients with pterygium or glaucoma		
12										Patients with diabetic peripheral neuropathy	Fasudil + methylcobalamin or lipoic acid	Methylcobalamin or lipoic acid alone
13										Adult women with pathologically confirmed epithelial ovarian cancer	Antiangiogenic therapy (7 included) alone or combined with chemotherapy	Placebo or chemotherapy alone
14	Han <sup>114</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/7	18	2007-2016	Patients with advanced non-small cell lung cancer	Immune checkpoint inhibitors: anti-PD1/PD-L1 therapies - 3 types	Chemotherapy - 6 regimens
15										Patients undergoing total knee or hip arthroplasty	Acetaminophen	Normal saline or placebo
16										Adults with social anxiety disorder	Fluvoxamine	Placebo
17										Children and adults requiring nasogastric intubation	Lidocaine	Normal saline, K-Y lubricant gel, or no treatment
18										Adults with intertrochanteric fractures preparing for internal fixation	Tranexamic acid	Placebo, no treatment
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20	Hu <sup>115</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/5	4	2010-2016			
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23	Huang <sup>116</sup>	2018	Medicine	2.0	Medicine, General & Internal	Not reported	0/5	18	2010-2015			
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25	Jiang <sup>117</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/5	13	2010-2017			
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28	Jiang <sup>118</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/4	15	2011-2016			
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30	Khan <sup>119</sup>	2018	Medicine	2.0	Medicine, General & Internal	Non-industry	0/8	7	2015-2017			
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33	Liang <sup>120</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/4	3	2016-2017			
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35	Liu <sup>121</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/7	5	1999-2007			
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37	Lor <sup>122</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/8	10	1999-2015			
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41	Wang <sup>123</sup>	2017	Medicine	2.0	Medicine, General & Internal	No funding	0/2	4	2015-2017			
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Zhou <sup>137</sup>	2018	Medicine	2.0	Medicine, General & Internal	No funding	0/4	6	2013-2017	symptomatic cholelithiasis and acute cholecystitis who prepared for laparoscopic cholecystectomy Adults with end-staged knee osteoarthritis undergoing total knee arthroplasty	Dexamethasone	Placebo, no treatment
Zhu <sup>138</sup>	2018	Medicine Postgraduate	2.0	Medicine, General & Internal	Not reported	0/3	8	2002-2016	Patients who underwent total hip arthroplasty	Selective non-steroidal anti-inflammatory drugs (selective COX-2 inhibitors) - 4 types	Non-selective non-steroidal anti-inflammatory drugs (non-selective COX-2 inhibitors) - 4 types
Zhou <sup>139</sup>	2018	Medicine	2.1	Medicine, General & Internal	No funding	0/5	10	2007-2017	Patients with dyslipidemia	Anacetrapib	Placebo, placebo + usual care
Zhang <sup>140</sup>	2018	Revista da Associação Médica Brasileira	0.7	Medicine, General & Internal	Non-industry	Not reported/6	6	2012-2016	Patients with complicated intra-abdominal infections and complicated urinary tract infections	Ceftazidime-avibactam	Other antibiotics - 3 types, usual care

**Specialty medicine (n = 100)**

Li <sup>141</sup>	2018	Acta Ophthalmologica	3.3	Ophthalmology	Non-industry	Not reported/3	72	1995-2015	Patients with primary open-angle glaucoma or ocular hypertension	Prostaglandin analogues, alpha-2 adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors, miotics	Placebo - Network meta-analysis
Tarantini <sup>142</sup>	2018	American Heart Journal	4.2	Cardiac & Cardiovascular Systems	No funding	0/7	5	2007-2016	Patients with acute coronary syndrome	P2Y12 receptor inhibitors - 2 types	Clopidogrel
Wang <sup>143</sup>	2018	American Journal of Cardiovascular Drugs	2.7	Cardiac & Cardiovascular Systems; Pharmacology & Pharmacy	Non-industry	0/3	5	2014-2017	Adults aged 18-65 years with hyperlipidemia	Inclisiran	Placebo, other lipid-lowering agents - Network meta-analysis
Aman <sup>144</sup>	2018	Anaesthesia and Intensive Care	1.7	Anesthesiology; Critical Care Medicine	Non-industry	Not reported/5	10	1995-2015	Patients undergoing caesarean section under general anaesthesia	Opioid analgesics - 3 types, non-opioid analgesics - 5 types	Placebo
Li <sup>145</sup>	2018	Autoimmunity Reviews	8.7	Immunology	Non-industry	0/7	15	2004-2017	Patients with rheumatoid arthritis	Statins - 2 types	Conventional treatment, placebo + conventional treatment
Wang <sup>146</sup>	2018	Biomed Research International	2.6	Biotechnology & Applied Microbiology; Medicine, Research & Experimental	Non-industry	0/4	15	2006-2017	Patients with left ventricular dysfunction undergoing cardiac surgery	Levosimendan	Placebo, milrinone, dopamine, intra-aortic balloon pump (IABP), and standard inotropic agents

