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Characteristics of funding of clinical trials: a methodological survey and a proposed guidance

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Characteristics of funding of clinical trials: a methodological survey and a proposed guidance

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data mining, AI training, and similar technologies

Keywords: funding, role of funder, randomised controlled trial

Word count: 3,225 words

ABSTRACT

Objectives: The objectives of this study were to describe the characteristics of funding of clinical trials and to develop guidance and an instrument for standardised reporting of funding information.

Methods: We addressed the extent to which clinical trials published in 2015 in any of the 119 Core Clinical Journals included a statement on the funding source (e.g., whether a not-for-profit organisation was supported by a private-for-profit), type of funding, amount and role of funder. We used a stepwise approach to develop a guidance and an instrument for standardised reporting of funding information.

Results: Of 200 trials, 178 (89%) included a funding statement, of which 171 (96%) reported being funded. Funding statements in the 171 funded trials indicated the source in 100%, amount in 1% and roles of funders in 50%. The most frequent sources were governmental (58%) and private-for-profit (40%). Of 54 funding statements in which the source was not-for-profit organisation, we found evidence of undisclosed support of those organisations from private-for-profit organisation(s) in 26 (48%). The most frequently reported roles of funders in the 171 funded trials related to study design (42%) and data analysis, interpretation, or management (41%). Of 139 RCTs addressing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or device. The proposed guidance addresses both the funding information that RCTs should report and the reporting process. Attached to the guidance is a fillable PDF document for use as an instrument for standardised reporting of funding information.

Conclusion: Although the majority of RCTs report funding, there is considerable variability in the reporting of funding source, amount and roles of funders. A standardised approach to

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reporting of funding information would address these limitations. Future research should explore the implications of funding by not-for profit organisations that are supported by for-profit organisations.

Strengths and limitations of this study:

- First methodological survey of a large and representative sample of clinical RCTs to describe the characteristics of the funding statements in detail.
- Provides a proposed guidance and instrument for standardised reporting of funding information.
- Use of systematic and transparent methods, e.g., duplicate and independent processes in screening and data collection.
- Includes trials limited to the clinical field and so our findings may not apply similarly to other fields such as public health research.

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BACKGROUND

Funding sources often influence the reporting of research findings and the interpretation of results.[1-6] One study found 86% of trial protocols documented an industry partner's right to disapprove or review proposed manuscripts.[7] Reporting of funding in trials may appropriately influence how physicians interpret and use trial findings in clinical practice.[8, 9] The Consolidated Standards of Reporting Trials (CONSORT) checklist recognises this issue in its inclusion of a section on reporting of funding.[10, 11]

Reports in the lay media have documented how for-profit organisations support research through not-for-profit organisations.[12, 13] In one example, The Independent recently highlighted a systematic review suggesting that the consumption of low-energy sweeteners in place of sugar reduces energy intake and body weight.[14] The review authors list the International Life Sciences Institute as the study funder. While the Institute describes itself as "a nonprofit, worldwide organisation whose mission is to provide science that improves human health", it receives funding primarily from companies such as the Coca-Cola Company, PepsiCo and Nestlé.[15] Other examples of not-for-profit organisations funded by industry and supporting research are the Sugar Association, Inc. [16, 17] and the now defunct Global Energy Balance Network.[18]

At least 22 studies have assessed reporting of funding in clinical trials (table 1), all of which focused on trials published in specific clinical areas or journals. Most (14, 64%) reported only on funded trials or did not differentiate between non-funded trials and those that do not report on funding and 17 (77%) did not always distinguish trials with no funding from those funded by the

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government or by not-for-profit sources. Moreover, these studies seldom assessed reporting on the role of funder (4), provision of supplies (2), and the amount of funding (0).

Table 1: Comparative chart including 23 related methodological surveys of reporting of funding information in trials

| Survey | Eligibility criteria | Numbe | Year of trial | Characteristics of funding | Main findings |
|--------------------------|--|--------|---------------|---|---|
| | | r of | publication | statement assessed in the | |
| | | trials | | survey | |
| Als-Nielsen 2003 [19] | RCTs included in eligible meta-analyses in Cochrane reviews | 370 | 1971 - 2000 | - Source of funding | Funding was not reported in 29%. 39% were funded by for-profit organisations. |
| Etter 2007 [20] | RCTs on nicotine replacement therapy in Cochrane review | 90 | 1979 - 2003 | - Source of funding | 54% received pharmaceutical company support.46% showed no evidence of pharmaceutical company support. |
| Mugambi 2013 [5] | RCTs on infant formula supplementation of symbiotics, probiotics, or prebiotics | 67 | 1980 - 2012 | - Source of funding | 60% were funded by food industry. 24% did not specify their source of funding. |
| Rochon 1994 [21] | Manufacturer-associated RCTs of NSAIDs listed in MEDLINE | 52 | 1987 - 1990 | Grant support Pharmaceutical authorship Provision of supplies Published in a pharmaceutical sponsored journal supplement | 19% reported grant support. 36.5% reported pharmaceutical authorship. 13.5% reported that manufacturer supplied drug. 31% were published in a pharmaceutical sponsored journal supplement. |
| Momeni 2008 [22] | Trials published in 4 major plastic surgery journals | 346 | 1990 - 2005 | - Source of funding | 20% reported on financial support, of which 60% were supported by industrial sponsorship. |
| Yaphe 2001 [23] | RCTs of drugs or food products published in 5 medical journals | 314 | 1992 - 1994 | Source of funding Pharmaceutical authorship | 68% received pharmaceutical industry support.33% received support as manpower |

| | | | | - Provision of supplies | (authorship or statistical help).21% received support as supply of drugs. |
|--------------------------|---|-----|---------------------|--|---|
| Peppercorn 2007 [24] | Breast cancer clinical trials published in 10 medical journals | 140 | 1993, 1998, 2003 | Source of funding Pharmaceutical authorship | 48% were categorised as pharmaceutical studies. 26% reported pharmaceutical industry authorship. |
| Bero 2007 [25] | Reports of RCTs comparing statin drugs | 192 | 1995 - 2005 | - Source of funding - Role of funder | 39% had no disclosure or no funding (Table 1). 49% disclosed funding from industry, of which 21% disclosed the role of the sponsor. |
| Djulbegovic 2000 [26] | RCTs for multiple myeloma | 130 | 1996 - 1998 | - Source of funding | 26% reported funding solely or in part by commercial organisations. |
| Clifford 2002 [27] | RCTs published in 5 high impact factor general medical journals | 100 | 1999 - 2000 | - Source of funding | 94% were funded, of which 66% were funded in whole or in part by industry.6% did not disclose their source of funding. |
| Bhandari 2004 [28] | RCTs published in 8 surgical and 5 medical journals | 332 | 1999 - 2001 | - Source of funding | 44% had no reported funding.37% reported funding by industry. |
| Tuech 2005 [29] | Phase III cancer RCTs published in 12 journals | 655 | 1999 - 2003 | - Source of funding - Role of funder | 35% were industry-sponsored, of which 18% reported the role of the study sponsor. 21% did not disclose funding and only 1 trial disclosed no financial support. |
| Shah 2005 [30] | Articles published in the Spine journal | 34 | 2000 - 2003 | - Source of funding | 23% were industry funded. |
| Tungaraza 2007 [31] | Original papers on psychiatric drug treatment published in two journals | 132 | 2000 - 2004 | Source of funding Pharmaceutical authorship | 85% were industry-funded.40% were industry-authored studies. |

| Ridker 2006 [32] | Cardiovascular medicine RCTs published in 3 medical journals | 349 | 2000 - 2005 | - Source of funding | 31% were financed by not-for-profit organisations, 44% by for-profit manufacturers, and 19% by both. 6% noted no source of funding. |
|------------------------------|--|-----|----------------------------|--|---|
| Voineskos 2016 [33] | Surgical RCTs | 173 | 2000 - 2013 | - Source of funding | 58% did not acknowledge a source of funding. 14% reported funding from for-profit sources. 10% explicitly reported 'no funding received'. |
| Montogome ry 2004 [34] | RCTs on second generation antipsychotics for the management of schizophrenia | 86 | 2002 | - Source of funding | 84% were industry-funded. 16% were non-industry-funded. |
| Perlis 2005 [35] | RCTs published in one of the four dermatology journals with the highest science citation impact factor scores and total citations | 179 | 2002 | - Source of funding | 57% reported receiving at least some industry support.26% had no information about funding. |
| Khan 2012 [36] | RCTs of drug therapy for rheumatoid arthritis | 103 | 2002 - 2003 2006 - 2007 | - Source of funding | 62% had complete or partial industry funding.19% had an unspecified funding source. |
| Hodgson 2014 [37] | RCTs in chronic wound care | 167 | 2004 - 2011 | - Source of funding | 35% were reported as having been commercially funded. 26% either did not report the source of funding or the status of funding source was unclear. |
| Bridoux 2014 [38] | Surgical trials published in 10 surgery journals with impact factor >2 | 657 | 2005 - 2010 | Source of fundingRole of funder | 47% disclosed funding. Of those, 39% reported funding from industry or mixed funding, of which 35% reported the role of study sponsor. |

| Lundh | RCTs published in The | 69 | 2008 - 2009 | - Role of funder | Sponsor had a role in: |
|-----------|-------------------------------|-----|-------------|-------------------------|--|
| 2012 [39] | Lancet and fully funded by | | | | Review and verification of information |
| | a drug or device company | | | | (71%) |
| | | | | | Entry of data into the study database |
| | | | | | (75%) |
| | | | | | Data storage (64%) |
| | | | | | Data analysis (58%) |
| | | | | | Coordinating writing of the manuscript |
| | | | | | (35%) |
| | | | | | Medical writing assistance (54%) |
| | | | | | Protocol writing (99%) |
| | | | | | Co-authorship (81%) |
| | | | | | Publication of results through co- |
| | | | | | authorship or approval/review of the |
| | | | | | paper (93%) |
| Current | RCTs published in any of | 200 | 2015 | - Source of funding | 89% included a funding statement, of |
| survey | the 119 Core Clinical | | | - Amount | which 96% reported being funded. |
| | Journals, not restricted to a | | | - Provision of supplies | |
| | specific clinical domain | | | - Role of funder | Of the funded trials (N=171): |
| | | | | | - 100% specified the source; |
| | | | | | - 40% received funding from private |
| | | | | | for-profit sources; |
| | | | | | - 1% reported the amount of funding |
| | | | | | - 21% of pharmacological/surgical |
| | | | | | trials (N=139) reported information |
| | | | | | on supplies. |
| | | | | | ✓- 50% reported on the roles of funder |
| | | | | | (26% as involved and 24% as not |
| | | | | | involved). |

RCT: randomised controlled trial

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The current literature lacks a detailed, current characterisation of funding of a representative sample of trials. The objectives of this study were to provide such a characterisation and to develop guidance for standardised reporting of funding information and a form that would aid such reporting.

METHODS

Design overview and definitions

We followed systematic review methodology to conduct a methodological survey of published randomised controlled trials (RCTs). We define funding as any support (e.g. monetary support, provision of supplies, assistance in manuscript writing). We considered as funding statement any text in the trial report providing any information regarding the funding of the trial, including a statement of no funding. A funding statement could indicate more than one funding contribution.

We used a stepwise approach for developing the proposed guidance for standardised reporting of funding information. Our starting point consisted of a simple classification we had used in a number of our previous studies (governmental, private not-for-profit, and private-for-profit).[40, 41] which we modified based on a review of relevant literature.[5, 36, 38] and of journals' policies on reporting of funding information (unpublished data from another methodological survey).[42] We further refined the classification (table 2) through an iterative process of discussion and revisions based on funding statements reported in this sample of RCTs, as well as in a sample of systematic reviews.[43] That process included both in person discussions and email feedback among the authors of this article. We used Adobe[®] Acrobat XI[®] software to

develop a fillable PDF document for use as an instrument for standardised reporting of funding information.

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| Types of sources of funding |
|-----------------------------|
| Fypes of sources of funding |

| Internal funding | author is the "Chair of –"; intramural fund; provided by institution, university, hospital affiliation, academic affiliation |
|--|---|
| External funding: | |
| 1. Government | national, regional (province, county), or governmental body, organisation, or association |
| 2. Private-for-profit | drug/device industry or private company |
| 3. Private not-for-profit with evidence of support by private-for-profit that is a health industry | foundation or organisation that receives funding from a drug industry, as stated in information provided online |
| 4. Private not-for-profit with evidence of support by private-for-profit that is not a health industry | foundation or philanthropy that was founded by billionaires or that receives funding from a private industry that is not known to produce drugs/devices, as stated in information provided online |
| 5. Private not-for-profit with no evidence of support by private-for- profit | foundation or organisation that is not known to receive funding from any governmental or private company, as stated in information provided online |
| | |



Eligibility criteria

We included reports of studies described as RCTs enrolling humans and published in English in any one of the 119 Core Clinical Journals during 2015. We excluded non-randomised trials, trials addressing basic sciences topics and non-clinical interventions, and research letters. We included RCTs with cross-over designs and secondary reports of trials (i.e. follow-up study; post-hoc analysis; interim analysis; pre-specified analysis or secondary outcomes or sub-study of a trial).

Search strategy

We searched using Ovid Medline in September 2015 for the 119 Core Clinical Journals (Abridged Index Medicus (AIM)). We applied the search filter obtained from the Cochrane handbook to identify RCTs. See appendix 1 for the detailed search strategy.

Selection process

We used an online sequence generator (www.random.org/sequences) to select a random sample from the citations captured. Following calibration exercises, three reviewers worked in teams of two to screen titles and abstracts in duplicate and independently. We obtained the full-texts of citations judged as potentially eligible by either reviewer.

The two teams of reviewers screened full-texts in duplicate and independently. They resolved disagreements by discussion, or with the help of a third reviewer as needed. A PRISMA study flow diagram [44] presents the results of the selection process (figure 1).

Data abstraction process

We developed a standardised data abstraction form along with specific instructions. After pilot testing the form, we embedded it electronically into Research Electronic Data Capture (REDCap), a secure web-based application designed to support data capture for research studies.[45] After completing calibration exercises, nine authors divided into teams of two abstracted data in duplicate and independently. Each team compared results and resolved disagreements through discussion with the help of a third review author as needed.

Data abstracted

We abstracted the following characteristics of the RCTs:

- Number of trialists;
- Whether it was the first full-text report of the trial findings;
- Classification of the income level of the country in which the first author's institution is located (according to the July 2015 World Bank list of economies);
- Type of intervention and type of control;
- Number of randomised participants;
- Level of risk of bias associated with allocation concealment;
- Whether authors reported conflicts of interest;
- Whether the report included a funding statement.

We then focused on trials that included a funding statement. We abstracted the following characteristics of the statement:

• Whether it reported funding versus no funding;

- The type of source(s) of funding. Table 2 presents the main types of sources of funding along with illustrative examples. As needed, we performed an online search to accurately assign the type of the source of funding. When a source of funding was identified as a not-for-profit organisation, we searched the organisation's website for any information on partnership with or support from a for-profit organisation;
- Amount of funding;
- Whether it differentiated source of funding from sponsor;
- Whether information was reported on supplies in trials on pharmacological or surgical interventions (i.e., drugs, devices, equipment, samples, or placebos) and whether the supplier is a funding source.

Finally, and in trials that reported being funded, we assessed whether the role of funder was explicitly reported for any funder as involved or not involved in the process of the research study.

Data analysis

Our sample size allows for a narrow 95% confidence interval (+/- 5%) around proportions of studies reporting sources of funding. We assessed agreement between reviewers for inclusion of RCTs at the full-text screening stage using chance-corrected agreement (kappa statistic). We conducted descriptive analyses of the general characteristics of the RCT, as well as the characteristics of the funding statement. We present summary data for categorical variables as frequencies and percentages and for continuous variables as median and interquartile range (IQR). All calculations used SPSS, version 21.0 for Windows (SPSS INC., Chicago, IL, USA).

Candidate independent variables for multiple logistic regression analyses to assess the predictors of reported funding and the role of funder included characteristics of the RCT and variables related to Journal policy for reporting funding (i.e., journal requirement for reporting of funding; journal requirement for reporting on the role of funder). For variables related to journal policy for reporting funding, we used unpublished data we had collected for another methodological survey.[42]

RESULTS

Figure 1 presents the study flow diagram. Agreement proved near perfect (kappa=0.82) at the full-text screening stage.

Characteristics of the randomised controlled trial

The first authors of most trials (90%) had affiliations in high-income countries and almost half (49%) assessed pharmacological interventions (table 3). Most trials (94%) reported on conflicts of interest and 54% disclosed presence of conflicts of interest. Almost all (178, 89%) included a funding statement.

| $\begin{array}{c}1\\2&3\\4&5\\6&7\\8&9\\10&112\\13&14\\15&16\\17&18\\9&21\\22&23\\24&25\\26\\27&28\end{array}$ | |
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| 43 46 47 48 49 50 | |
| 51 52 53 54 | |
| 55 56 57 58 59 60 | |

| | Overall |
|---|-----------|
| | N (%) § |
| Number of trialists; median (IQR) | 9 (6 - 14 |
| Paper is the first full-text report of the trial findings | 171 (86% |
| Classification of the income level of the country in which the first author's | |
| nstitution is located: | |
| High-income | 179 (90% |
| Upper middle-income | 15 (8%) |
| Lower middle-income | 4 (2%) |
| Low-income | 2 (1%) |
| Type of intervention | |
| Pharmacological | 97 (49%) |
| Surgical/invasive procedure | 42 (21%) |
| Non-invasive procedure | 11 (6%) |
| Lifestyle intervention | 15 (8%) |
| Screening/diagnostic intervention | 9 (5%) |
| Psycho-therapeutic intervention | 4 (2%) |
| Rehabilitation | 6 (3%) |
| Other | 16 (8%) |
| Гуре of control | |
| Active control (as opposed to non-active) | 82 (41%) |

d trials **T** 11 0 C /1 . 1 .11. (N = 200)2 1 1 1 1 1 1

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| Number of randomised participants; median (IQR) | 160 (60 - 485) |
|--|----------------|
| Level of risk of bias associated with allocation concealment | |
| High risk | 4 (2%) |
| Low risk | 59 (30%) |
| Unclear | 137 (69%) |
| Paper with authors reporting conflicts of interest | |
| Not reported | 12 (6%) |
| Reported with no conflicts of interest disclosed | 80 (40%) |
| Reported with conflicts of interest disclosed | 108 (54%) |
| Paper included a funding statement | |
| Included (as opposed to not included) | 178 (89%) |

§ For continuous variables, numbers refer to median (IQR); indicated in the relevant row.

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Characteristics of the reported funding

Table 4 presents the characteristics of the reported funding of the 178 trials with a funding statement, of which 171 (96%) reported being funded. The median number (IQR) of sources of funding per trial was 1 (1-3), with a range of 1 to 12. The top most frequent sources of funding were governmental (58%) and private-for-profit (40%). Of the 54 funding contribution statements in which the source was identified as being a not-for-profit organisation, we found evidence of support of those organisations from private-for-profit organisation(s) in 29 (54%), of which 26 (48%) did not disclose this support in the study report. Twenty-one trials (12%) reported funding from private-for-profit in addition to another source. Two trials reported the amount of funding received. Of the 139 RCTs assessing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or device.



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Table 4: Characteristics of the funding statements included in the randomised controlled trials

 (N=178 trials)

| | Overall |
|--|-----------|
| | N (%) |
| Funding statement reported being: | |
| Funded (as opposed to not funded) | 171 (96%) |
| Source of funding (when reported as funded; N=171) | |
| Internally funded | 26 (15%) |
| Externally funded by: | |
| Government | 99 (58%) |
| Private-for-profit | 68 (40%) |
| Private not-for-profit with evidence of support by private-for-profit | 14 (8%) |
| that is a health industry | |
| Private not-for-profit with evidence of support by private-for-profit | 15 (9%) |
| that is not a health industry | |
| Private not-for-profit with no evidence of support by private-for- | 25 (15%) |
| profit | |
| Statement included amount of funding received | 2 (1%) |
| Paper reported to be sponsored by a source different than the source of | 2 (1%) |
| funding/support | |
| Paper reported information on supplies (i.e., drugs, devices, equipment, | |
| samples, or placebos) \$ | |

| Yes, supplied by manufacturer same as funder | 12 (9% |
|---|---------|
| Yes, supplied by manufacturer different than funder | 17 (129 |
| Not reported | 110 (79 |

\$ Calculated using the number of trials on pharmacological interventions and surgical/invasive procedures (N=139).

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The reported roles of funders

Table 5 presents the reported roles of funders in the 171 trials that reported being funded. 85 trials (50%) indicated the role of funders and provided descriptions of 22 different roles. The most frequent roles indicated in these 85 trials were participation in the design of the study (42%), data collection (27%), data analysis, interpretation, or management (41%), manuscript preparation (32%), decision to submit the manuscript (15%) and conduct of the study (15%).

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Table 5: Reporting on the roles of funders in the randomised controlled trials that reported being funded (N=171)

| Image: Not involved Involved Involved N (%) N (%) N (%) N (%) Any role of the below 41 (24%) 44 (26%) 86 (50%) Protocol/design of the study 41 (24%) 30 (18%) 100 (58%) Data collection 31 (18%) 16 (9%) 124 (73%) Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 8 (5%) 146 (85%) Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Approval of study conduct 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) Team assembly 0 (0%) 2 (1%) 169 (99%) | | Reported role as: | | Did not report |
|--|---|-------------------|----------|----------------|
| N (%) N (%) N (%) Any role of the below 41 (24%) 44 (26%) 86 (50%) Protocol/design of the study 41 (24%) 30 (18%) 100 (58%) Data collection 31 (18%) 16 (9%) 124 (73%) Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 7 (4%) 146 (85%) Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board | | | | role |
| Any role of the below 41 (24%) 44 (26%) 86 (50%) Protocol/design of the study 41 (24%) 30 (18%) 100 (58%) Data collection 31 (18%) 16 (9%) 124 (73%) Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 7 (4%) 147 (86%) Approval of the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) | | Not involved | Involved | |
| Protocol/design of the study 41 (24%) 30 (18%) 100 (58%) Data collection 31 (18%) 16 (9%) 124 (73%) Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 7 (4%) 147 (86%) Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Approval of the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) | | N (%) | N (%) | N (%) |
| Data collection 31 (18%) 16 (9%) 124 (73%) Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 7 (4%) 147 (86%) Approval of the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) | Any role of the below | 41 (24%) | 44 (26%) | 86 (50%) |
| Verifying data accuracy/ fact checking 0 (0%) 3 (2%) 168 (98%) Outcome adjudication 0 (0%) 1 (1%) 170 (99%) Data analysis/ interpretation/ management 40 (23%) 31 (19%) 100 (58%) Funded a medical writer 1 (1%) 19 (11%) 151 (88%) Preparation of the manuscript 34 (20%) 20 (12%) 117 (68%) Review of the manuscript 17 (10%) 7 (4%) 147 (86%) Approval of the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) | Protocol/design of the study | 41 (24%) | 30 (18%) | 100 (58%) |
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| Review of the manuscript 17 (10%) 7 (4%) 147 (86%) Approval of the manuscript 17 (10%) 8 (5%) 146 (85%) Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 2 (1%) 169 (99%) | Funded a medical writer | 1 (1%) | 19 (11%) | 151 (88%) |
| Approval of the manuscript 17 (10%) 8 (5%) 146 (85%) Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) Team assembly 0 (0%) 2 (1%) 169 (99%) | Preparation of the manuscript | 34 (20%) | 20 (12%) | 117 (68%) |
| Decision to submit the manuscript 18 (10%) 6 (4%) 147 (86%) Appointed an independent data and safety 0 (0%) 1 (1%) 170 (99%) monitoring board 0 (0%) 3 (2%) 168 (98%) Auditing of study conduct 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 2 (1%) 169 (99%) | Review of the manuscript | 17 (10%) | 7 (4%) | 147 (86%) |
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| Auditing of study conduct 0 (0%) 3 (2%) 168 (98%) Management 0 (0%) 3 (2%) 168 (98%) Team assembly 0 (0%) 2 (1%) 169 (99%) | Appointed an independent data and safety | 0 (0%) | 1 (1%) | 170 (99%) |
| Management 0 (0%) 3 (2%) 168 (98%) Team assembly 0 (0%) 2 (1%) 169 (99%) | monitoring board | | | |
| Team assembly 0 (0%) 2 (1%) 169 (99%) | Auditing of study conduct | 0 (0%) | 3 (2%) | 168 (98%) |
| | Management | 0 (0%) | 3 (2%) | 168 (98%) |
| Conduct of study 13 (8%) 12 (7%) 146 (85%) | Team assembly | 0 (0%) | 2 (1%) | 169 (99%) |
| | Conduct of study | 13 (8%) | 12 (7%) | 146 (85%) |

| Generated randomisation list | 0 (0%) | 3 (2%) | 168 (98%) |
|-------------------------------|---------|---------|------------|
| Enrollment of participants | 0 (0%) | 1 (1%) | 170 (99%) |
| | 0 (070) | 1 (170) | 170 (5576) |
| Logistical support | 0 (0%) | 3 (2%) | 168 (98%) |
| Holding study data | 0 (0%) | 1 (1%) | 170 (99%) |
| Study oversight | 0 (0%) | 2 (1%) | 169 (99%) |
| Steering committee | 0 (0%) | 1 (1%) | 170 (99%) |
| Measurement of study variable | 0 (0%) | 5 (3%) | 166 (97%) |

Results of the regression analyses

Appendix 2 presents the details of the multiple logistic regression analyses. The two models had the following statistically significant associations:

- 'Reporting being funded' model: journal impact factor (odds ratio [OR] = 1.51, 95% confidence interval [CI] 1.15-1.96); and affiliation with an institution from a high-income country (reference category being middle or low-income countries; OR=14.17, 95% CI 3.95-50.90).
- 'Explicit reporting on the role of funder' model: paper is the first reporting on the findings of the trial (OR=3.47, 95% CI 1.21-9.96); journal impact factor (OR= 1.06, 95% CI 1.03-1.10); journal requires the reporting on the role of funder (OR=3.25, 95% CI 1.43-7.38); and funding from private-for-profit source (reference category being any other source of funding; OR=4.9, 95% CI 2.11-11.83).

Proposed guidance

The proposed guidance provides suggestions for both funding information and the reporting process. Box 1 lists the funding information that relates to the phases of the research study for which the funding was received, the funding sources and the involvement of the funders in the process of the research study.

Box 1: Suggestions for what funding information to report

Research phases for which funding was received

• Funding received to plan, conduct and/or report the research study under consideration.

Funding sources

• All funders, including the following, with specifications:

- Internal funding (specifying institution)
- Government(s) (specifying granting agency, level of government)
- Inter-government (two or more government agencies such as the European Union)
- Private-for-profit (listing companies/organisations)
- Not-for-profit (specifying support by private-for-profit if it exists, including the companies/organisations that provide support)
- Type of funding received including monetary support, provision of supplies, assistance in manuscript writing, etc.
- Value of monetary support and value of other supports.

Involvement (role) of funders

- Involvement (role) of each funder in the process of the research study, including:
 - Study planning and conduct: design, participant recruitment, data collection, data management, data analysis, quality control.
 - Study reporting (manuscript): medical writing assistance, preparation, review, approval, decision to submit.
 - Authorship: authors employed by the funder.

As for the process of reporting funding information, we suggest that the corresponding author plays the role of the guarantor of this information and take responsibility for:

- Collecting funding information and filling a standardised form;
- Sending the form to all co-authors for approval and verification of accuracy and completeness of the information;
- Submitting the up-to-date form at the time of submission of the manuscript for consideration for publication;
- Updating and re-submitting the form at the time of acceptance of the manuscript for final publication.

Appendix 3 provides a fillable PDF document for use as an instrument for standardised reporting of funding information.