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4										Adults with history of colorectal cancer or adenoma	Aspirin, non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs)	Placebo, no treatment
5	Veettil <sup>147</sup>	2017	BMC Cancer	3.3	Oncology	No funding	0/6	8	2003-2014		Purine-like xanthine oxidase inhibitors - 2 types, non-purine-like xanthine oxidase inhibitors - 2 types	
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8			BMC Cardiovascular Disorders	1.8	Cardiac & Cardiovascular Systems	No funding	0/9	91	1973-2017	Adults under treatment for any clinical condition		Placebo, no treatment
9	Bredemeier <sup>148</sup>	2018								Patients with post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP)	Nonsteroidal anti-inflammatory drugs (NSAIDs) - 6 types	
10												
11			BMC Gastroenterology	2.7	Gastroenterology & Hepatology	Non-industry	0/5	22	2003-2017	Patients with invasive fungal infections		Placebo
12	Lyu <sup>149</sup>	2018										
13			BMC Infectious Diseases	2.6	Infectious Diseases	Non-industry	0/6	16	2001-2016	Patients undergoing total shoulder arthroplasty or reverse shoulder arthroplasty	Voriconazole	Other antifungal agents - 7 types
14	Xing <sup>150</sup>	2017										
15			BMC Musculoskeletal Disorders	2.0	Orthopedics; Rheumatology	No funding	0/4	3	2015-2017		Tranexamic acid	Placebo
16											Pharmacological agents for traumatic brain injury – 14 types, pharmacological agents for stroke – 23 types, pharmacological agents for bacterial meningitis – 1 type, pharmacological agents for intracerebral haemorrhage – 6 types, pharmacological agents for aneurysmal subarachnoid hemorrhage – 19 types	
17										Patients with ischemic or hemorrhagic stroke, traumatic brain injury, or bacterial meningitis		Unspecified control
18			BMC Neurology	2.2	Clinical Neurology	No funding	0/3	110 <sup>a</sup>	1983-2015	Patients with primary or recurrent pterygium undergoing surgical removal combined with toxic agents	Anti-fibrotic and anti-VEGF (vascular endothelial growth factor) medications - 3 types	Placebo - Network meta-analysis
19	Beez <sup>152</sup>	2017								Patients with acute coronary syndrome and patients who underwent percutaneous coronary intervention		
20			BMC Ophthalmology	1.8	Ophtamology	No funding	0/7	32	1990-2016			
21	Zeng <sup>153</sup>	2017										
22			BMC Pharmacology & Toxicology	1.9	Pharmacology & Pharmacy; Toxicology	Non-industry	0/3	4	2013-2016		Prasugrel	Ticagrelor
23	Bundhun <sup>154</sup>	2017										
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Zhang <sup>155</sup>	2017	BMC Psychiatry	2.4	Psychiatry	No funding	0/11	47	2003-2015	People with schizophrenia or related disorders that had a duration of treatment that was no more than 1 year	Antipsychotic drugs - 12 types	Placebo - Network meta-analysis
Zhang <sup>156</sup>	2017	BMC Pulmonary Medicine	2.7	Respiratory System	No funding	0/5	19	1996-2016	Patients with acute exacerbations of chronic obstructive pulmonary disease (COPD)	Antibiotics - 17 types	Placebo - Network meta-analysis
Zhang <sup>157</sup>	2017b	BMC Pulmonary Medicine	2.7	Respiratory System	Non-industry	0/4	25	1993-2016	Preterm infants	Corticosteroids	Placebo
Ramos-Esquivel <sup>158</sup>	2018	Breast Cancer British Journal of Sports Medicine	1.8	Oncology; Obstetrics & Gynecology	No funding	0/4	3	2016-2017	Post-menopausal women with metastatic HR-positive, HER2-negative breast cancer	Cyclin-dependent kinase 4/6 inhibitors - 3 types + aromatase inhibitor - 2 types	Aromatase inhibitors - 2 types
Zeng <sup>159</sup>	2018	Sport Sciences	7.9	Sport Sciences	Non-industry	0/12	36	1979-2016	Patients with osteoarthritis in any joint	Non-steroidal anti-inflammatory drugs - 9 types	Network meta-analysis FOLFOX (leucovorin + fluorouracil + oxaliplatin) + bevacizumab, FOLFIRI (leucovorin + fluorouracil + irinotecan) + bevacizumab
Shui <sup>160</sup>	2018	Cellular Physiology and Biochemistry	5.5	Cell Biology; Physiology	Not reported	0/6	4	2015-2017	Patients with metastatic colorectal cancer	FOLFOXIRI (leucovorin + fluorouracil + oxaliplatin + irinotecan) + bevacizumab	Miltefosine, paromomycin, antimonial compounds - 2 types, pentamidine, sitamaquine
Rodrigo <sup>161</sup>	2018	Clinical Microbiology and Infection	5.4	Infectious Diseases; Microbiology	No funding	0/4	28	1996-2017	Patients with visceral leishmaniasis	Amphotericin B	Placebo, nonsteroidal anti-inflammatory drugs (NSAIDs), disease modifying antirheumatic drugs (DMARDs)
Wang <sup>162</sup>	2018	Clinical Rheumatology	2.1	Rheumatology	Non-industry	0/3	25	2002-2014	Patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis	Tumor necrosis factor (TNF) inhibitors - 5 types, non-tumor necrosis factor (TNF) inhibitors - 2 types	Low molecular-weight heparin (LMWH) – 5 types, enoxaparin + vitamin K antagonists (VKA)
Hong <sup>163</sup>	2018	Critical Reviews in Oncology / Hematology	4.5	Oncology; Hematology	No funding	1/5	13	1996-2015	Adults with acute venous thromboembolism	Proprotein convertase subtilisin/kexin type 9 gene inhibitors (PCSK9i)	Rivaroxaban, unfractionated heparin (UFH)
de Carvalho <sup>164</sup>	2018	Diabetes Care	13.4	Endocrinology & Metabolism	Not reported <sup>f</sup>	0/3	20	2012-2017	Patients with familial or nonfamilial		Placebo, placebo + other lipid-lowering therapy