DISCUSSION

Summary of findings

The objective of this study was to describe the characteristics of the funding statements in reports of clinical trials. About nine in ten trial reports included a funding statement and 96% of those statements indicated that funding existed (tables 1 and 2). The latter statements specified the source, amount, and role of funders in 100%, 1%, and 50% of cases respectively (tables 2 and 3). The most commonly reported sources of funding were government and private-for-profit sources (table 2). Of all funding contribution statements in which the source was identified as being a not-for-profit organisation, about half related to not-for-profit organisations for which we found evidence of support by private-for-profit organisation(s). Only three of those statements disclosed the support by the private-for profit-organisations. For trials of pharmacological or surgical interventions, only a fifth reported information on the supplier of the medication or device (table 3). We identified descriptions of a total of 22 different roles for the funders. Trials most frequently reported on roles related to the design of the study, data collection, data analysis, and manuscript preparation (table 4). We also propose a guidance and instrument for standardised reporting of funding information.

Reporting of funding

The high percentage of trials that reported being funded may be explained by the fact that conducting an RCT typically requires a large number of resources.[46-48] Also, we found a positive association between reporting being funded and affiliation with an institution from a

high-income country. This may reflect better opportunities for, and higher ability of, institutions from high-income countries to obtain funding.

Explicit reporting on the role of funder was associated with journal requirement for reporting on the role of funder. This might explain the relatively low percentage of trials that reported on the roles of funders given that only 31% of clinical journals require authors to state the role of funder (unpublished data from another methodological survey [3]). Explicit reporting on the role of funder was positively associated with trial funding from private-for-profit sources. This may be due to the adherence of the industry to higher standards of reporting. Indeed, several studies found that industry-funded trials had higher quality scores as compared to trials funded by other sources.[26, 49-52]

Both reporting being funded and explicit reporting on the role of funder were associated with higher journal impact factor. This is consistent with our previous findings that better reporting of authors' conflicts of interest is associated with higher journal impact factor for both systematic reviews and trials published in Core Clinical Journals.[43, 53]

We found that half of not-for-profit organisations included in funding contribution statements were supported by private-for-profit organisation(s). This is probably an underestimate due to lack of reporting of such support by authors. This also suggests that these types of relationships are prevalent. Indeed, one recent study found that 96 national health organisations accepted money from the Coca-Cola Company, PepsiCo, or both,[54] with a number of these organisations known to fund research (e.g., Juvenile Diabetes Research Foundation). This is very

concerning given that the appearance of support by a not-for-profit may portray confidence in the study findings, in spite of the fact that the indirect for-profit support may have biased those findings.

Strengths and limitations

This is the first methodological survey of a large and representative sample of clinical RCTs to describe the characteristics of the funding statements in detail. Our proposed guidance and instrument for standardised reporting of funding information may serve researchers from different fields of health. Moreover, they may be used for other types of research studies and manuscripts and not only trials (e.g., systematic reviews). In addition, we used systematic and transparent methods for screening and data collection. As our study focused on clinical trials, our findings may not apply similarly to other fields, for example, health policy and systems research.

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Comparison to similar studies

We identified 22 studies on the reporting of funding information in clinical trials (see table 1) [5, 19-39]. While all 22 studies focused on trials published in specific clinical areas or journals, our study assessed a wide sample of clinical trials published in any of the Core Clinical Journals. None of the 22 studies looked at whether the amount of funding was reported. In fact, we found that two trials in our sample reported amount. Two out of the 22 studies assessed reporting of provision of supplies in trials published between 1987 and 1994.[21, 23] To our knowledge, our study is the first one to survey a recent sample of trials for reporting of amount of funding and information on supplies.

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Only four out of the 22 studies assessed reporting on the roles of funders.[25, 29, 38, 39]. Whereas these studies assessed this in industry-funded or partially industry-funded trials, we assessed this across all types of funders. For example, we found that 44% of trials funded solely by governmental sources reported on the role of funder. Example statements from those that reported involvement of the government as a funder include: "appointed an independent data and safety monitoring board", "had input into the study design and data interpretation" and "reviewed and approved the report".

Our previous study on clinical systematic reviews found that a third of systematic reviews did not report on funding or reported no funding in comparison to 15% of trials in this study.[43] When the included systematic reviews reported being funded, the most commonly reported sources of funding were internal funding and government (52% and 67% respectively). While only 2% of clinical systematic reviews reported funding from private-for-profit sources, we found that 40% of clinical trials reported such funding. Moreover, trials were twice more likely than systematic reviews to report on not-for-profit as their funding source (32% and 16% respectively). While half of funded trials reported on the role of the funder, a quarter of funded systematic reviews did so.

In comparison to the CONSORT Checklist section on funding,[10, 11] our guidance provides specific recommendations for the reporting of funding information and includes detailed definitions and examples of types of funders. It also includes a clear classification of roles in which funders may be involved in the process of the trial.

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Implications for practice

Our proposed guidance may help with clearer and more detailed reporting of the characteristics of funding in trials. This may in turn help readers and systematic reviewers better assess the significance of the funding and how it might affect the credibility of findings.[8, 55] Specifically, we recommend that trialists explicitly report more details on the funders, whether they are supported by for-profit organisations, the provision of drugs and equipment,[11] and on the role of funders.[25, 29, 38, 39] Authors have to be careful not to report funding information (i.e., grants received for the conduct of the study) in the conflict of interest section of the manuscript. Also, our findings have implications for reporting statements (such as CONSORT) for improving the reporting of funding information.

Implications for future research

Future research should further explore the issue of funding of not-for profit organisations by forprofit organisations and the role of the latter in the planning, conduct and reporting of research studies. Future research could also assess for the accuracy and completeness of reporting of trial funding and roles of funders. Moreover, it would be interesting to explore reporting of funding in primary studies of other research fields (e.g., health policy and systems), especially that roles of funders may vary from those described in clinical trials.

FIGURES

Figure 1: Study flow diagram

SUPPLEMENTARY FILE

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Appendix 1: Search strategy

<text> Appendix 2: Details of the multiple logistic regression analyses

Appendix 3: Instrument for reporting of funding information

CONTRIBUTIONS

MBH, GG, and EAA conceived and designed the study. MBH coordinated the study throughout. EAA had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MBH, NJ, and MK screened papers for inclusion. MBH, NJ, EAA-J, DJH, EAA-J, LCL, MZH, MA-G, and SA extracted the data. MBH and EAA analysed and interpreted the data. MBH wrote the first draft of the manuscript with EAA. MBH and EAA developed the first draft of the fillable PDF document. All authors critically revised the manuscript and approved the final version. The lead author EAA affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

COMPETING INTERESTS

All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare no conflicts of interest.

FUNDING

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ETHICAL APPROVAL

Not required.

DATA SHARING

Data available upon request.

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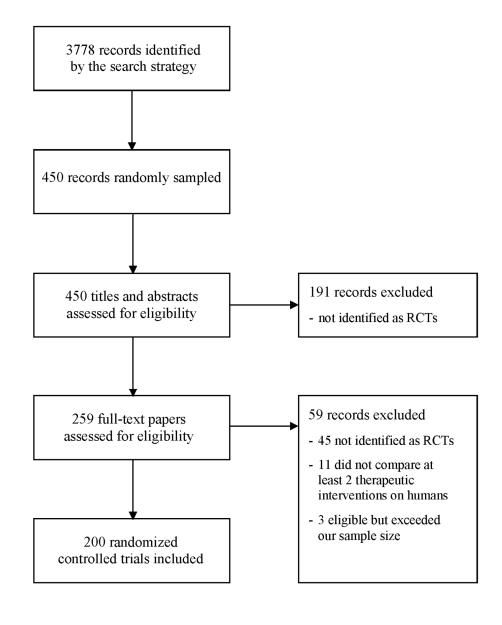
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Study flow diagram 130x160mm (300 x 300 DPI)

APPENDICES

Appendix 1: Search strategy

MEDLINE (Ovid interface) search strategy for randomized controlled trials (Filter obtained from the Cochrane Handbook, under the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)

- 1. randomized controlled trial.pt.
- 2. controlled clinical trial.pt.

- 3. randomized.ab.
 4. placebo.ab.
 5. clinical trials as topic.sh.
 6. randomly.ab.
 7. trial.ti.
 8. 1 or 2 or 3 or 4 or 5 or 6 or 7
 9. exp animals/ not humans.sh.
 10. 8 not 9
 11. limit 10 to ("core clinical journals (aim)" and yr="2015")

Appendix 2: Details of the multiple logistic regression analyses

Analysis 1

Dependent variable (categorical)

• Reporting being funded (funded vs. not funded/not reported); all trials (N=200)

Independent variables

- 1. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)
- 2. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)
- 3. Conflict of interest disclosure (COI present vs. COI absent/not reported) We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.
- 4. Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)

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- 5. Journal impact factor (continuous)
- 6. Number of randomized participants (continuous)
- 7. Classification of the country of the institution to which the first author is affiliated (categorical, high-income vs. middle or low-income)

| | Adjusted OR (95% CI) | p-value |
|---|-------------------------|---------|
| Type of intervention (pharmacologic as opposed to non- pharmacologic) | 1.79 (0.61 – 5.22) | 0.284 |
| Paper is the first one reporting on the findings of the trial | 0.63 (0.12 - 3.22) | 0.577 |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 2.30 (0.62 - 8.38) | 0.209 |
| Journal impact factor * | 1.43 (1.11 – 1.86) | 0.006 |
| Number of randomized participants | 1.00 (1.00 - 1.00) | 0.477 |
| Classification of the country of the institution to which the first author is affiliated * (high-income as opposed to middle or low- income) | 16.25 (4.03 – 65.5) | <0.0001 |
| Journal requirement for reporting on the role of funder | 1.02 (0.36 – 2.84) | 0.974 |
| DR = odds ratio; CI = confidence interval p-values for statistically significant associations. | 0 | |

Analysis 2

Dependent variable (categorical)

• Explicit reporting of the role of funder (reported vs. not reported); trials that reported being funded (N=171)

Independent variables

- 1. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)
- 2. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)
- 3. Conflict of interest disclosure (COI present vs. COI absent/not reported) We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.
- Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)
- 5. Journal impact factor (continuous)
- 6. Number of randomized participants (continuous)
- 7. Classification of the country of the institution to which the first author is affiliated (categorical, high-income vs. middle or low-income)
- 8. Journal requirement for reporting on the role of funder (categorical, yes vs. no)
- Funding from private-for-profit source(s) as opposed to all other sources of funding (categorical, yes vs. no)

| | Adjusted OR (95% CI) | p-value |
|---|-------------------------|----------|
| Type of intervention (pharmacologic as opposed to non- pharmacologic) | 1.60 (0.71 – 3.58) | 0.261 |
| Paper is the first one reporting on the findings of the trial * | 3.47 (1.21 – 9.96) | 0.021 |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 0.53 (0.22 – 1.32) | 0.174 |
| Journal impact factor * | 1.06 (1.03 – 1.10) | < 0.0001 |
| Number of randomized participants | 1.00 (1.00 - 1.00) | 0.152 |
| Classification of the country of the institution to which the first author is affiliated (high-income as opposed to middle or low- income) | 3.30 (0.41 – 26.60) | 0.262 |
| Journal requirement for reporting on the role of funder * | 3.25 (1.43 - 7.38) | 0.005 |
| Funding from private-for-profit source(s) * | 4.9 (2.11 – 11.83) | < 0.0001 |
| DR = odds ratio; CI = confidence interval p-values for statistically significant associations. | | |

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Keywords: funding, role of funder, randomised controlled trial

15 Word count: 3,675 words

1 ABSTRACT

Objectives: To provide a detailed and current characterisation of funding of a representative
sample clinical trials. We also aimed to develop guidance for standardised reporting of funding
information.

Methods: We addressed the extent to which clinical trials published in 2015 in any of the 119
Core Clinical Journals included a statement on the funding source (e.g., whether a not-for-profit
organisation was supported by a private-for-profit), type of funding, amount and role of funder.
We used a stepwise approach to develop a guidance and an instrument for standardised reporting
of funding information.

Results: Of 200 trials, 178 (89%) included a funding statement, of which 171 (96%) reported being funded. Funding statements in the 171 funded trials indicated the source in 100%, amount in 1% and roles of funders in 50%. The most frequent sources were governmental (58%) and private-for-profit (40%). Of 54 funding statements in which the source was a not-for-profit organisation, we found evidence of undisclosed support of those organisations from private-for-profit organisation(s) in 26 (48%). The most frequently reported roles of funders in the 171 funded trials related to study design (42%) and data analysis, interpretation, or management (41%). Of 139 RCTs addressing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or device. The proposed guidance addresses both the funding information that RCTs should report and the reporting process. Attached to the guidance is a fillable PDF document for use as an instrument for standardised reporting of funding information.

22 Conclusion: Although the majority of RCTs report funding, there is considerable variability in23 the reporting of funding source, amount and roles of funders. A standardised approach to

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| reporting of funding information would address these limitations. Future research should explore |
|---|
| reporting of running information would address these initiations. I uture research should explore |
| the implications of funding by not-for profit organisations that are supported by for-profit |
| organisations. |
| |
| Strengths and limitations of this study: |
| • First cross-sectional survey of a large and representative sample of clinical RCTs to |
| describe the characteristics of the funding statements in detail. |
| • Provides a proposed guidance and instrument for standardised reporting of funding |
| information. |
| • Use of systematic and transparent methods, e.g., duplicate and independent processes in |
| screening and data collection. |
| • Includes trials limited to the clinical field and so our findings may not apply similarly to |
| other fields such as public health research. |
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1 BACKGROUND

Funding sources may influence the reporting of research findings and the interpretation of results.[1-6] One study found that 86% of trial protocols documented an industry partner's right to disapprove or review proposed manuscripts.[7] This might also apply to other types of funders, for example, government. Reporting of funding in trials may appropriately influence how physicians interpret and use trial findings in clinical practice.[8, 9] The Consolidated Standards of Reporting Trials (CONSORT) checklist recognises this issue by including a section on reporting of funding.[10, 11]

Reports in the lay media have documented how for-profit organisations support research through not-for-profit organisations.[12, 13] In one example, The Independent recently highlighted a systematic review suggesting that the consumption of low-energy sweeteners in place of sugar reduces energy intake and body weight.[14] The review authors list the International Life Sciences Institute as the study funder. While the Institute describes itself as "a nonprofit, worldwide organisation whose mission is to provide science that improves human health", it receives funding primarily from companies such as the Coca-Cola Company, PepsiCo and Nestlé.[15] Other examples of not-for-profit organisations funded by industry and supporting research are the Sugar Association, Inc. [16, 17] and the now defunct Global Energy Balance Network.[18]

We conducted a comprehensive review of the literature and found 22 studies that assessed reporting of funding in clinical trials (see appendix 1).[5, 19-39] The main gap we identified in this literature is a detailed and current characterisation of funding of a representative sample of

trials. Indeed, all of the identified studies focused on trials published in specific clinical areas or journals. Most (14, 64%) reported only on funded trials or did not differentiate between nonfunded trials and those that do not report on funding. Seventeen studies (77%) did not always distinguish trials with no funding from those funded by the government or by not-for-profit sources. Moreover, these studies seldom assessed reporting on the role of funder (n=4), provision of supplies (n=2), and the amount of funding (n=0). None of the studies explored the relationship between not-for-profit organizations funding trials and for-profit organizations.

9 Therefore the main objective of this study was to provide a detailed and current characterisation
10 of funding of a representative sample of clinical trials. We also aimed to develop guidance for
11 standardised reporting of funding information.

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METHODS

14 Design overview and definitions

We followed systematic methodology to conduct a cross-sectional survey of published randomised controlled trials (RCTs). We define funding as any support (e.g. monetary support, provision of supplies, assistance in manuscript writing). We considered as funding statement any text in the trial report providing any information regarding the funding of the trial, including a statement of no funding. A funding statement could indicate more than one funding contribution.

21 Eligibility criteria

22 We included reports of studies described as RCTs comparing at least two therapeutic 23 interventions of any type in humans and published in English. We included RCTs with cross-

over designs and secondary reports of trials (i.e. follow-up study; post-hoc analysis; interim
analysis; pre-specified analysis or secondary outcomes or sub-study of a trial). We excluded nonrandomised trials, trials addressing basic sciences topics and non-clinical interventions, and
research letters.

6 Search strategy

We searched Ovid Medline in September 2015 and limited our search to the year 2015 and the 119 Core Clinical Journals (Abridged Index Medicus (AIM)).[40] We applied the search filter obtained from the Cochrane handbook to identify RCTs. See appendix 2 for the detailed search strategy.

Selection process

We used an online sequence generator (www.random.org/sequences) to randomise the citations captured by the search. We followed the order of the randomization list to screen citations until we obtained 200 eligible RCTs. Our sample size allows for a narrow 95% confidence interval (+/- 5%) around proportions of studies reporting sources of funding.

Following calibration exercises, three reviewers (MBH, NJ, MK) worked in teams of two (MBH was the reviewer on both) to screen titles and abstracts in duplicate and independently, using EndNoteTM X7.5 software (Thomson Reuters, Philadelphia, PA, USA). We obtained the fulltexts of citations judged as potentially eligible by either reviewer. The two teams of reviewers screened full-texts in duplicate and independently. They resolved disagreements by discussion,

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| 1 | or with the help of a third reviewer (EAA) as needed. A PRISMA study flow diagram [41] |
|----|---|
| 2 | presents the results of the selection process (figure 1). |
| 3 | |
| 4 | Data extraction process |
| 5 | We developed a standardised data extraction form along with specific instructions. After pilot |
| 6 | testing the form, we embedded it electronically into Research Electronic Data Capture |
| 7 | (REDCap), a secure web-based application designed to support data capture for research |
| 8 | studies.[42] After completing calibration exercises, nine authors divided into teams of two |
| 9 | extracted data in duplicate and independently (MBH was a reviewer on each of the eight teams). |
| 10 | Each team compared results and resolved disagreements through discussion, or with the help of a |
| 11 | third reviewer (EAA) as needed. |
| 12 | |
| 13 | Data extracted |
| 14 | We extracted the following characteristics of the RCTs: |
| 15 | • Number of trial authors; |
| 16 | • Whether it is the first full-text report of the trial findings; |
| 17 | • Classification of the income level of the country in which the first author's institution is |
| 18 | located (as high, upper-middle, lower-middle, or low income country according to the |
| 19 | July 2015 World Bank list of economies); |
| 20 | • Type of intervention and type of control; |
| 21 | • Number of randomised participants; |
| 22 | • Level of risk of bias associated with allocation concealment (based on the Cochrane |
| 23 | Collaboration's tool for assessing risk of bias)[43]; |
| | |

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- Whether authors reported conflicts of interest;
- Whether the report included a funding statement.

We then focused on trials that included funding information. We extracted the following fundingcharacteristics reported in the paper:

• Whether it reported funding versus no funding;

• The type of source(s) of funding (see appendix 3). These included internal funding (when it is an academic or hospital affiliation) and external funding, categorized into: government, private-for-profit, private not-for-profit with evidence of support by private-for-profit that is a health industry, private not-for-profit with evidence of support by private-for-profit that is not a health industry, and private not-for-profit with no evidence of support by private-for-profit. As needed, we performed an online search to accurately assign the type of the funding source. When a funding source was identified as a not-for-profit organisation, we searched the organisation's website for any information on partnership with or support from a for-profit organisation (see appendix 4 for details);

- Amount of funding;
 - Whether the paper reported to be sponsored by a source different than the source of funding/support;
 - Whether information was reported (across the paper) on supplies in trials on pharmacological or surgical interventions (i.e., drugs, devices, equipment, samples, or placebos) and whether the supplier is a funding source. We looked for that information in the funding statements, acknowledgement statements and the methods section.

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Finally, and in trials that reported being funded, we assessed whether the role of funder was
 explicitly reported for any funder as involved or not involved in the process of the research
 study.

5 Data analysis

We assessed agreement between reviewers of each team for inclusion of RCTs at the full-text
screening stage using chance-corrected agreement (kappa statistic). We conducted descriptive
analyses of the general characteristics of the RCT, as well as the characteristics of the funding
statement. We present summary data for categorical variables as frequencies and percentages and
for continuous variables as median and interquartile range (IQR). All calculations used SPSS,
version 21.0 for Windows (SPSS INC., Chicago, IL, USA).

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Candidate independent variables for multivariable logistic regression analyses to assess the predictors of reported funding and the role of funder included characteristics of the RCT and variables related to Journal policy for reporting funding (i.e., journal requirement for reporting of funding; journal requirement for reporting on the role of funder). For variables related to journal policy for reporting funding information, we used unpublished data we had collected in mid 2014 for another cross-sectional survey.[44]

20 Development of the guidance

We used the following approach for developing the proposed guidance for standardised reporting of funding information. First, our classification of funding sources was based on one we had used in a previous study (governmental, private not-for-profit, and private-for-profit)[45] that we modified after a review of relevant literature[5, 22, 27] and of journals' policies on reporting of

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funding information (unpublished data from another cross-sectional survey).[44] Second, we refined the classification through an iterative process of discussion and revisions based on funding statements reported in this sample of RCTs, as well as in a sample of systematic reviews.[46] Finally, we used Adobe[®] Acrobat XI[®] software to develop a fillable PDF document for use as an instrument for standardised reporting of funding information.

The process included both in-person and email discussions among the authors of this article and feedback from external experts. The individuals involved have the following profiles: author EAA is a clinical epidemiologist and was an associate journal editor for Health and Quality of Life Outcomes journal; author GG is a clinical epidemiologist and has been a member of editorial boards of 8 journals. The external experts we consulted include Dr. Elie Al-Chaer (health researcher with a law degree and editor-in-chief of International Journal of Women's Health and Dove Press), Dr. Joerg Meerpohl (associate editor of Health and Quality of Life Outcomes journal), and Dr. Peter Tugwell (co-editor of the Journal of Clinical Epidemiology).

RESULTS

Figure 1 presents the study flow diagram. Agreement proved substantial (kappa= 0.78) and near perfect (kappa= 0.86) respectively for each of the two teams at the full-text screening stage.

Characteristics of the randomised controlled trial

The first authors of most trials (90%) had affiliations in high-income countries and almost half (49%) assessed pharmacological interventions (table 1). Most trials (94%) reported on conflicts

| 1 2 | | |
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| 3 4 5 | 1 | of interest and 54% disclosed presence of conflicts of interest. Almost all (178, 89%) included a |
| 5 6 7 | 2 | funding statement. |
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| 1 [| Table 1: General | characteristics of | f the included | randomised c | controlled trials (N=200) |
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|-----|------------------|--------------------|----------------|--------------|---------------------------|

| | Overall |
|---|--------------|
| | n (%) \$ |
| Number of trial authors; median (IQR) | 9 (6 - 14) * |
| Paper is the first full-text report of the trial findings | 171 (86%) |
| Classification of the income level of the country in which the first author's | |
| institution is located: | |
| High-income | 179 (90%) |
| Upper middle-income | 15 (8%) |
| Lower middle-income | 4 (2%) |
| Low-income | 2 (1%) |
| Type of intervention | |
| Pharmacological | 97 (49%) |
| Surgical/invasive procedure | 42 (21%) |
| Non-invasive procedure | 11 (6%) |
| Lifestyle intervention | 15 (8%) |
| Screening/diagnostic intervention | 9 (5%) |
| Psycho-therapeutic intervention | 4 (2%) |
| Rehabilitation | 6 (3%) |
| Other | 16 (8%) |
| Type of control | |
| Active control (as opposed to non-active) | 82 (41%) |

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| Number of randomised participants; median (IQR) | 160 (60 - 485) |
|--|----------------|
| Level of risk of bias associated with allocation concealment | |
| High risk | 4 (2%) |
| Low risk | 59 (30%) |
| Unclear | 137 (69%) |
| Reporting of conflicts of interest | |
| Not reported | 12 (6%) |
| Reported with no conflicts of interest disclosed | 80 (40%) |
| Reported with conflicts of interest disclosed | 108 (54%) |
| Inclusion of a funding statement | |
| Included (as opposed to not included) | 178 (89%) |

1

2 \$ For continuous variables, numbers refer to median (IQR); indicated in the relevant row.

3 * The number of trial authors per trial ranged between 1 and 91.

Characteristics of the reported funding

Table 2 presents the characteristics of the reported funding of the 178 trials with a funding statement, of which 171 (96%) reported being funded. The median number (IQR) of funding sources for each funded trial was 1 (1-3), with a range of 1 to 12 sources per trial. The top most frequent sources of funding were governmental (58%) and private-for-profit (40%). Of the 54 funding contribution statements in which the source was identified as being a not-for-profit organisation, we found evidence of support of those organisations from private-for-profit entity(ies) in 29 (54%), of which 26 (48%) did not disclose this support in the study report. Twenty-one trials (12%) reported funding from private-for-profit in addition to another source. Two trials reported the amount of funding received. Of the 139 RCTs assessing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or

12 device.

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Table 2: Characteristics of the funding statements included in the randomised controlled trials

2 (N=178 trials)

| | Overall |
|--|-----------|
| | n (%) |
| Funding statement reported being: | |
| Funded (as opposed to not funded) | 171 (96%) |
| Source(s) of funding (when reported as funded; N=171) \$ | |
| Internally funded | 26 (15%) |
| Externally funded by: | |
| Government | 99 (58%) |
| Private-for-profit | 68 (40%) |
| Private not-for-profit with evidence of support by private-for-profit | 14 (8%) |
| that is a health industry | |
| Private not-for-profit with evidence of support by private-for-profit | 15 (9%) |
| that is not a health industry | |
| Private not-for-profit with no evidence of support by private-for- | 25 (15%) |
| profit | |
| Statement included amount of funding received | 2 (1%) |
| Paper reported to be sponsored by a source different than the source of | 2 (1%) |
| funding/support | |
| Paper reported information on supplies (i.e., drugs, devices, equipment, | |
| samples, or placebos) * | |

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| Yes, supplied by manufacturer same as funder | 12 (9%) |
|---|-----------|
| Yes, supplied by manufacturer different than funder | 17 (12%) |
| Not reported | 110 (79%) |

\$ More than one type could apply for trials reporting more than one source of funding.

app. ber of t * Calculated using the number of trials on pharmacological interventions and surgical/invasive

procedures (N=139).

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1 The reported roles of funders

Table 3 presents the reported roles of funders in the 171 trials that reported being funded. 85 trials (50%) indicated the role of funders and provided descriptions of 22 different roles. The most frequent roles indicated in these 85 trials were participation in the design of the study (42%), data collection (27%), data analysis, interpretation, or management (41%), manuscript preparation (32%), decision to submit the manuscript (15%) and conduct of the study (15%).

decision .