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5			Digestive							a		
6	Jaafar <sup>165</sup>	2018	Diseases and Sciences	2.8	Gastroenterology & Hepatology	Not reported	0/5	17	2000-2016	Adults (18 and over) with organic or functional dyspepsia	Rebamipide	Placebo, standard treatment, no treatment
7										Patients with neurodegenerative movement disorders		
8	Liu <sup>166</sup>	2018	Drug Delivery	3.1	Pharmacology & Pharmacy	Not reported	0/2	9	2002-2015	Patients undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI)	Riluzole	Placebo
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12			Drug Design, Development and Therapy	2.9	Chemistry, Medicinal; Pharmacology & Pharmacy	Not reported	0/5	9	2010-2016	Adults (≥ 18 years) undergoing spinal anesthesia	Atorvastatin	Placebo
13	Liu <sup>167</sup>	2018										
14			Drug Design, Development and Therapy	2.9	Chemistry, Medicinal; Pharmacology & Pharmacy	Not reported	0/5	9	2009-2016	Adults with traumatic brain injuries and depressive disorders	Dexmedetomidine	Fentanyl
15	Sun <sup>168</sup>	2017										
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18			East Asian Archives of Psychiatry	None	Not applicable	Not reported	0/2	4	2005-2010	Adults with traumatic brain injuries and depressive disorders	Antidepressants - 2 types	Placebo
19	Paraschakis <sup>169</sup>	2017	Emergency Medicine Journal	2.0	Emergency Medicine	No funding	0/8	4	2001-2016	Patients taking acute antiemetic drugs	Diphenhydramine	Placebo
20	D'Souza <sup>170</sup>	2018								Adult women with epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer who have achieved complete clinical remission after debulking surgery and first-line chemotherapy		
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28			European Journal of Gynecological Oncology	0.6	Oncology; Obstetrics & Gynecology	Not reported	Not reported/4	4	2004-2013	Patients with chronic breathlessness	CA125-targeted antibody – 2 types	Placebo
29	Mei <sup>171</sup>	2016										
30			Respiratory Journal	12.2	Respiratory System	Non-industry	3/9 <sup>a</sup>	35	1982-2015	Critically ill patients receiving stress ulcer prophylaxis (SUP)	Opioids - 8 types	Placebo
31	Verberkt <sup>172</sup>	2017	Expert Opinion on Pharmacotherapy	3.5	Pharmacology & Pharmacy	No funding	0/3	51	1980-2016	Patients undergoing coronary artery bypass surgery	Antacids, proton pump inhibitors (PPI), histamine-2 receptor antagonists (H2RA), and sucralfate	Placebo - Network meta-analysis
32												
33			Expert Review of Clinical Pharmacology	2.8	Pharmacology & Pharmacy	No funding	0/4	5	1999-2012	Patients undergoing coronary artery bypass surgery	Lidocaine	Placebo
34	Sridharan <sup>173</sup>	2018										
35												
36			Expert Review of Clinical Pharmacology	2.8	Pharmacology & Pharmacy	Non-industry	0/4	14	2002-2017	Patients with stable angina pectoris requiring elective percutaneous	Nicorandil	Placebo (saline, isosorbide dinitrate), no treatment
37	Habibi <sup>174</sup>	2018										
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40	Li <sup>175</sup>	2018										
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5	Zhu <sup>189</sup>	2018	Clinical	2.6	Oncology	Non-	0/7	35	2005-2016	Cancer patients	Anti-EGFR monoclonal	Placebo, usual care
6			Oncology			industry					antibodies (EGFR-MoAbs)	
7			International									
8	Liu <sup>190</sup>	2018	Journal of	1.8	Neurosciences	Not	0/2	4	2007-2016	Patients with	Lacosamide	Placebo
9			Neuroscience			reported				seizures		
10										Patients with		
11	Coccolini <sup>191</sup>	2018	International	2.7	Surgery	No	0/12	15	1993-2014	advanced gastric and	Neoadjuvant chemotherapy	No neoadjuvant
12			Journal of			funding				esophago-gastric	(with surgery)	chemotherapy (only
13			Surgery							cancer		surgery)
14	Fan <sup>192</sup>	2018	International	2.7	Surgery	Non-	0/8	7	2005-2016	Patients with	Dexamethasone	Placebo, no treatment
15			Journal of			industry				scheduled total knee		("nothing controlled
16			Surgery							arthroplasty		multimodal analgesia
17										Patients with a		method")
18										diagnosis of		
19	Li <sup>193</sup>	2018	International	2.7	Surgery	No	0/5	6	2008-2017	symptomatic	Lidocaine	Placebo, saline
20			Journal of			funding				cholelithiasis and		
21			Surgery							acute cholecystitis		
22										who prepared for		
23										laparoscopic		
24	Li <sup>194</sup>	2018	International	2.7	Surgery	No	0/4	17	1998-2017	cholecystectomy	Anaesthetic medications -	No drug - Network
25			Journal of			funding				Patients undergoing	12 types	meta-analysis
26			Surgery							anaesthesia as part		
27										of endoscopic		
28	Liu <sup>195</sup>	2018	International	2.7	Surgery	Non-	0/5	3 <sup>†</sup>	2005-2017	retrograde	Tranexamic acid	Aminocaproic acid
29			Journal of			industry				cholangiopancreatog		
30			Surgery							raphy		
31	Ran <sup>196</sup>	2018	International	2.7	Surgery	No	0/5	5	2002-2016	Patients undergoing	Hyaluronic acid	Methylprednisolone
32			Journal of			funding				total knee		
33			Surgery							arthroplasty or total		
34	Zhu <sup>198</sup>	2018	International	2.7	Surgery	Non-	0/5	6	2004-2017	hip arthroplasty	Ketamine	Saline
35			Journal of			industry				Patients with		
36			Surgery							symptomatic knee		
37	Wagner <sup>199</sup>	2018	International	3.8	Clinical Neurology; Psychiatry	No	0/5	5	2002-2016	osteoarthritis	Second generation	Placebo - Network
38			Journal of			funding				hepatocellular	antidepressants - 16 types	meta-analysis
39			Surgery							carcinoma		
40	Hickman <sup>200</sup>	2018	International	2.8	Genetics & Heredity; Obstetrics & Gynecology;	No	0/5	10	2007-2016	Adult patients	Gonadotropin-releasing	Standard treatment
41			Journal of			reported				prepared for	hormone agonists (GnRHa)	(chemotherapy only)
42			Assisted							laparoscopic	- 7 types	
43			Reproduction							cholecystectomy		
44			and Genetics							Adults with major		
45										depressive disorder		
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3					Reproductive							
4				Biology						cancer undergoing		
5										chemotherapy		
6											Programmed death 1 (PD-	
7											1)/programmed death	
8	Luo <sup>201</sup>	2018	Journal of Cancer Research and Clinical Oncology	3.3	Oncology	Non-industry	0/4	8	2015-2017	Patients with non-small-cell lung carcinoma	ligand 1 (PD-L1) inhibitors - 3 types	Chemotherapy - 2 types
9			Journal of Cancer Research and Clinical Oncology									
10										Patients with metastatic castration-resistant prostate cancer	Targeted agents - 16 types	Placebo - Network meta-analysis
11	Wang <sup>202</sup>	2018	Journal of Cancer Research and Therapeutics	3.3	Oncology	Non-industry	0/5	26	2010-2017			
12												
13												
14	Wang <sup>203</sup>	2018		0.8	Oncology	No funding	0/4	35	1997-2011	Cancer patients with moderate to severe pain	Fentanyl	Morphine
15										Adults (18 years and over) undergoing any type of cardiac surgery	Aspirin	Placebo, discontinuation of aspirin greater than 7 days before surgery
16	Aboul-Hassan <sup>204</sup>	2017	Journal of Cardiac Surgery	1.2	Cardiac & Cardiovascular Systems; Surgery	No funding	0/8	12	1985-2016			
17												
18												
19												
20												
21	Wang <sup>205</sup>	2018	Journal of Cardiovascular Surgery	1.2	Cardiac & Cardiovascular Systems; Surgery; Peripheral Vascular Disease	Not reported	0/6	5	1999-2010	Patients undergoing isolated coronary artery bypass graft (CABG) surgery	Statins - 3 types	No preoperative statin
22											Antiandrogens, insulin sensitizers, estrogen-progestin oral contraceptives pills (OCPs), OCPs + antiandrogen, OCPs + insulin sensitizer, antiandrogen + insulin sensitizer	
23												
24												
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27												
28	Barrionuevo <sup>206</sup>	2018	Journal of Clinical Endocrinology and Metabolism	5.8	Endocrinology & Metabolism	Non-industry	0/8	32	1989-2016	Women with hirsutism		Placebo - Network meta-analysis
29												
30												
31	Cui <sup>207</sup>	2018	Journal of Clinical Pharmacy and Therapeutics	1.7	Pharmacology & Pharmacy	Not reported	0/6	23	1993-2014	Patients with type 2 diabetes	Statins - 6 types	Placebo - Network meta-analysis
32												
33												
34	Sawyer <sup>208</sup>	2018	Journal of Dermatological Treatment	2.1	Dermatology	Industry	6/6	54	2001-2016	Adults with moderate-to-severe chronic plaque-type psoriasis	Apremilast, biological therapies - 7 types	Placebo - Network meta-analysis
35												
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40	Markey <sup>209</sup>	2018	Journal of Emergency Medicine	1.2	Emergency Medicine	Not reported	Not reported/3	11	1989-2004	Patients with onset of atrial fibrillation (AF) within 48 h, who were hemodynamically stable and without evidence of acute coronary syndrome,	Flecainide	Placebo, verapamil, and other active anti-dysrhythmics
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									congestive heart failure, or structural heart disease		
									Adult patients (18 years and over) taking low-dose aspirin for a minimum of 2 weeks	Proton-pump inhibitors (PPIs) - 5 types	Histamine-2 receptor antagonists (H2RAs) - 2 types
Szabó <sup>210</sup>	2017	Journal of Gastrointestinal and Liver Diseases	2.0	Gastroenterology & Hepatology	Not reported	0/15	10 <sup>w</sup>	2009-2016	Patients with histologically confirmed solid cancer		
Su <sup>211</sup>	2018	Journal of Immunology Research	3.3	Immunology	Non-industry	0/6	15	2011-2017		Immune checkpoint inhibitors (ICIs) - 5 types	Placebo or chemotherapy
Chen <sup>212</sup>	2018	Journal of Interventional Cardiac Electrophysiology	1.5	Cardiac & Cardiovascular Systems	Non-industry	0/9	8	2006-2017	Patients with persistent atrial fibrillation	Antiarrhythmic drugs	Catheter ablation
Chen <sup>213</sup>	2017	Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	No funding	0/4	6	2008-2014	Patients undergoing knee arthroscopy	Midazolam	Placebo
Li <sup>214</sup>	2018	Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	Not reported	0/5	3 <sup>x</sup>	2002-2017	Patients undergoing a primary total hip or knee arthroplasty	Aminocaproic acid	Placebo or no treatment
Luo <sup>215</sup>	2018	Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	Not reported	0/4	3 <sup>y</sup>	2002-2017	Patients treated with spine surgery	Tranexamic acid	Control (not specified)
Ma <sup>216</sup>	2018	Journal of Orthopaedic Surgery and Research	1.6	Orthopedics	No funding	0/4	4	1991-2015	Patients who underwent hip surgery	Naproxen	Placebo
He <sup>217</sup>	2018	Journal of Psychiatric Research	4.0	Psychiatry	Non-industry	0/8	22	2009-2015	Patients with a primary diagnosis of major depressive disorder (MDD)	Vortioxetine, levomilnacipran, vilazodone	Placebo
Wang <sup>218</sup>	2018	Journal of Stroke & Cerebrovascular Diseases	1.6	Neurosciences; Peripheral Vascular Disease	Non-industry	4/8	6	2003-2013	Asian patients with non-valvular atrial fibrillation (AF)	Warfarin, direct oral anticoagulants (DOACs) - 5 types	Network meta-analysis
Dhana <sup>219</sup>	2018	Journal of the American Academy of Dermatology	6.9	Dermatology	No funding	0/6	15	2000-2016	People with scabies	Permethrin	Ivermectin
Karatasakis <sup>220</sup>	2017	Journal of the American Heart Association	4.5	Cardiac & Cardiovascular Systems	Not reported	3/12 <sup>z</sup>	35	2012-2017	Adults with hypercholesterolemia	Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors - 2 types	Placebo, ezetimibe, standard therapy