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1 Table 3: Reporting on the roles of funders in the randomised controlled trials that reported being

2 funded (N=171)

| | Reported | role as: | Did not report |
|---|--------------|----------|----------------|
| | | | role |
| <u>^</u> | Not involved | Involved | |
| | n (%) | n (%) | n (%) |
| Any role of the below | 41 (24%) | 44 (26%) | 86 (50%) |
| Protocol/design of the study | 41 (24%) | 30 (18%) | 100 (58%) |
| Data collection | 31 (18%) | 16 (9%) | 124 (73%) |
| Verifying data accuracy/ fact checking | 0 (0%) | 3 (2%) | 168 (98%) |
| Outcome adjudication | 0 (0%) | 1 (1%) | 170 (99%) |
| Data analysis/ interpretation/ management | 40 (23%) | 31 (19%) | 100 (58%) |
| Funded a medical writer | 1 (1%) | 19 (11%) | 151 (88%) |
| Preparation of the manuscript | 34 (20%) | 20 (12%) | 117 (68%) |
| Review of the manuscript | 17 (10%) | 7 (4%) | 147 (86%) |
| Approval of the manuscript | 17 (10%) | 8 (5%) | 146 (85%) |
| Decision to submit the manuscript | 18 (10%) | 6 (4%) | 147 (86%) |
| Appointed an independent data and safety | 0 (0%) | 1 (1%) | 170 (99%) |
| monitoring board | | | |
| Auditing of study conduct | 0 (0%) | 3 (2%) | 168 (98%) |
| Management | 0 (0%) | 3 (2%) | 168 (98%) |
| Team assembly | 0 (0%) | 2 (1%) | 169 (99%) |
| Conduct of study | 13 (8%) | 12 (7%) | 146 (85%) |

| Generated randomisation list | 0 (0%) | 3 (2%) | 168 (98%) |
|-------------------------------|--------|--------|-----------|
| Enrollment of participants | 0 (0%) | 1 (1%) | 170 (99%) |
| Logistical support | 0 (0%) | 3 (2%) | 168 (98%) |
| Holding study data | 0 (0%) | 1 (1%) | 170 (99%) |
| Study oversight | 0 (0%) | 2 (1%) | 169 (99%) |
| Steering committee | 0 (0%) | 1 (1%) | 170 (99%) |
| Measurement of study variable | 0 (0%) | 5 (3%) | 166 (97%) |

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1 Results of the regression analyses

2 Appendix 5 presents the details of the multivariable logistic regression analyses. Reporting being

- 3 funded was positively associated with two variables (table 4), based on data from all included
- 4 trials (n=200). Explicit reporting on the role of funder was positively associated with four
- 5 variables (table 4), based on data from trials reporting being funded (n=171).

| Dependent variables | Independent variables | Adjusted OR | p-val |
|------------------------|--|----------------|---------|
| | | (95% CI) | |
| 'Reporting being | Journal impact factor | 1.43 | 0.00 |
| funded' model (N=200) | | (1.11 – 1.86) | |
| | Affiliation with an institution from a | 16.25 | < 0.00 |
| | high-income country (reference category | (4.03 - 65.5) | |
| | being middle or low-income countries) | | |
| 'Explicit reporting on | Paper is the first reporting on the findings | 3.47 | 0.02 |
| the role of funder' | of the trial | (1.21 – 9.96) | |
| model (N=171) | Journal impact factor | 1.06 | < 0.000 |
| | 6 | (1.03 – 1.10) | |
| | Journal requirement for reporting on the | 3.25 | 0.005 |
| | role of funder | (1.43 – 7.38) | |
| | Funding from private-for-profit source(s) | 4.9 | <0.000 |
| | (reference category being all other types | (2.11 – 11.83) | |
| | of funding sources) | | |

Proposed guidance

The proposed guidance provides suggestions for both funding information and the reporting
process. Box 1 lists the funding information that relates to the phases of the research study for
which the funding was received, the funding sources and the involvement of the funders in the
process of the research study.

> **Box 1:** Suggestions for what funding information to report Funding sources (and Grant ID if applicable)

- All types of funding sources, including the following with specifications:
 - Internal funding (specifying institution)
 - Government(s) (specifying granting agency, level of government)
 - Inter-government (two or more government agencies such as the European Union)
 - Private-for-profit (listing companies/entities)
 - Private not-for-profit (listing organisations/philanthropies)
- Research phases for which funding was received: planning, conduct and/or reporting of the research study under consideration. When funding relates to provision of supplies, the appropriate answer is 'conduct'.
- Type of funding received including monetary support, provision of supplies, etc.
- Value of monetary support and value of other supports.
- Whether the funding provided by any of the funding sources is supported by an entity other than/external to the funding source.

Involvement (role) of funding sources

- Involvement (role) of each funder in the process of the research study, including:
 - Study planning and conduct: design and protocol drafting, study management, participant recruitment, data collection, data management, data analysis, quality control.
 - Study reporting (manuscript): preparation, review, approval, decision to submit.
 - Authorship: authors employed by the funder.

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| 2 3 4 | 1 | |
|----------------|----|--|
| 4 5 6 | 2 | As for the process of reporting funding information, we suggest that the corresponding author |
| 7 8 | 3 | plays the role of the guarantor of this information (given his/her primary responsibility of |
| 9 10 11 | 4 | communicating with both the journal and the readers) and take responsibility for: |
| 12 13 | 5 | • Collecting funding information and filling a standardised form; |
| 14 15 16 | 6 | • Sending the form to all co-authors for approval and verification of accuracy and |
| 17 18 | 7 | completeness of the information; |
| 19 20 21 | 8 | • Submitting the up-to-date form at the time of submission of the manuscript for |
| 21 22 23 | 9 | consideration for publication; |
| 24 25 | 10 | • Updating and re-submitting the form at the time of acceptance of the manuscript for final |
| 26 27 28 | 11 | publication. |
| 29 30 | 12 | |
| 31 32 33 | 13 | Appendix 6 provides a fillable PDF document for use as an instrument for standardised reporting |
| 34 35 | 14 | of funding information. |
| 36 37 38 | 15 | |
| 39 40 | 16 | DISCUSSION |
| 41 42 | 17 | Summary of findings |
| 43 44 45 | 18 | The objective of this study was to describe the characteristics of the funding statements in reports |
| 46 47 | 19 | of clinical trials. About nine in ten trial reports included a funding statement and 96% of those |
| 48 49 50 | 20 | statements indicated that funding existed. The latter statements specified the source, amount, and |
| 51 52 | 21 | role of funders in 100%, 1%, and 50% of cases respectively. The most commonly reported |
| 53 54 | 22 | sources of funding were government and private-for-profit sources. Of all funding contribution |
| 55 56 57 | 23 | statements in which the source was identified as being a not-for-profit organisation, about half |
| 58 59 60 | | 25 |

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related to not-for-profit organisations for which we found evidence of support by private-forprofit entity(ies). Only three of those statements disclosed the support by the private-for profitentities. For trials of pharmacological or surgical interventions, only a fifth reported information on the supplier of the medication or device. We identified descriptions of a total of 22 different roles for the funders. Trials most frequently reported on roles related to the design of the study, data collection, data analysis, and manuscript preparation. We also propose a guidance and instrument for standardised reporting of funding information.

Reporting of funding

10 The high percentage of trials that reported being funded may be explained by the fact that 11 conducting an RCT typically requires a large number of resources.[47-49] Also, we found a 12 positive association between reporting being funded and affiliation with an institution from a 13 high-income country. This may reflect better opportunities for, and higher ability of, institutions 14 from high-income countries to obtain funding.

Explicit reporting on the role of funder was associated with journal requirement for reporting on the role of funder. This might explain the relatively low percentage of trials that reported on the roles of funders given that only 31% of clinical journals require authors to state the role of funder (unpublished data from another cross-sectional survey [44]). Explicit reporting on the role of funder was positively associated with trial funding from private-for-profit sources. This may be due to the adherence of the industry to higher standards of reporting. Indeed, several studies found that industry-funded trials had higher quality scores as compared to trials funded by other sources.[24, 50-53]

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Both reporting being funded and explicit reporting on the role of funder were associated with higher journal impact factor. This is consistent with our previous findings that better reporting of authors' conflicts of interest is associated with higher journal impact factor for both systematic reviews and trials published in Core Clinical Journals.[46, 54]

We found that half of not-for-profit organisations included in funding contribution statements were supported by private-for-profit entity(ies). This is probably an underestimate due to lack of reporting of such support by authors. This also suggests that these types of relationships are prevalent. Indeed, one recent study found that 96 national health organisations accepted money from the Coca-Cola Company, PepsiCo, or both, [55] with a number of these organisations known to fund research (e.g., Juvenile Diabetes Research Foundation). This is very concerning given that the appearance of support by a not-for-profit may portray confidence in the study findings, in spite of the fact that the indirect for-profit support may have biased those findings. Indeed, while we explored whether private not-for-profit organizations were supported by private-for-profit entity(ies), this may also apply to other types of funding sources.

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18 Strengths and limitations

19 This is the first cross-sectional survey of a large and representative sample of clinical RCTs to 20 describe the characteristics of the funding statements in detail. Our proposed guidance and 21 instrument for standardised reporting of funding information may serve researchers from 22 different fields of health. Moreover, they may be used for other types of research studies and

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manuscripts and not only trials (e.g., systematic reviews). In addition, we used systematic and transparent methods for screening and data collection.

> As our study focused on clinical trials, our findings may not apply similarly to other fields, for example, health policy and systems research. While we did not conduct a formal and extensive validation of the guidance (and instrument), we believe that it has both face and content validity given that we based it on a thorough review of the related literature, on the cross-sectional survey of trials, and we revised it based on feedback from journal editors and a lawyer.

- 10 Comparison to similar studies

We identified 22 studies on the reporting of funding information in clinical trials (see appendix 1) [5, 19-39]. While all 22 studies focused on trials published in specific clinical areas or journals, our study assessed a wide sample of clinical trials published in any of the Core Clinical Journals. None of the 22 studies looked at whether the amount of funding was reported. In fact, we found that two trials in our sample reported amount. Two out of the 22 studies assessed reporting of provision of supplies in trials published between 1987 and 1994.[34, 39] To our knowledge, our study is the first one to survey a recent sample of trials for reporting of amount of funding and information on supplies.

20 Only four out of the 22 studies assessed reporting on the roles of funders.[20, 22, 28, 36]. 21 Whereas these studies assessed this in industry-funded or partially industry-funded trials, we 22 assessed this across all types of funders. For example, we found that 44% of trials funded solely 23 by governmental sources reported on the role of funder. Example statements from those that

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reported involvement of the government as a funder include: "appointed an independent data and safety monitoring board", "had input into the study design and data interpretation" and "reviewed and approved the report".

Our previous study on clinical systematic reviews found that a third of systematic reviews did not report on funding or reported no funding in comparison to 15% of trials in this study.[46] When the included systematic reviews reported being funded, the most commonly reported sources of funding were internal funding and government (52% and 67% respectively). While only 2% of clinical systematic reviews reported funding from private-for-profit sources, we found that 40% of clinical trials reported such funding. Moreover, trials were twice more likely than systematic reviews to report on not-for-profit as their funding source (32% and 16% respectively). While half of funded trials reported on the role of the funder, a quarter of funded systematic reviews did so.

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In comparison to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[56, 57] and the CONSORT checklist sections on funding,[10, 11] our guidance provides more detailed and specific recommendations for the reporting of funding information and includes detailed definitions and examples of types of funders. It also includes a clear classification of roles in which funders may be involved in the process of the trial. Whereas the International Committee of Medical Journal Editors (ICMJE) conflict of interest disclosure form includes a section for the reporting of "financial support", the questions and options that follow imply types of financial conflicts of interest for each individual author rather than the study's funding.[58]

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2 Implications for practice

Our proposed guidance may help with clearer and more detailed reporting of the characteristics of funding in trials. This may in turn help readers and systematic reviewers better assess the significance of the funding and how it might affect the credibility of findings.[8, 59] Specifically, we recommend that trial authors explicitly report more details on the funders, whether they are supported by for-profit organisations, the provision of drugs and equipment, [11] and on the role of funders. [20, 22, 28, 36] We suggest that authors do not to report funding information (i.e., grants received for the conduct of the study) in both the funding section and the conflict of interest section of the manuscript, but only in the former one. Also, our findings have implications for reporting statements (such as SPIRIT and CONSORT) for improving the reporting of funding information.

14 Implications for future research

Future research should further explore the issue of funding of not-for profit organisations by forprofit organisations and the role of the latter in the planning, conduct and reporting of research studies. Future research could also assess for the accuracy and completeness of reporting of trial funding and roles of funders. Moreover, it would be interesting to explore reporting of funding in primary studies of other research fields (e.g., health policy and systems), especially that roles of funders may vary from those described in clinical trials. Finally, our proposed guidance and instrument for the standardised reporting of funding information would benefit from formal and extensive validation.

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| 5 6 | 2 | FIGURES |
| 7 8 9 | 3 | Figure 1: Study flow diagram |
| 10 11 | 4 | |
| 12 13 14 | 5 | SUPPLEMENTARY FILE |
| 15 16 | 6 | Appendix 1: Comparative chart including 23 related surveys of reporting of funding information |
| 17 18 10 | 7 | in trials |
| 19 20 21 | 8 | Appendix 2: Search strategy |
| 22 23 | 9 | Appendix 3: Types of funding sources |
| 24 25 26 | 10 | Appendix 4: Process followed to verify whether a private not-for-profit organisation was |
| 27 28 | 11 | supported by a private-for-profit entity |
| 29 30 | 12 | Appendix 5: Details of the multivariable logistic regression analyses |
| 31 32 33 | 13 | Appendix 6: Instrument for reporting of funding information |
| 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 4 55 56 57 58 59 | 14 | 81 |
| 60 | | 51 |

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funding information. We also thank the reviewers whose suggestions helped improve this
manuscript.

7 CONTRIBUTIONS

MBH, GG, and EAA conceived and designed the study. MBH coordinated the study throughout. EAA had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MBH, NJ, and MK screened papers for inclusion. MBH, NJ, EAA-J, DJH, EAA-J, LCL, MZH, MA-G, and SA extracted the data. MBH and EAA analysed and interpreted the data. MBH wrote the first draft of the manuscript with EAA. MBH and EAA developed the first draft of the fillable PDF document. All authors critically revised the manuscript and approved the final version. The lead author EAA affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

19 COMPETING INTERESTS

20 All authors have completed the ICMJE uniform disclosure form at
21 http://www.icmje.org/coi disclosure.pdf and declare no conflicts of interest.

23 FUNDING

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ETHICAL APPROVAL

Not required.

DATA SHARING

Data available upon request.

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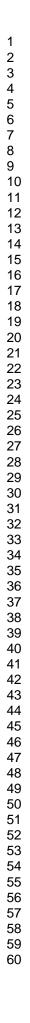
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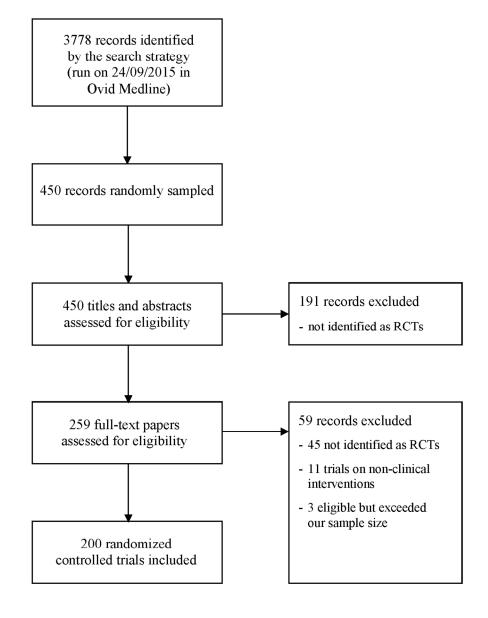
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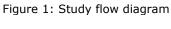
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| 2 3 4 5 6 | APPENDICE Appendix 1: (| | related surv | veys of reportin | g of funding information in trials | njopen-2017-015997 on 5 by copyright, including for uses |
| 7 8 9 10 | Survey | Eligibility criteria | Number of trials | Year of trial publication | Characteristics of funding statement assessed in the | or O Main findings |
| 11 12 13 14 | | 0 | | publication | survey | 2017. Dow ignement selated to to |
| 15 16 17 18 | Als-Nielsen 2003 [19] | RCTs included in eligible meta-analyses in Cochrane reviews | 370 | 1971 - 2000 | - Source of funding | Funding was not reported in 29%. 39% avere funded by for-profit organase fors. |
| 19 20 21 22 | Etter 2007 [25] | RCTs on nicotine replacement therapy in Cochrane review | 90 | 1979 - 2003 | - Source of funding | 54% For Section 2000 Support 54% For Section 2000 Support 55 46% Section 2000 Support 55 46% Section 2000 Support 2000 Sup |
| 23 24 25 26 27 | Mugambi 2013 [5] | RCTs on infant formula supplementation of symbiotics, probiotics, or prebiotics | 67 | 1980 - 2012 | - Source of funding | 60% average funded by food industry. 24% did not specify their source of funding. |
| 28 29 30 31 32 33 34 35 36 37 | Rochon 1994 [34] | Manufacturer-associated RCTs of NSAIDs listed in MEDLINE | 52 | 1987 - 1990 | Grant support Pharmaceutical authorship Provision of supplies Published in a pharmaceutical sponsored journal supplement | 19% geported grant support. 36.5% reported pharmaceutical authorship. 13.5% reported that manufacturer suppled drug. 31% reported in a pharmaceutical sponsored journal supplement. |
| 38 39 40 | Momeni 2008 [29] | Trials published in 4 major plastic surgery journals | 346 | 1990 - 2005 | - Source of funding | 20% reperted on financial support, of which 60% were supported by industrial sponsors |
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| Yaphe 2001 [39] | RCTs of drugs or food products published in 5 medical journals | 314 | 1992 - 1994 | Source of funding Pharmaceutical authorship Provision of supplies | 68% received pharmaceutical industry support. 9 33% received support as manpower (authorship or statistical help). 21% received support as supply of drugs |
| Peppercorn 2007 [31] | Breast cancer clinical trials published in 10 medical journals | 140 | 1993, 1998, 2003 | Source of funding Pharmaceutical authorship | 48% & B categorised as pharmaceutical studies: 26% apported pharmaceutical industry authors by |
| Bero 2007 [20] | Reports of RCTs comparing statin drugs | 192 | 1995 - 2005 | - Source of funding - Role of funder | 39% and no disclosure or no funding. 49% and no disclosure or no funding. whice a funding from industry, of whice a funding from industry, of spon |
| Djulbegovic 2000 [24] | RCTs for multiple myeloma | 130 | 1996 - 1998 | - Source of funding | 26% read funding solely or in part by comments all organisations. |
| Clifford 2002 [23] | RCTs published in 5 high impact factor general medical journals | 100 | 1999 - 2000 | - Source of funding | 94% were funded, of which 66% were funded in whole or in part by industry. 6% ded not disclose their source of funding. |
| Bhandari 2004 [21] | RCTs published in 8 surgical and 5 medical journals | 332 | 1999 - 2001 | - Source of funding | 44% had no reported funding. 37% reported funding by industry. |
| Tuech 2005 [36] | Phase III cancer RCTs published in 12 journals | 655 | 1999 - 2003 | - Source of funding - Role of funder | 35% Fivere industry-sponsored, of which 18% fiepfitted the role of the study sponsor. 21% field bot disclose funding and only 1 trial fiscussed no financial support. |
| Shah 2005 [35] | Articles published in the Spine journal | 34 | 2000 - 2003 | - Source of funding | 23% were industry funded. |
| Tungaraza 2007 [37] | Original papers on psychiatric drug treatment published in two journals | 132 | 2000 - 2004 | Source of funding Pharmaceutical authorship | 85% were industry-funded. 40% were industry-authored studies. |

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| 3 4 5 6 7 | Ridker 2006 [33] | Cardiovascular medicine RCTs published in 3 medical journals | 349 | 2000 - 2005 | - Source of funding | 31% were financed by not-for-profit organisations, 44% by for-profit manufacturers, and 19% by both. 6% rection source of funding. |
| 8 9 10 11 12 13 14 | Voineskos 2016 [38] | Surgical RCTs | 173 | 2000 - 2013 | - Source of funding | 58% did Rot acknowledge a source of funding for 14% set orted funding from for-profit sources 10% combicitly reported 'no funding received s |
| 15 16 17 18 19 | Montogom -ery 2004 [30] | RCTs on second generation antipsychotics for the management of schizophrenia | 86 | 2002 | - Source of funding | 84% were industry-funded. 16% avere non-industry-funded. |
| 20 21 22 23 24 25 26 | Perlis 2005 [32] | RCTs published in one of the four dermatology journals with the highest science citation impact factor scores and total citations | 179 | 2002 | - Source of funding | 57% is by ted receiving at least some inducery support. 26% ≩ad no information about funding. |
| 27 28 29 30 | Khan 2012 [27] | RCTs of drug therapy for rheumatoid arthritis | 103 | 2002 - 2003 2006 - 2007 | - Source of funding | 62% ad complete or partial industry funding g. 19% ad an unspecified funding source. |
| 31 32 33 34 35 36 | Hodgson 2014 [26] | RCTs in chronic wound care | 167 | 2004 - 2011 | - Source of funding | 35% sivers reported as having been commercially funded. 26% sither did not report the source of funding of the status of funding source was unclear. |
| 37 38 39 40 41 | Bridoux 2014 [22] | Surgical trials published in 10 surgery journals with impact factor >2 | 657 | 2005 - 2010 | - Source of funding - Role of funder | 47% discosed funding. Of those 39% reported funding from industry or mixed funding, of which 35% reported the role of study sponsor. |
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| Lundh 2012 [28] | RCTs published in The Lancet and fully funded by a drug or device company | 69 | 2008 - 2009 | - Role of funder | Sponsor had a role in: Review and verification of information (71%) of the study database (75%) Of the study datab |
| Current survey | RCTs published in any of the 119 Core Clinical Journals, not restricted to a specific clinical domain | 200 | 2015 | Source of funding Amount Provision of supplies Role of funder | pape (22%) 89% ancluded a funding statement, of which 96% reported being funded. Of the funded trials (N=171): 160% specified the source; 46% received funding from private-fog-profit sources; 1% reported the amount of funding; 2% of pharmacological/surgical trails (N=139) reported information or supplies. 56% reported on the roles of funders (26% as involved and 24% as not involved). |
| RCT: random | nised controlled trial For pee | r review onl | y - http://bmjop | en.bmj.com/site/about/guidelines | nce Bibliographique de I s.xhtml I |

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We searched Ovid Medline (In-Process & Other Non-Indexed Citations and Ovid MEDLINE) in September 2015 using the MEDLINE (Ovid interface) search strategy for randomized controlled trials (Filter obtained from the Cochrane Handbook, under the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision):

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- 2. controlled clinical trial.pt.
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- 3. randomized.ab.
 4. placebo.ab.
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 8. 1 or 2 or 3 or 4 or 5 or 6 or 7
 9. exp animals/ not humans.sh.
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| Internal funding | author is the "Chair of –"; intramural fund provided by institution, university, hospital affiliation, academic affiliation |
|--|---|
| External funding: | |
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| 2. Private-for-profit | drug/device industry or private company |
| 3. Private not-for-profit with evidence of support by private-for-profit that is a health industry | foundation or organisation that receives funding from a drug industry, as stated in information provided online |
| 4. Private not-for-profit with evidence of support by private-for-profit that is not a health industry | foundation or philanthropy that was founded by billionaires or that receives funding from a private industry that is not known to produce drugs/devices, as stated in information provided online |
| 5. Private not-for-profit with no evidence of support by private-for-profit | foundation or organisation that is not known to receive funding from any governmental or private company, as stated in information provided online |

Appendix 4: Process followed to verify whether a private not-for-profit organisation was supported by a private-for-profit entity

- 1- We searched for the official website of the funding source reported in the trial using an online search engine (e.g., Google).
- 2- We searched for relevant information in the following sections: About Us, Who we are, Supporters, Donors, Partners, Partnerships, Sponsors, Financial support, Financial statements, Finances, Financials.
- 3- If no relevant information was obtained from the official website, we searched the organisation on Wikipedia, LinkedIn profiles and Facebook.
- PS: We did not contact funding sources to obtain any additional information.

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Appendix 5: Details of the multivariable logistic regression analyses

Analysis 1

Dependent variable (categorical)

• Reporting being funded (funded vs. not funded/not reported); all trials (N=200)

Independent variables

- 1. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)
- 2. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)
- 3. Conflict of interest disclosure (COI present vs. COI absent/not reported) We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.
- 4. Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)
- 5. Journal impact factor (continuous)
- 6. Number of randomized participants (continuous)
- 7. Classification of the country of the institution to which the first author is affiliated (categorical, high-income vs. middle or low-income)
- 8. Journal requirement for reporting on the role of funder (categorical, yes vs. no)

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Dependent variable (categorical)

• Explicit reporting of the role of funder (reported vs. not reported); trials that reported being funded (N=171)

Independent variables

In addition to the eight independent variables listed in analysis 1, we also included the following variable:

Funding from private-for-profit source(s) as opposed to all other types of funding sources (categorical, yes vs. no)

Results

| | Anal | ysis 1 | Analys | is 2 |
|---|-------------------------|-----------|-------------------------|------------|
| | Adjusted OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value |
| Type of intervention (pharmacologic as opposed to non-pharmacologic) | 1.79 (0.61 – 5.22) | 0.284 | 1.60 (0.71 – 3.58) | 0.261 |
| Paper is the first one reporting on the findings of the trial | 0.63 (0.12 – 3.22) | 0.577 | 3.47 (1.21 – 9.96) | 0.021 * |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 2.30 (0.62 - 8.38) | 0.209 | 0.53 (0.22 – 1.32) | 0.174 |
| Journal impact factor | 1.43 (1.11 – 1.86) | 0.006 * | 1.06 (1.03 - 1.10) | < 0.0001 * |
| Number of randomized participants | 1.00 (1.00 – 1.00) | 0.477 | 1.00 (1.00 - 1.00) | 0.152 |
| Classification of the country of the institution to which the first author is affiliated (high-income as opposed to middle or low-income) | 16.25 (4.03 – 65.5) | <0.0001 * | 3.30 (0.41 – 26.60) | 0.262 |
| Journal requirement for reporting on the role of funder | 1.02 (0.36 - 2.84) | 0.974 | 3.25 (1.43 – 7.38) | 0.005 * |
| Funding from private-for-profit source(s) (as opposed to all other types of funding sources) | N/A | N/A | 4.9 (2.11 – 11.83) | <0.0001 * |

OR = odds ratio; CI = confidence interval

* p-values for statistically significant associations.

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| Question 4 addresses characteristics of the funding sources. Explanations on type of funder: | use | ctok | |
| | ۳ e | oer N | |
| • Internal funder: refers to a funder that is the author's own institution or employer. This term typically refers to Conceivably, it could refer to a non-academic institution (e.g., pharmaceutical company) when it funded a study <i>Example statements: internal research account, support through being the "Chair of –", intramural fund, fund the academic institution, university, or hospital.</i> | 803 | acted by its employees. | |
| External funder: refers to a funder different than the author's own institution or employer. Types of external for a second secon | emin | gl (e.g., provincial), or | |
| - Inter-governmental: refers to two or more government agencies. Examples: European Union. | Al training, | tp://bmjopen.bmj.com/ | |
| - Private-for-profit: refers to an entity that operates to make profit. <i>Examples: drug or device industry, private company, insurance company, private laboratory.</i> | g, and siı | bmj.com/ | |
| - Private not-for-profit: refers to an organization that is not conducted primarily to make profit. <i>Examples: Doctors Without Borders, Bill and Melinda Gates Foundation.</i> | and similar tech | on June | |
| Questions 5 and 6 address whether the funding provided by any of the funding sources listed in Section 3 is suppo han/external to the listed source. | ndeogies. | 15y an entity other 1920 1920 1920 1920 | |
| • Example: a private not-for-profit organization that is a partner of, or receives support (typically in the form o other than itself. | | ding), from at least one ent | tity |
| - "The Epilepsy Foundation's mission is funded through the generous gifts of individual donors and man corporations and corporate foundations, member organizations, and both state and federal governmen for Disease Control and Prevention." | | recties, including the Center | |
| - "The Pfizer Foundation is a charitable organization established by Pfizer Inc." | | ographique | |
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| Page 55 | of 69 BMJ Open | cted t | 36/bm | |
|---|--|---|--|-----|
| 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 5 26 27 28 29 30 31 23 33 | of 69 BM J Open Section 4 Questions 7 and 8 address the involvement of funding sources. Funders may play a role in one or more steps of the research study. It is important to indicate whether a funder is involveming steps: • Study planning and conduct • Study planning and conduct • Study planning and conduct • Study management • Participant recruitment • Data management (e.g., verifying accuracy, storing data) • Data management (e.g., verifying accuracy, storing data) • Data management (e.g., oversight, auditing) • Data management (e.g., oversight, auditing) • Data management (e.g., oversight, auditing) • Augustion: relates to affaing the manuscript or medical writing assistance (providing a medical writer • Review of the manuscript • Approval of the final version of the manuscript or medical writing assistance (providing a medical writer • Review of the manuscript for publication (e.g., to what journal) • Approval of the final version of the manuscript • Automation • Automation • Date roles to at least one of the employees of the funder being an author on the manuscript. • Dimenter • In the relates to at least one of the employees of the funder being an author on the manuscript. </td <td>${\mathfrak{g}}$ Enseignement Superieur (ABES) . ${\mathfrak{g}}$ training, and similar</td> <td>tober 2017. Downloaded from http://bgjopen.bmj.com/ on June 13, Enseignement Superieur (ABES) .</td> <td>)</td> | ${\mathfrak{g}}$ Enseignement Superieur (ABES) . ${\mathfrak{g}}$ training, and similar | tober 2017. Downloaded from http://bgjopen.bmj.com/ on June 13, Enseignement Superieur (ABES) . |) |
| 29 30 31 32 | This relates to at least one of the employees of the funder being an author on the manuscript. Other roles | technologies | 'on June 13, 2025 | |
| 37 38 39 40 41 42 43 44 45 46 47 | ©2017. Elie Akl and Maram Hakoum, American University of Beirut. All rights reserved. The instrument may not be us | | at Agence Bibliographique de disseminated, reproduced, | moc |