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3			Journal of the									
4			European									
5			Academy of							Adult patients (≥ 18)		
6			Dermatology and			Non-				with moderate-to-		
7	Kuo <sup>221</sup>	2018	Venereology	4.3	Dermatology	industry	2/4	4	2012-2016	severe plaque	Tofacitinib	Placebo
8			Journal of									
9			Traditional									
10	Liu <sup>222</sup>	2016	Chinese	0.9	Integrative &	Non-	Not	16	2005-2015	Patients with	Methotrexate	Sinomenine
11			Medicine		Complementary	industry	reported/6			rheumatoid arthritis		
12					Biochemistry &							
13					Molecular Biology;							
14			Journal of		Biotechnology &					Adult patients		
15	Zheng <sup>223</sup>	2017	Zhejiang	1.8	Applied	Not	0/7	8	1990-2014	undergoing cardiac	Amiodarone, lidocaine	Placebo
16			University-		Microbiology;	reported				aortic cross-clamp		
17			SCIENCE B		Medicine, Research					Patients with		
18					& Experimental					isoniazid-resistant,		Usual care (REZ =
19	Fregonese <sup>224</sup>	2018	Lancet	21.5	Critical Care	Non-	0/57	2	2010-2014	rifampicin-	Fluoroquinolone,	rifampicin,
20			Respiratory		Medicine;	industry			2010-	susceptible	streptomycin	ethambutol,
21			Medicine		Respiratory System				2010-	tuberculosis		pyrazinamide)
22									Unpublishe			
23	Bornstein <sup>225</sup>	2018	Neurological	2.3	Clinical Neurology;	Not	Not	9	d	Patients during early	Cerebrolysin	Placebo
24			Sciences		Neurosciences	reported	reported/10			post-stroke period	Bevacizumab,	Placebo,
25										Patients arranged for	bevacizumab +	antimetabolite - 2
26	Chen <sup>226</sup>	2018	Ophthalmic	1.8	Ophthalmology		0/4	3	2013-2015	primary	antimetabolite - 2	types
27			Research		Anesthesiology;					trabeculectomy		
28	Han <sup>227</sup>	2017	Pain Physician	2.6	Clinical Neurology	No	0/4	10	2004-2016	Patients undergoing	Gabapentin	Placebo
29						funding				spinal surgery		
30										Adult patients		
31	Peng <sup>228</sup>	2017	Pain Physician	2.6	Anesthesiology;	No	0/5	18	2004-2016	undergoing surgical	Dexmedetomidine +	Opioids
32					Clinical Neurology	funding				procedures	opioids	
33					Chemistry,							
34					Medicinal;							
35					Chemistry,							
36					Multidisciplinary;							
37	Feng <sup>229</sup>	2016	Pharmazie	1.0	Pharmacology &	Not	0/7	2 <sup>aa</sup>	2011-2012	Patients with	V-5 immunitor	Usual care
38					Pharmacy	reported				tuberculosis		(chemotherapy), usual
39					Chemistry,							care + placebo
40					Medicinal;							
41					Chemistry,							
42					Multidisciplinary;							
43					Pharmacology &							
44					Pharmacy							
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4										Adults with			
5										persistent depressive			
6										disorder (DSM-5),			
7										chronic major	Antidepressants - 6 types,		
8										depression, recurrent	cognitive-behavioral		
9										major depression	analysis system of		
10										with incomplete	psychotherapy,		
11			Psychotherapy							interepisode	combination of		
12	Furukawa <sup>232</sup>	2018	and Psychosomatics	13.1	Psychiatry;	Non-	2/11	3	2000-2015	recovery or	antidepressants and		
13					Psychology	industry				dysthymia (DSM-	cognitive-behavioral		Network meta-analysis
14										IV), or any	analysis system of		
15	Liu <sup>233</sup>	2018	Renal Failure	1.4	Urology &	Not	0/6	12	2006-2015	corresponding	psychotherapy		
16					Nephrology	reported				conditions			
17										Adult patients with	Uric acid-lowering therapy	Placebo, usual therapy,	
18										chronic kidney	- 2 types	no treatment	
19	Miravitlles <sup>234</sup>	2017	Respiratory	3.8	Respiratory System	Industry	3/4	10	2014-2016	disease		Tiotropium or	
20			Research							Adults with a		olodaterol as	
21										history of chronic		monotherapy,	
22										obstructive		salmeterol +	
23										pulmonary disease	Tiotropium + olodaterol	fluticasone	
24										(COPD)		Corticosteroid + fast-	
25										Patients with		onset-acting β2-	
26										intermittent or mild	Corticosteroids, fast-onset-	agonist	
27										persistent asthma	acting β2-agonists		
28										Adults (18 years and			
29										over) with moderate	Tumor necrosis factor		
30										to severe psoriatic	(antiTNF)-α inhibitors - 4	Placebo - Network	
31										arthritis (PsA)	types	meta-analysis	
32										Adult patients (18			
33										years and over)			
34										treated for the			
35										secondary			
36										prevention of			
37										cardiovascular,			
38										peripheral vascular,			
39										and cerebrovascular	Proton pump inhibitors	Thienopyridines - 2	
40										disease	(PPI) + thienopyridines	types	
41										Adults (18 and over)			
42										undergoing			
43										gastrointestinal			
44										endoscopy	Midazolam	Propofol	
45										Asian and non-			
46										Asian adults (18			
47										years and older)			
										with acute venous	Direct oral anticoagulants	Vitamin K antagonists	
										thromboembolism	(DOACs) - 4 types	(VKAs), heparin	
										HIV-positive people	Influenza vaccine, Placebo	Network meta-analysis	