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APPENDICES

Appendix 1: Comparative chart including 23 related surveys of reporting of funding information in trials

| Survey | Eligibility criteria | Number | Year of trial | Characteristics of funding | Main findings |
|--------------------------|--|-----------|---------------|---|---|
| | | of trials | publication | statement assessed in the | |
| | 0 | | | survey | |
| Als-Nielsen 2003 [19] | RCTs included in eligible meta-analyses in Cochrane reviews | 370 | 1971 - 2000 | - Source of funding | Funding was not reported in 29%. 39% were funded by for-profit organisations. |
| Etter 2007 [25] | RCTs on nicotine replacement therapy in Cochrane review | 90 | 1979 - 2003 | - Source of funding | 54% received pharmaceutical company support. 46% showed no evidence of pharmaceutical company support. |
| Mugambi 2013 [5] | RCTs on infant formula supplementation of symbiotics, probiotics, or prebiotics | 67 | 1980 - 2012 | - Source of funding | 60% were funded by food industry. 24% did not specify their source of funding. |
| Rochon 1994 [34] | Manufacturer-associated RCTs of NSAIDs listed in MEDLINE | 52 | 1987 - 1990 | Grant support Pharmaceutical authorship Provision of supplies Published in a pharmaceutical sponsored journal supplement | 19% reported grant support. 36.5% reported pharmaceutical authorship. 13.5% reported that manufacturer supplied drug. 31% were published in a pharmaceutical sponsored journal supplement. |
| Momeni 2008 [29] | Trials published in 4 major plastic surgery journals | 346 | 1990 - 2005 | - Source of funding | 20% reported on financial support, of which 60% were supported by industrial sponsorship. |

| Yaphe 2001 [39] | RCTs of drugs or food products published in 5 | 314 | 1992 - 1994 | - Source of funding - Pharmaceutical | 68% received pharmaceutical industry support. |
|--------------------------|---|-----|---------------------|--|---|
| | medical journals | | | authorship - Provision of supplies | 33% received support as manpower(authorship or statistical help).21% received support as supply of drugs |
| Peppercorn 2007 [31] | Breast cancer clinical trials published in 10 medical journals | 140 | 1993, 1998, 2003 | Source of funding Pharmaceutical authorship | 48% were categorised as pharmaceutical studies. 26% reported pharmaceutical industry authorship. |
| Bero 2007 [20] | Reports of RCTs comparing statin drugs | 192 | 1995 - 2005 | - Source of funding - Role of funder | 39% had no disclosure or no funding (Table 1). 49% disclosed funding from industry, of which 21% disclosed the role of the sponsor. |
| Djulbegovic 2000 [24] | RCTs for multiple myeloma | 130 | 1996 - 1998 | - Source of funding | 26% reported funding solely or in part b commercial organisations. |
| Clifford 2002 [23] | RCTs published in 5 high impact factor general medical journals | 100 | 1999 - 2000 | - Source of funding | 94% were funded, of which 66% were funded in whole or in part by industry.6% did not disclose their source of funding. |
| Bhandari 2004 [21] | RCTs published in 8 surgical and 5 medical journals | 332 | 1999 - 2001 | - Source of funding | 44% had no reported funding. 37% reported funding by industry. |
| Tuech 2005 [36] | Phase III cancer RCTs published in 12 journals | 655 | 1999 - 2003 | - Source of funding - Role of funder | 35% were industry-sponsored, of which 18% reported the role of the study sponsor. 21% did not disclose funding and only 1 trial disclosed no financial support. |
| Shah 2005 [35] | Articles published in the Spine journal | 34 | 2000 - 2003 | - Source of funding | 23% were industry funded. |
| Tungaraza 2007 [37] | Original papers on psychiatric drug treatment published in two journals | 132 | 2000 - 2004 | Source of funding Pharmaceutical authorship | 85% were industry-funded.40% were industry-authored studies. |

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| Page | 58 | of | 69 |
|------|----|----|----|
|------|----|----|----|

| Ridker 2006 [33] | Cardiovascular medicine RCTs published in 3 medical journals | 349 | 2000 - 2005 | - Source of funding | 31% were financed by not-for-profit organisations, 44% by for-profit manufacturers, and 19% by both. 6% noted no source of funding. |
|-------------------------------|--|-----|----------------------------|---|---|
| Voineskos 2016 [38] | Surgical RCTs | 173 | 2000 - 2013 | - Source of funding | 58% did not acknowledge a source of funding. 14% reported funding from for-profit sources. 10% explicitly reported 'no funding received'. |
| Montogom -ery 2004 [30] | RCTs on second generation antipsychotics for the management of schizophrenia | 86 | 2002 | - Source of funding | 84% were industry-funded. 16% were non-industry-funded. |
| Perlis 2005 [32] | RCTs published in one of the four dermatology journals with the highest science citation impact factor scores and total citations | 179 | 2002 | - Source of funding | 57% reported receiving at least some industry support.26% had no information about funding. |
| Khan 2012 [27] | RCTs of drug therapy for rheumatoid arthritis | 103 | 2002 – 2003 2006 - 2007 | - Source of funding | 62% had complete or partial industry funding.19% had an unspecified funding source. |
| Hodgson 2014 [26] | RCTs in chronic wound care | 167 | 2004 - 2011 | - Source of funding | 35% were reported as having been commercially funded. 26% either did not report the source of funding or the status of funding source was unclear. |
| Bridoux 2014 [22] | Surgical trials published in 10 surgery journals with impact factor >2 | 657 | 2005 - 2010 | - Source of funding - Role of funder | 47% disclosed funding. Of those, 39% reported funding from industry or mixed funding, of which 35% reported the role of study sponsor. |

| Lundh | RCTs published in The | 69 | 2008 - 2009 | - Role of funder | Sponsor had a role in: |
|-----------|-------------------------------|-----|-------------|-------------------------|---|
| 2012 [28] | Lancet and fully funded by | | | | Review and verification of information |
| | a drug or device company | | | | (71%) |
| | | | | | Entry of data into the study database |
| | | | | | (75%) |
| | | | | | Data storage (64%) |
| | | | | | Data analysis (58%) |
| | | | | | Coordinating writing of the manuscript |
| | | | | | (35%) |
| | | | | | Medical writing assistance (54%) |
| | | | | | Protocol writing (99%) |
| | | | | | Co-authorship (81%) |
| | | | | | Publication of results through co- |
| | | | | | authorship or approval/review of the |
| ~ | | | | a | paper (93%) |
| Current | RCTs published in any of | 200 | 2015 | - Source of funding | 89% included a funding statement, of |
| survey | the 119 Core Clinical | | | - Amount | which 96% reported being funded. |
| | Journals, not restricted to a | | | - Provision of supplies | |
| | specific clinical domain | | | - Role of funder | Of the funded trials (N=171): |
| | | | | | - 100% specified the source; |
| | | | | | - 40% received funding from private |
| | | | | | for-profit sources; |
| | | | | | - 1% reported the amount of funding |
| | | | | | - 21% of pharmacological/surgical |
| | | | | 4 | trials (N=139) reported information |
| | | | | | on supplies. 50% reported on the roles of funder |
| | | | | | \sim - 50% reported on the roles of funder |
| | | | | | (26% as involved and 24% as not involved). |
| | | | | | involved). |

RCT: randomised controlled trial

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Appendix 12: Search strategy

We searched Ovid Medline (In-Process & Other Non-Indexed Citations and Ovid MEDLINE) in September 2015 using the MEDLINE (Ovid interface) search strategy for randomized controlled trials (Filter obtained from the Cochrane Handbook, under the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision):

- 1. randomized controlled trial.pt.
- 2. controlled clinical trial.pt.
- randomized.ab. 3.
- placebo.ab. 4.
- clinical trials as topic.sh. 5.
- 6. randomly.ab.
- 7. trial.ti.
- 8. 1 or 2 or 3 or 4 or 5 or 6 or 7
- 9. exp animals/ not humans.sh.
- 10.8 not 9
- 915") 11. limit 10 to ("core clinical journals (aim)" and yr="2015")

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Appendix 3: Types of funding sources

| Internal funding | author is the "Chair of –"; intramural fund; provided by institution, university, hospital affiliation, academic affiliation |
|--|---|
| External funding: | |
| 1. Government | national, regional (province, county), or governmental body, organisation, or association |
| 2. Private-for-profit | drug/device industry or private company |
| 3. Private not-for-profit with evidence of support by private-for-profit that is a health industry | foundation or organisation that receives funding from a drug industry, as stated in information provided online |
| 4. Private not-for-profit with evidence of support by private-for-profit that is not a health industry | foundation or philanthropy that was founded by billionaires or that receives funding from a private industry that is not known to produce drugs/devices, as stated in information provided online |
| 5. Private not-for-profit with no evidence of support by private-for- profit | foundation or organisation that is not known to receive funding from any governmental or private company, as stated in information provided online |
| | |



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Appendix 4: Process followed to verify whether a private not-for-profit organisation was supported by a private-for-profit entity

- 1- We searched for the official website of the funding source reported in the trial using an online search engine (e.g., Google).
- 2- We searched for relevant information in the following sections: About Us, Who we are, Supporters, Donors, Partners, Partnerships, Sponsors, Financial support, Financial statements, Finances, Financials.
- 3- If no relevant information was obtained from the official website, we searched the organisation on Wikipedia, LinkedIn profiles and Facebook.
- PS: We did not contact funding sources to obtain any additional information.

Appendix 25: Details of the multiplevariable logistic regression analyses

Analysis 1

Dependent variable (categorical)

• Reporting being funded (funded vs. not funded/not reported); all trials (N=200)

Independent variables

- 1. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)
- 2. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)
- 3. Conflict of interest disclosure (COI present vs. COI absent/not reported) We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.
- 4. Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)
- 5. Journal impact factor (continuous)
- 6. Number of randomized participants (continuous)
- 7. Classification of the country of the institution to which the first author is affiliated (categorical, high-income vs. middle or low-income)
- 8. Journal requirement for reporting on the role of funder (categorical, yes vs. no)

Results

| Adjusted OR (95% CI) | p-value |
|---|---|
| 1.79 (0.61 – 5.22) | 0.284 |
| 0.63 (0.12 3.22) | 0.577 |
| 2.30 (0.62 – 8.38) | 0.209 |
| 1.43 (1.11 1.86) | 0.006 |
| 1.00 (1.00 1.00) | 0.477 |
| 16.25 (4.03 65.5) | <0.0001 |
| 1.02 (0.36 2.84) | 0.97 4 |
| 0, | |
| | $\frac{(95\% \text{ CI})}{1.79}$ $(0.61 - 5.22)$ $\frac{0.63}{(0.12 - 3.22)}$ $\frac{2.30}{(0.62 - 8.38)}$ $\frac{1.43}{(1.11 - 1.86)}$ $\frac{1.00}{(1.00 - 1.00)}$ $\frac{16.25}{(4.03 - 65.5)}$ $\frac{1.02}{(1.02 - 1.00)}$ |

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Dependent variable (categorical)

• Explicit reporting of the role of funder (reported vs. not reported); trials that reported being funded (N=171)

Independent variables

In addition to the eight independent variables listed in analysis 1, we also included the following variable:

9. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)

10. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)

11. Conflict of interest disclosure (COI present vs. COI absent/not reported)

12. We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.

13.

- 14. Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)
- 15. Journal impact factor (continuous)
- 16. Number of randomized participants (continuous)
- 17. Classification of the country of the institution to which the first author is affiliated

(categorical, high-income vs. middle or low-income)

18. Journal requirement for reporting on the role of funder (categorical, yes vs. no)

<u>19.9.</u> Funding from private-for-profit source(s) as opposed to all other <u>types of</u> funding sources (categorical, yes vs. no)

Results

| | Adjusted OR (95% CI) | p-value |
|---|--|-----------------------|
| Type of intervention (pharmacologic as opposed to non- pharmacologic) | 1.60 (0.71 3.58) | 0.261 |
| Paper is the first one reporting on the findings of the trial * | 3.47 (1.21 9.96) | 0.021 |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 0.53 (0.22 1.32) | 0.174 |
| Journal impact factor * | 1.06 (1.03 – 1.10) | <0.0001 |
| Number of randomized participants | 1.00 (1.00 – 1.00) | 0.152 |
| Classification of the country of the institution to which the first author is affiliated (high-income as opposed to middle or low- income) | 3.30 (0.41—26.60) | 0.262 |
| Journal requirement for reporting on the role of funder * | 3.25 (1.43 7.38) | 0.005 |
| Funding from private-for-profit source(s) * | 4.9 (2.11-11.83) | <0.0001 |
| OR = odds ratio; CI = confidence interval * p-values for statistically significant associations. | | |

MERGED-Results

| | Anal | ysis 1 | Analys | <u>is 2</u> |
|---|--|-----------|-------------------------|-------------|
| | Adjusted OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value |
| Type of intervention (pharmacologic as opposed to non-pharmacologic) | 1.79 (0.61 – 5.22) | 0.284 | 1.60 (0.71 – 3.58) | 0.261 |
| Paper is the first one reporting on the findings of the trial | 0.63 (0.12 - 3.22) | 0.577 | 3.47 (1.21 – 9.96) | 0.021 * |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 2.30 (0.62 - 8.38) | 0.209 | 0.53 (0.22 – 1.32) | 0.174 |
| Journal impact factor | 1.43 (1.11 – 1.86) | 0.006 * | 1.06 (1.03 - 1.10) | <0.0001 * |
| Number of randomized participants | 1.00 (1.00 – 1.00) | 0.477 | 1.00 (1.00 – 1.00) | 0.152 |
| Classification of the country of the institution to which the first author is affiliated (high-income as opposed to middle or low-income) | 16.25 (4.03 – 65.5) | <0.0001 * | 3.30 (0.41 – 26.60) | 0.262 |
| Journal requirement for reporting on the role of funder | $ \begin{array}{r} 1.02 \\ (0.36 - 2.84) \end{array} $ | 0.974 | 3.25 (1.43 – 7.38) | 0.005 * |
| Funding from private-for-profit source(s) (as opposed to all other types of funding sources) | N/A | N/A | 4.9 (2.11 – 11.83) | <0.0001 * |