**Multidisciplinary sciences (n = 10)**

Chen <sup>241</sup>	2018	Medical Science Monitor	1.9	Medicine, Research & Experimental	Non-industry	0/5	20 <sup>cc</sup>	2000-2016	Patients with essential hypertension Adult patients (over 18 years old) that underwent the extraction of any tooth	Anti-hypertensive drugs - 8 types	Acupuncture
Arteagoitia <sup>242</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/3	8	1989-2015	Adults with osteoarthritis or rheumatoid arthritis of the knee or hip	Chlorhexidine	Placebo, standard treatment
Feng <sup>243</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/4	9	2002-2009	Pediatric surgical patients	Etoricoxib	Placebo, other non-steroidal anti-inflammatory drugs (NSAIDs) - 2 included
Kawakami <sup>244</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/5	6	2007-2017	Adults (18 years and over) diagnosed with generalized anxiety disorder (GAD)	Magnesium	Placebo, no treatment
Li <sup>245</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/7	8	2007-2014	Patients with hypertension and chronic kidney disease stage 3 to 5 and dialysis	Duloxetine	Placebo
Lin <sup>246</sup>	2017	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	0/6	21	1992-2012	Adults (19 years and over) undergoing cardiac surgery	Calcium channel blockers	Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers
Ling <sup>247</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	Not reported/6	9	2003-2017	Cancer patients	Dexmedetomidine	Propofol, morphine, placebo
Rohner <sup>248</sup>	2017	PLOS ONE	2.8	Multidisciplinary Sciences	Non-industry	2/7	94	1993-2014	Patients with atrial fibrillation or atrial flutter	Erythropoiesis-stimulating agents	Usual care
Sethi <sup>249</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	No funding	0/6	28	1986-2017	Post renal transplant patients	Digoxin	Placebo, no intervention, beta blockers, calcium antagonists, amiodarone
Wolf <sup>250</sup>	2018	PLOS ONE	2.8	Multidisciplinary Sciences	Industry	1/9	13	2002-2016		mTOR-inhibitors - 2 types	Calcineurin-inhibitors

<sup>a</sup>Only 3 studies reported that authors were employed by industry and therefore we included them as ties for the purposes of this table; <sup>b</sup>11/12 included RCTs had a drug arm; <sup>c</sup>33/38 included RCTs had a drug arm; <sup>d</sup>4/14 included RCTs had a drug arm; <sup>e</sup>One author reported pharmaceutical company employment; <sup>f</sup>9/11 included RCTs had a drug arm; <sup>g</sup>71/120 included studies were RCTs; <sup>h</sup>24/25 included studies were RCTs; <sup>i</sup>Meta-analysis funding sources reported as 'None, Other' we coded as no study funding; <sup>j</sup>10/27 included RCTs had a drug arm; <sup>k</sup>Flow chart indicates that 0 RCTs were included in the quantitative synthesis, but 2 RCTs were quantitatively synthesized and 13 were included; <sup>l</sup>Declarations of interest were provided for only 3 out of 5 meta-analysis authors; <sup>m</sup>24/31 included RCTs had a drug arm; <sup>n</sup>103/106 included RCTs had a drug arm; <sup>o</sup>3/5 included RCTs had a drug arm; <sup>p</sup>34/60 included RCTs had a drug arm; <sup>q</sup>110/123 included RCTs had an eligible drug arm; <sup>r</sup>Salary was reported under 'funding' but they did not specify whether there was any funding for the study itself; <sup>s</sup>ICMJE forms only provided for 5/9 authors; <sup>t</sup>3/4 included studies were RCTs; <sup>u</sup>4/11 included studies were RCTs; <sup>v</sup>Four authors reported financial ties with a pharmaceutical company and employment by Symmetron, a company that provides health economic research services to pharmaceutical companies, and two authors reported employment by a pharmaceutical company; <sup>w</sup>10/12 included studies were RCTs; <sup>x</sup>3/7 included studies were RCTs; <sup>y</sup>3/4 included studies were RCTs; <sup>z</sup> Of the 3 authors that reported financial ties, one also reported industry employment; <sup>aa</sup>2/4 included studies were RCTs; <sup>bb</sup>14/30 included studies were RCTs; <sup>cc</sup>20/30 included studies were RCTs with a drug arm

eTable2. – Detailed reporting of study funding sources (F), author-industry financial ties (T), and author-industry employment (E) form included RCTs

First Author	Year	Journal	Funding Sources of Included Trials Reported in Meta-analysis?	Author-Industry Financial Ties of Included Trials Reported in Meta-analysis?	Author-Industry Employment of Included Trials Reported in Meta-analysis?	Location Reported					Abstract	Lay summary	Online appendix
						Risk of Bias Text	Risk of Bias Figure or Table	Main Text, Other than Risk of Bias	Other in Main Document (Characteristics of Included Studies Table, other table, footnote)				
<b>Cochrane Reviews (n = 107)</b>													
Abdel-Rahman <sup>1</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F	F		F		F	F	
Adams <sup>2</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F		F	F				
Agabio <sup>3</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No			F, T	F, T			F	
Al-Shahi Salman <sup>4</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	No			F	F				
Alabed <sup>5</sup>	2018	Cochrane Database of Systematic Reviews	Partial	No	Partial				F, E				
Allegretti <sup>6</sup>	2017	Cochrane Database of Systematic Reviews	Full	No	No	F	F				F	F	
Arechabala <sup>7</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	Partial	F	F, E	F, T	F, T, E			F	
Baandrup <sup>8</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	Partial	F	F	F	F, T, E			F	
Bala <sup>9</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No	F			F				
Barbato <sup>10</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No								
Bergman <sup>11</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No				F, T				
Bighelli <sup>12</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	Partial	F	F, T, E	F	F, T, E	F		F	
Birks <sup>13</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No			F	F, T	F			
Boyapati <sup>14</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No								
Brown <sup>15</sup>	2018	Cochrane Database of Systematic Reviews	Partial	Partial	No	F	F	F	F, T	F		F	
Bruins Slot <sup>16</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F				
Bryan <sup>17</sup>	2017	Cochrane Database of Systematic Reviews	Partial	No	No				F				



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Bryant-Smith <sup>18</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F
Burry <sup>19</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No		F	F	F
Campschroer <sup>20</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No				F, T
Candy <sup>21</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No			F	F
Chiew <sup>22</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No				
Das <sup>23</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No			F	F F
Demicheli <sup>24</sup>	2018	Cochrane Database of Systematic Reviews	Full <sup>a</sup>	Partial	Partial				F, T, E
Demicheli <sup>25</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No				
Di Nisio <sup>26</sup>	2018	Cochrane Database of Systematic Reviews	Partial	Partial	No				F, T
El-Sayeh <sup>27</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No		F		F
Engelen <sup>28</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No				
Eshun-Wilson <sup>29</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No				F, T
Essali <sup>30</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F
Everitt <sup>31</sup>	2018	Cochrane Database of Systematic Reviews	Partial	Partial	No		F, T	F, T	F F, T
Fanshawe <sup>32</sup>	2017	Cochrane Database of Systematic Reviews	No	No	No				
Franik <sup>33</sup>	2018	Cochrane Database of Systematic Reviews	Full	Partial	No				F, T
González <sup>34</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F
Grabosch <sup>35</sup>	2018	Cochrane Database of Systematic Reviews	No	No	No				
Graves <sup>36</sup>	2018	Cochrane Database of Systematic Reviews	Partial <sup>b</sup>	No	No				F
Haas <sup>37</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No			F, T	F, T
Hakoum <sup>38</sup>	2018	Cochrane Database of Systematic Reviews	Full	Full	No				F, T
Heras-Mosteiro <sup>39</sup>	2017	Cochrane Database of Systematic Reviews	Partial <sup>c</sup>	Partial <sup>d</sup>	Partial				F, T, E
Janmaat <sup>40</sup>	2017	Cochrane Database of Systematic Reviews	No	No	No				
Jefferson <sup>41</sup>	2018	Cochrane Database of Systematic Reviews	Full	No	No				F
Jung <sup>42</sup>	2017	Cochrane Database of Systematic Reviews	Full	Full	Partial			F, T	F, T, E



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2												
3			Cochrane Database of									
4	Norman <sup>68</sup>	2018	Systematic Reviews	Full	No	Partial			F		F, E	
5	Normansell <sup>69</sup>	2018	Cochrane Database of	Full	No <sup>h</sup>	No			F		F	
6			Systematic Reviews									
7	Novoa <sup>70</sup>	2018	Cochrane Database of	Full	Partial <sup>h</sup>	No	F	F			F, T	F
8			Systematic Reviews									
9	Ohlsson <sup>71</sup>	2017	Cochrane Database of	Partial	No	No			F		F	
10			Systematic Reviews									
11	Ostinelli <sup>72</sup>	2018	Cochrane Database of	Full	No	No			F	F		
12			Systematic Reviews	Partial	Partial	No	F	F, T		F		
13	Ostinelli <sup>73</sup>	2018	Cochrane Database of	Full	Partial	No	F	F, T		F		
14	Ostuzzi <sup>74</sup>	2018	Systematic Reviews	Full	Partial	No	F	F, T		F		
15	Parker <sup>75</sup>	2018	Cochrane Database of	No	No	No						
16			Systematic Reviews	Partial	Partial	No	F, T	F, T		F		F
17	Pasquali <sup>76</sup>	2018	Cochrane Database of	Full	No	No			F		F	
18	Pike <sup>77</sup>	2018	Systematic Reviews	Full	No	No						
19			Cochrane Database of									
20	Rirash <sup>78</sup>	2017	Systematic Reviews	No	No	No						
21			Cochrane Database of									
22	Robertson <sup>79</sup>	2017	Systematic Reviews	No	No	No						
23			Cochrane Database of									
24	Romero <sup>80</sup>	2017	Systematic Reviews	Full	No	No	F	F	F	F	F	F
25			Cochrane Database of									
26	Rosumeck <sup>81</sup>	2018	Systematic Reviews	Full	Full	No					F, T	
27			Cochrane Database of									
28	Rüschen <sup>82</sup>	2018	Systematic Reviews	Full	Full	No			F, T		F, T	
29			Cochrane Database of									
30	Ruthirakuhan <sup>83</sup>	2018	Systematic Reviews	Full	No	Partial			F		F, E	
31			Cochrane Database of									
32	Sankar <sup>84</sup>	2018	Systematic Reviews	No	No	No						
33			Cochrane Database of									
34	Schumann <sup>85</sup>	2018	Systematic Reviews	Full	Partial	Partial	F, T		F		F, T, E	F, T
35			Cochrane Database of									
36	Simancas-Racines <sup>86</sup>	2018	Systematic Reviews	Full	Full	No	F	F	F		F, T	
37			Cochrane Database of									
38	Smith <sup>87</sup>	2017	Systematic Reviews	Full	Full	Full	F, T, E	F, T, E				
39			Cochrane Database of									
40	Smith <sup>88</sup>	2018	Systematic Reviews	Full	Full	No			F, T		F, T	
41			Cochrane Database of									
42	Soares-Weiser <sup>89</sup>	2018	Systematic Reviews	Partial	No	No					F	
43			Cochrane Database of									
44	Squizzato <sup>90</sup>	2017	Systematic Reviews	Full	Partial <sup>i</sup>	No	F	F, T	F			F
45			Cochrane Database of									
46	St George <sup>91</sup>	2018	Systematic Reviews	Full	Partial	Partial	F, T	F, T, E	F		F, T, E	
47			Cochrane Database of									
48	Stern <sup>92</sup>	2017	Systematic Reviews	Full	No	No			F		F	F

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3			Cochrane Database of									
4	Sturman <sup>93</sup>	2017	Systematic Reviews	Full	Full	No	F, T	F, T	F, T			
5	Tammenmaa- Aho <sup>94</sup>	2018	Cochrane Database of	Partial	No	No				F		
6			Cochrane Database of									
7	Temmingh <sup>95</sup>	2018	Systematic Reviews	Full	Partial	Partial	F, T	F, T, E	F, T, E	F, T		
8			Cochrane Database of									
9	Tenforde <sup>96</sup>	2018	Systematic Reviews	Full	Full	No	F, T	F, T		F, T		
10			Cochrane Database of									
11	Toews <sup>97</sup>	2018	Systematic Reviews	Full	Full	Partial		F, E	F	F, T		
12			Cochrane Database of									
13	Venekamp <sup>98</sup>	2018	Systematic Reviews	Full	Full	No			F	F, T		
14			Cochrane Database of									
15	Vermeij <sup>99</sup>	2018	Systematic Reviews	No	No	No						
16			Cochrane Database of									
17	Vietto <sup>100</sup>	2018	Systematic Reviews	Full	No	No				F	F	
18			Cochrane Database of									
19	Wall <sup>101</sup>	2018	Systematic Reviews	Full	Full	No	F, T	F	F	F		
20			Cochrane Database of									
21	Weibel <sup>102</sup>	2018	Systematic Reviews	Full	No	No			F	F		
22			Cochrane Database of									
23	Wright <sup>103</sup>	2018	Systematic Reviews	Partial	Partial	No	F	F, T				
24			Cochrane Database of									
25	Xiao <sup>104</sup>	2018	Systematic Reviews	Full	No	No				F		
26			Cochrane Database of									
27	Zhang <sup>105</sup>	2017	Systematic Reviews	Full	No	No	F	F	F	F	F	
28			Cochrane Database of									
29	Zhou <sup>106</sup>	2017	Systematic Reviews	Full	Full	No			F	F, T	F	
30			Cochrane Database of									
31	Zonneveld <sup>107</sup>	2018	Systematic Reviews	Partial <sup>l</sup>	No	No		F				
32	<b>General Medicine (n = 33)</b>											
33	López-López <sup>108</sup>	2017	BMJ	Full	No	No			F		F	
34			BMJ Open									
35	Wang <sup>109</sup>	2018	BMJ Open	No	No	No						
36			Lancet						F		F	
37	Cipriani <sup>110</sup>	2018	Lancet	Full <sup>k</sup>	No	No						
38			Medicine									
39	Chen <sup>111</sup>	2018	Medicine	No	No	No						
40			Medicine									
41	Ding <sup>112</sup>	2018	Medicine	No	No	No						
42			Medicine									
43	Guo <sup>113</sup>	2018	Medicine	No	No	No						
44			Medicine									
45	Han <sup>114</sup>	2018	Medicine	No	No	No						
46			Medicine									
47	Hu <sup>115</sup>	2018	Medicine	No	No	No						
48			Medicine									
49	Huang <sup>116</sup>	2018	Medicine	Full	Partial	No	F, T					
50			Medicine									
51	Jiang <sup>117</sup>	2018	Medicine	No	No	No						
52			Medicine									
53	Jiang <sup>118</sup>	2018	Medicine	No	No	No						
54			Medicine									
55	Khan <sup>119</sup>	2018	Medicine	No	No	No						
56			Medicine									
57	Liang <sup>120</sup>	2017	Medicine	No	No	No						
58			Medicine									
59	Liu <sup>121</sup>	2018	Medicine	Partial <sup>l</sup>	No	No			F			
60			Medicine									
61	Lor <sup>122</sup>	2017	Medicine	No	No	No						
62			Medicine									
63	Wang <sup>123</sup>	2017	Medicine	No	No	No						
64			Medicine									
65	Wang <sup>124</sup>	2018	Medicine	No	No	No						
66			Medicine									
67	Wang <sup>125</sup>	2018	Medicine	No	No	No						
68			Medicine									
69	Wei <sup>126</sup>	2017	Medicine	No	No	No						

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Woo <sup>127</sup>	2018	Medicine	No	No	No		
Xia <sup>128</sup>	2018	Medicine	No	No	No		
Yang <sup>129</sup>	2017	Medicine	No	No	No		
Ye <sup>130</sup>	2017	Medicine	No	No	No		
Yu <sup>131</sup>	2018	Medicine	No	No	No		
Yuan <sup>132</sup>	2018	Medicine	No	No	No		
Zhang <sup>133</sup>	2018	Medicine	No	No	No		
Zhang <sup>134</sup>	2018	Medicine	No	No	No		
Zhao <sup>135</sup>	2018	Medicine	No	No	No		
Zhao <sup>136</sup>	2018	Medicine	No	No	No		
Zhou <sup>137</sup>	2018	Medicine	No	No	No		
Zhu <sup>138</sup>	2018	Medicine	No	No	No		
Zhou <sup>139</sup>	2018	Postgraduate Medicine Revista da Associação Médica Brasileira	No	No	No		
Zhang <sup>140</sup>	2018	Full	Full <sup>m</sup>	No		F, T	
<b>Specialty medicine (n = 100)</b>							
Li <sup>141</sup>	2018	Acta Ophthalmologica American Heart Journal	Full <sup>n</sup>	No	No	F	F
Tarantini <sup>142</sup>	2018	American Journal of Cardiovascular Drugs	No	No	No		
Wang <sup>143</sup>	2018	Anaesthesia and Intensive Care	No	No	No		
Aman <sup>144</sup>	2018	Autoimmunity Reviews	No	No	No		
Li <sup>145</sup>	2018	Biomed Research International	No	No	No		
Wang <sup>146</sup>	2018	BMC Cancer	No	No	No		
Veetil <sup>147</sup>	2017	BMC Cardiovascular Disorders	Full	No	No		F
Bredemeier <sup>148</sup>	2018	BMC Gastroenterology BMC Infectious Diseases	No	No	No		
Lyu <sup>149</sup>	2018	BMC Musculoskeletal Disorders	No	No	No		
Xing <sup>150</sup>	2017	BMC Neurology	No	No	No		
Kuo <sup>151</sup>	2018	BMC Ophthalmology	No	No	No		
Beez <sup>152</sup>	2017	BMC Pharmacology & Toxicology	No	No	No		
Zeng <sup>153</sup>	2017	BMC Psychiatry	No	No	No		
Bundhun <sup>154</sup>	2017	BMC Pulmonary Medicine	No	No	No		
Zhang <sup>155</sup>	2017	BMC Pulmonary Medicine	No	No	No		
Zhang <sup>156</sup>	2017	Medicine	Full	No	No		
Zhang <sup>157</sup>	2017	Medicine	Full	No	No		
Ramos-Esquivel <sup>158</sup>	2018	Breast Cancer British Journal of Sports Medicine	No	No	No		
Zeng <sup>159</sup>	2018	Sports Medicine	Partial <sup>o</sup>	No	No	F	F

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3			Cellular Physiology					
4	Shui <sup>160</sup>	2018	and Biochemistry	No	No	No		
5	Rodrigo <sup>161</sup>	2018	Clinical Microbiology	Partial	No	No		F
6			and Infection					
7	Wang <sup>162</sup>	2018	Clinical	No	No	No		
8			Rheumatology					
9	Hong <sup>163</sup>	2018	Critical Reviews in					
10	de Carvalho <sup>164</sup>	2018	Oncology /					
11			Hematology	No	No	No		
12	Jaafar <sup>165</sup>	2018	Diabetes Care	No	No	No		
13	Liu <sup>166</sup>	2018	Digestive Diseases and					
14			Sciences	No	No	No		
15	Liu <sup>167</sup>	2018	Drug Delivery	No	No	No		
16			Drug Design,					
17	Sun <sup>168</sup>	2017	Development and					
18	Paraschakis <sup>169</sup>	2017	Therapy	No	No	No		
19			Drug Design,					
20	D'Souza <sup>170</sup>	2018	Development and					
21			Therapy	No	No	No		
22	Mei <sup>171</sup>	2016	East Asian Archives of					
23	Verberkt <sup>172</sup>	2017	Psychiatry	No	No	No		
24			Emergency Medicine					
25	Sridharan <sup>173</sup>	2018	Journal	No	No	No		
26			European Journal of					
27	Habibi <sup>174</sup>	2018	Gynecological					
28			Oncology	No	No	No		
29	Lj <sup>175</sup>	2018	European Respiratory					
30	Sangroongruangsr i <sup>176</sup>	2018	Journal	No	No	No		F
31	Hickey <sup>177</sup>	2018	Expert Opinion on					
32	Zhao <sup>178</sup>	2018	Pharmacotherapy	No	No	No		
33	Khera <sup>179</sup>	2018	Expert Review of					
34			Clinical Pharmacology	No	No	No		
35	Lj <sup>180</sup>	2018	Expert Review of					
36	Zhuge <sup>181</sup>	2018	Clinical Pharmacology	No	No	No		
37	Kim <sup>182</sup>	2017	Expert Review of					
38			Clinical Pharmacology	No	No	No		
39	Garg <sup>183</sup>	2018	Foot and Ankle	No	No	No		
40	Rosanova <sup>184</sup>	2017	Surgery	No	No	No		
41	Yu <sup>185</sup>	2018	Gastric Cancer	Partial <sup>P</sup>	No	No	F	F
42			Gastroenterology					
43			Gynecologic					
44			Oncology	No	No	No		
45			Helicobacter	No	No	No		
46			Indian Journal of					
47			Cancer	No	No	No		
			Indian Journal of					
			Gastroenterology	No	No	No		
			Infectious Diseases	No	No	No		
			Inflammopharmacolog y	No	No	No		

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3			International				
4	Kakkos <sup>186</sup>	2018	Angiology	No	No	No	
5	Ou <sup>187</sup>	2018	International				F
6			Immunopharmacology	Full	No	No	
7	Yin <sup>188</sup>	2018	International	No	No	No	
8			Immunopharmacology				
9	Zhu <sup>189</sup>	2018	International Journal	No	No	No	
10			of Clinical Oncology				
11	Liu <sup>190</sup>	2018	International Journal	No	No	No	
12			of Neuroscience				
13	Coccolini <sup>191</sup>	2018	International Journal	No	No	No	
14			of Surgery				
15	Fan <sup>192</sup>	2018	International Journal	No	No	No	
16			of Surgery				
17	Li <sup>193</sup>	2018	International Journal	No	No	No	
18			of Surgery				
19	Li <sup>194</sup>	2018	International Journal	No	No	No	
20			of Surgery				
21	Liu <sup>195</sup>	2018	International Journal	No	No	No	
22			of Surgery				
23	Ran <sup>196</sup>	2018	International Journal	No <sup>a</sup>	No	No	
24			of Surgery				
25	Zhao <sup>197</sup>	2018	International Journal	No	No	No	
26			of Surgery				
27	Zhu <sup>198</sup>	2018	International Journal	No	No	No	
28			of Surgery				
29	Wagner <sup>199</sup>	2018	Journal of Affective	Partial	No	No	F
30			Disorders				
31	Hickman <sup>200</sup>	2018	Journal of Assisted	No	No	No	
32			Reproduction and				
33			Genetics				
34	Luo <sup>201</sup>	2018	Journal of Cancer	No	No	No	
35			Research and Clinical				
36			Oncology				
37	Wang <sup>202</sup>	2018	Journal of Cancer	Partial <sup>f</sup>	No	No	F F
38			Research and				
39	Wang <sup>203</sup>	2018	Therapeutics	No	No	No	
40			Journal of Cardiac				
41	Aboul-Hassan <sup>204</sup>	2017	Surgery	No	No	No	
42			Journal of				
43			Cardiovascular				
44	Wang <sup>205</sup>	2018	Surgery	No	No	No	
45			Journal of Clinical				F
46			Endocrinology and				
47	Barrionuevo <sup>206</sup>	2018	Metabolism	Full	No	No	F

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Cui <sup>207</sup>	2018	Journal of Clinical Pharmacy and Therapeutics	Full <sup>s</sup>	No	No	F
Sawyer <sup>208</sup>	2018	Journal of Dermatological Treatment	No	No	No	
Markey <sup>209</sup>	2018	Journal of Emergency Medicine	No	No	No	
Szabó <sup>210</sup>	2017	Journal of Gastrointestinal and Liver Diseases	No	No	No	
Su <sup>211</sup>	2018	Journal of Immunology Research	No	No	No	
Chen <sup>212</sup>	2018	Journal of Interventional Cardiac Electrophysiology	No	No	No	
Chen <sup>213</sup>	2017	Journal of Orthopaedic Surgery and Research	No	No	No	
Li <sup>214</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
Luo <sup>215</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
Ma <sup>216</sup>	2018	Journal of Orthopaedic Surgery and Research	No	No	No	
He <sup>217</sup>	2018	Journal of Psychiatric Research	Full	No	No	F
Wang <sup>218</sup>	2018	Journal of Stroke & Cerebrovascular Diseases	No	No	No	
Dhana <sup>219</sup>	2018	Journal of the American Academy of Dermatology	No	No	No	
Karatasakis <sup>220</sup>	2017	Journal of the American Heart Association	No	No	No	
Kuo <sup>221</sup>	2018	Journal of the European Academy of Dermatology and Venereology	Full	No	No	
Liu <sup>222</sup>	2016	Journal of Traditional Chinese Medicine	No	No	No	
Zheng <sup>223</sup>	2017	Journal of Zhejiang University-SCIENCE B	No	No	No	
Fregonese <sup>224</sup>	2018	Lancet Respiratory Medicine	No	No	No	
Bornstein <sup>225</sup>	2018	Neurological Sciences	No	No	No	
Chen <sup>226</sup>	2018	Ophthalmic Research	No	No	No	
Han <sup>227</sup>	2017	Pain Physician	No	No	No	
Peng <sup>228</sup>	2017	Pain Physician	No	No	No	



3	Feng <sup>229</sup>	2016	Pharmazie	No	No	No	
4	Xu <sup>230</sup>	2016	Pharmazie	No	No	No	
5	Palmeirim <sup>231</sup>	2018	PLOS Neglected Tropical Diseases	No	No	No	
6			Psychotherapy and				
7	Furukawa <sup>232</sup>	2018	Psychosomatics	No	No	No	
8	Liu <sup>233</sup>	2018	Renal Failure	No	No	No	
9	Miravittles <sup>234</sup>	2017	Respiratory Research	Full	No	No	F
10	Wang <sup>235</sup>	2017	Respiratory Research	No	No	No	
11			Rheumatology				
12	Kawalec <sup>236</sup>	2018	International	No	No	No	
13	Malhotra <sup>237</sup>	2018	Stroke	No	No	No	
14			Surgical Laparoscopy				
15			Endoscopy & Percutaneous				
16	Zhang <sup>238</sup>	2018	Techniques	No	No	No	
17	Yamashita <sup>239</sup>	2018	Thrombosis Research	No	No	Partial	E
18	Zhang <sup>240</sup>	2018	Vaccine	No	No	No	

**Other (n = 10)**

19	Chen <sup>241</sup>	2018	Medical Science				
20	Arteagoitia <sup>242</sup>	2018	Monitor	No	No	No	
21	Feng <sup>243</sup>	2018	PLOS ONE	No	No	No	
22	Kawakami <sup>244</sup>	2018	PLOS ONE	No	No	No	
23	Li <sup>245</sup>	2018	PLOS ONE	No	No	No	
24	Lin <sup>246</sup>	2017	PLOS ONE	No	No	No	
25	Ling <sup>247</sup>	2018	PLOS ONE	No	No	No	
26	Rohner <sup>248</sup>	2017	PLOS ONE	No	No	No	
27	Sethi <sup>249</sup>	2018	PLOS ONE	Partial	No	No	F
28	Wolf <sup>250</sup>	2018	PLOS ONE	No	No	No	

<sup>a</sup>Funding sources categorized as government funded, industry funded, or mixed for most trials. Specific details about funding were reported for 2 trials and details on author ties and employment were reported for a single trial; <sup>b</sup>Authors reported extracting funding sources from included RCTs but funding sources are only reported for a single study; <sup>c</sup>Reported funding sources for all included studies except for one; <sup>d</sup>Reported author financial ties for all included studies except for 2; <sup>e</sup>Non-industry author employment reported for some included RCTs; <sup>f</sup>Funding sources and author ties reported for all included RCTs except one that was a conference abstract; <sup>g</sup>Funding sources only reported for a single RCT; <sup>h</sup>Authors reported whether or not included RCTs had declared COI (yes, no) and, if yes, indicated the page of the original study the declaration could be found on. This was coded as partially reporting because the nature of these COI was not reported within the meta-analysis publication itself and it was unclear whether these were financial ties and whether they were with industry; <sup>i</sup>Non-industry author financial ties reported for some included RCTs; <sup>j</sup>A single RCT was reported as 'industry sponsored' with no specifics about the sponsor; <sup>k</sup>Authors coded studies as sponsored by industry or not, and any of author industry affiliation, industry funding, or data obtained from pharmaceutical company qualified an RCT as 'sponsored'; <sup>l</sup>Authors report that 'some trials had a high risk of reporting bias because they were sponsored by pharmaceutical companies' but do not specify which or even how many trials; <sup>m</sup>Authors reported that all included RCTs had authors with financial ties to industry but provided no further information; <sup>n</sup>Reported whether each included RCT was industry funded (yes or no) but provided no further information; <sup>o</sup>For some analyses the authors reported how many included RCTs were non-commercially funded and present results including only non-commercially funded trials, but do not provide further information on which trials were commercially funded; <sup>p</sup>Authors state 14 trials were industry-sponsored and reference figure 1 in the supplementary material where 14 studies were marked as high risk for other bias, but it is not explicitly specified what was considered as 'other bias'; <sup>q</sup>Authors considered RCT funding sources within 'other bias'. In their risk of bias assessment but did not report any specific information; <sup>r</sup>Authors report that most studies were funded by the pharmaceutical industry and refer readers to figure 2 (risk of bias figure), but the figure does not give any information about which RCTs; <sup>s</sup>Included RCTs were coded as having company funding (Yes/No).

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# PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	N/A
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3,4
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5,6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6,7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eMethods1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-10
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-12
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3, 10,11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	10,11



# PRISMA 2009 Checklist

Page 1 of 2

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	11
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	12, 13, 26, 27 (Table 1)
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	28 (Table 2)
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15-17
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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# PRISMA 2009 Checklist

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