OR = odds ratio; CI = confidence interval

* p-values for statistically significant associations.

| 1 | Appendix 6: Instrument for reporting of funding information |
|---|---|
| 2 3 | Please see the PDF supplementary file (does not include tracked changes). |
| $\begin{array}{c} 4\\ 5\\ 6\\ 7\\ 8\\ 9\\ 10\\ 11\\ 12\\ 13\\ 14\\ 15\\ 16\\ 17\\ 18\\ 19\\ 20\\ 21\\ 22\\ 32\\ 4\\ 25\\ 26\\ 27\\ 28\\ 29\\ 30\\ 31\\ 32\\ 33\\ 34\\ 55\\ 26\\ 27\\ 28\\ 29\\ 30\\ 31\\ 32\\ 33\\ 34\\ 55\\ 56\\ 57\\ 58\\ 9\\ 60\\ \end{array}$ | |

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Characteristics of funding of clinical trials: cross-sectional survey and proposed guidance

| Journal: | BMJ Open |
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| Manuscript ID | bmjopen-2017-015997.R2 |
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| Date Submitted by the Author: | 04-Jul-2017 |
| Complete List of Authors: | Hakoum, Maram; American University of Beirut Medical Center, Clinical Research Institute Jouni, Nahla; American University of Beirut, Faculty of Agriculture and Food Sciences Abou-Jaoude, Eliane; University at Buffalo - The State University of New York, Department of Internal Medicine Hasbani, Divina ; American University of Beirut Faculty of Medicine Abou-Jaoude, Elias; University at Buffalo - The State University of New York Lopes, Luciane; University of Sorocaba, Pharmacology Khaldieh, Mariam; American University of Beirut, Faculty of Sciences Hammoud, Mira; Massachusetts General Hospital, Department of Psychiatry Al-Gibbawi, Mounir; American University of Beirut, Department of Epidemiology and Population Health Guyatt, Gordon; McMaster University, Akl, Elie; American University of Beirut, Department of Internal Medicine |
| Primary Subject Heading : | Research methods |
| Secondary Subject Heading: | Ethics, Medical publishing and peer review, Research methods |
| Keywords: | funding, role of funder, randomised controlled trial |

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|---|----|---|
| - 3 4 5 6 7 8 9 10 112 13 14 15 16 7 8 9 20 12 23 24 25 26 7 8 9 31 32 33 45 36 7 8 9 40 | 1 | Characteristics of funding of clinical trials: cross-sectional survey and proposed guidance |
| | 2 | |
| | 3 | Maram B. Hakoum, Nahla Jouni, Eliane A. Abou-Jaoude, Divina Justina Hasbani, Elias A. |
| | 4 | Abou-Jaoude, Luciane Cruz Lopes, Mariam Khaldieh, Mira Z. Hammoud, Mounir Al-Gibbawi, |
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Keywords: funding, role of funder, randomised controlled trial

15 Word count: 3,706 words

1 ABSTRACT

Objectives: To provide a detailed and current characterisation of funding of a representative
sample clinical trials. We also aimed to develop guidance for standardised reporting of funding
information.

Methods: We addressed the extent to which clinical trials published in 2015 in any of the 119
Core Clinical Journals included a statement on the funding source (e.g., whether a not-for-profit
organisation was supported by a private-for-profit), type of funding, amount and role of funder.
We used a stepwise approach to develop a guidance and an instrument for standardised reporting
of funding information.

Results: Of 200 trials, 178 (89%) included a funding statement, of which 171 (96%) reported being funded. Funding statements in the 171 funded trials indicated the source in 100%, amount in 1% and roles of funders in 50%. The most frequent sources were governmental (58%) and private-for-profit (40%). Of 54 funding statements in which the source was a not-for-profit organisation, we found evidence of undisclosed support of those organisations from private-for-profit organisation(s) in 26 (48%). The most frequently reported roles of funders in the 171 funded trials related to study design (42%) and data analysis, interpretation, or management (41%). Of 139 RCTs addressing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or device. The proposed guidance addresses both the funding information that RCTs should report and the reporting process. Attached to the guidance is a fillable PDF document for use as an instrument for standardised reporting of funding information.

22 Conclusion: Although the majority of RCTs report funding, there is considerable variability in23 the reporting of funding source, amount and roles of funders. A standardised approach to

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| 3 4 | 1 | reporting of funding information would address these limitations. Future research should explore |
| 5 6 | 2 | the implications of funding by not-for profit organisations that are supported by for-profit |
| 7 8 9 | 3 | organisations. |
| 10 11 | 4 | |
| 12 13 | 5 | Strengths and limitations of this study: |
| 14 15 16 | 6 | • First cross-sectional survey of a large and representative sample of clinical RCTs to |
| 17 18 | 7 | describe the characteristics of the funding statements in detail. |
| 19 20 21 | 8 | • Provides a proposed guidance and instrument for standardised reporting of funding |
| 22 23 | 9 | information. |
| 24 25 | 10 | • Use of systematic and transparent methods, e.g., duplicate and independent processes in |
| 26 27 28 | 11 | screening and data collection. |
| 29 30 | 12 | • Includes trials limited to the clinical field and so our findings may not apply similarly to |
| 31 32 33 | 13 | other fields such as public health research. |
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1 BACKGROUND

Funding sources may influence the reporting of research findings and the interpretation of results.[1-6] One study found that 86% of trial protocols documented an industry partner's right to disapprove or review proposed manuscripts.[7] This might also apply to other types of funders, for example, government. Reporting of funding in trials may appropriately influence how physicians interpret and use trial findings in clinical practice.[8, 9] The Consolidated Standards of Reporting Trials (CONSORT) checklist recognises this issue by including a section on reporting of funding.[10, 11]

Reports in the lay media have documented how for-profit organisations support research through not-for-profit organisations.[12, 13] In one example, The Independent recently highlighted a systematic review suggesting that the consumption of low-energy sweeteners in place of sugar reduces energy intake and body weight.[14] The review authors list the International Life Sciences Institute as the study funder. While the Institute describes itself as "a nonprofit, worldwide organisation whose mission is to provide science that improves human health", it receives funding primarily from companies such as the Coca-Cola Company, PepsiCo and Nestlé.[15] Other examples of not-for-profit organisations funded by industry and supporting research are the Sugar Association, Inc. [16, 17] and the now defunct Global Energy Balance Network.[18]

We conducted a comprehensive review of the literature and found 22 studies that assessed reporting of funding in clinical trials (see appendix 1).[5, 19-39] The main gap we identified in this literature is a detailed and current characterisation of funding of a representative sample of

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trials. Indeed, all of the identified studies focused on trials published in specific clinical areas or journals. Most (14, 64%) reported only on funded trials or did not differentiate between nonfunded trials and those that do not report on funding. Seventeen studies (77%) did not always distinguish trials with no funding from those funded by the government or by not-for-profit sources. Moreover, these studies seldom assessed reporting on the role of funder (n=4), provision of supplies (n=2), and the amount of funding (n=0). None of the studies explored the relationship between not-for-profit organizations funding trials and for-profit organizations. Therefore the main objective of this study was to provide a detailed and current characterisation of funding of a representative sample of clinical trials. We also aimed to develop guidance for standardised reporting of funding information. **METHODS Design overview and definitions** We followed systematic methodology to conduct a cross-sectional survey of published randomised controlled trials (RCTs). We define funding as any support (e.g. monetary support, provision of supplies, assistance in manuscript writing). We considered as funding statement any text in the trial report providing any information regarding the funding of the trial, including a statement of no funding. A funding statement could indicate more than one funding contribution.

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21 Eligibility criteria

22 We included reports of studies described as RCTs comparing at least two therapeutic 23 interventions of any type in humans and published in English. We included RCTs with cross-

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over designs and secondary reports of trials (i.e. follow-up study, post-hoc analysis, interim
 analysis, pre-specified analysis or secondary outcomes or sub-study of a trial). We excluded non randomised trials, trials addressing basic sciences topics and non-clinical interventions, and
 research letters.

6 Search strategy

We searched Ovid Medline in September 2015 and limited our search to the year 2015 and the 119 Core Clinical Journals (Abridged Index Medicus (AIM)).[40] We applied the search filter obtained from the Cochrane handbook to identify RCTs. See appendix 2 for the detailed search strategy.

Selection process

We used an online sequence generator (www.random.org/sequences) to randomise the citations captured by the search. We followed the order of the randomization list to screen citations until we obtained 200 eligible RCTs. Our sample size allows for a narrow 95% confidence interval (+/- 5%) around proportions of studies reporting sources of funding.

Following calibration exercises, three reviewers (MBH, NJ, MK) worked in teams of two (MBH was the reviewer on both) to screen titles and abstracts in duplicate and independently, using EndNoteTM X7.5 software (Thomson Reuters, Philadelphia, PA, USA). We obtained the fulltexts of citations judged as potentially eligible by either reviewer. The two teams of reviewers screened full-texts in duplicate and independently. They resolved disagreements by discussion,

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| 1 | or with the help of a third reviewer (EAA) as needed. A PRISMA study flow diagram [41] |
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| 2 | presents the results of the selection process (figure 1). |
| 3 | |
| 4 | Data extraction process |
| 5 | We developed a standardised data extraction form along with specific instructions. After pilot |
| 6 | testing the form, we embedded it electronically into Research Electronic Data Capture |
| 7 | (REDCap), a secure web-based application designed to support data capture for research |
| 8 | studies.[42] After completing calibration exercises, nine authors divided into teams of two |
| 9 | extracted data in duplicate and independently (MBH was a reviewer on each of the eight teams). |
| 10 | Each team compared results and resolved disagreements through discussion, or with the help of a |
| 11 | third reviewer (EAA) as needed. |
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| 13 14 | Data extracted We extracted the following characteristics of the RCTs: |
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| 14 | We extracted the following characteristics of the RCTs: |
| 14 15 | We extracted the following characteristics of the RCTs:Number of trial authors, |
| 14 15 16 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, |
| 14 15 16 17 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, Classification of the income level of the country in which the first author's institution is |
| 14 15 16 17 18 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, Classification of the income level of the country in which the first author's institution is located (as high, upper-middle, lower-middle, or low income country according to the |
| 14 15 16 17 18 19 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, Classification of the income level of the country in which the first author's institution is located (as high, upper-middle, lower-middle, or low income country according to the July 2015 World Bank list of economies), |
| 14 15 16 17 18 19 20 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, Classification of the income level of the country in which the first author's institution is located (as high, upper-middle, lower-middle, or low income country according to the July 2015 World Bank list of economies), Type of intervention and type of control, |
| 14 15 16 17 18 19 20 21 | We extracted the following characteristics of the RCTs: Number of trial authors, Whether it is the first full-text report of the trial findings, Classification of the income level of the country in which the first author's institution is located (as high, upper-middle, lower-middle, or low income country according to the July 2015 World Bank list of economies), Type of intervention and type of control, Number of trial sites, |

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Level of risk of bias associated with allocation concealment, a methodological feature as an indicator of risk of bias (based on the Cochrane Collaboration's tool for assessing risk of bias) [43], Whether authors reported conflicts of interest, Whether the report included a funding statement. We then focused on trials that included funding information. We extracted the following funding characteristics reported in the paper: Whether it reported funding versus no funding, The type of source(s) of funding (see appendix 3). These included internal funding (when it is an academic or hospital affiliation) and external funding, categorized into: government, private-for-profit, private not-for-profit with evidence of support by private-for-profit that is a health industry, private not-for-profit with evidence of support by private-for-profit that is not a health industry, and private not-for-profit with no evidence of support by private-for-profit. As needed, we performed an online search to accurately assign the type of the funding source. When a funding source was identified as a not-for-profit organisation, we searched the organisation's website for any information on partnership with or support from a for-profit organisation (see appendix 4 for details), Amount of funding, Whether the paper reported to be sponsored by a source different than the source of funding/support, Whether information was reported (across the paper) on supplies in trials on pharmacological or surgical interventions (i.e., drugs, devices, equipment, samples, or

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placebos) and whether the supplier is a funding source. We looked for that information in the funding statements, acknowledgement statements and the methods section.

Finally, and in trials that reported being funded, we assessed whether the role of funder was explicitly reported for any funder as involved or not involved in the process of the research study.

8 Data analysis

9 We assessed agreement between reviewers of each team for inclusion of RCTs at the full-text 10 screening stage using chance-corrected agreement (kappa statistic). We conducted descriptive 11 analyses of the general characteristics of the RCT, as well as the characteristics of the funding 12 statement. We present summary data for categorical variables as frequencies and percentages and 13 for continuous variables as median and interquartile range (IQR). All calculations used SPSS, 14 version 21.0 for Windows (SPSS INC., Chicago, IL, USA). BMJ Open: first published as 10.1136/bmjopen-2017-015997 on 5 October 2017. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

16 Candidate independent variables for multivariable logistic regression analyses to assess the 17 predictors of reported funding and the role of funder included characteristics of the RCT and 18 variables related to Journal policy for reporting funding (i.e., journal requirement for reporting of 19 funding, journal requirement for reporting on the role of funder). For variables related to journal 20 policy for reporting funding information, we used unpublished data we had collected in mid 21 2014 for another cross-sectional survey.[44]

23 Development of the guidance

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We used the following approach for developing the proposed guidance for standardised reporting of funding information. First, our classification of funding sources was based on one we had used in a previous study (governmental, private not-for-profit, and private-for-profit)[45] that we modified after a review of relevant literature[5, 22, 27] and of journals' policies on reporting of funding information (unpublished data from another cross-sectional survey).[44] Second, we refined the classification through an iterative process of discussion and revisions based on funding statements reported in this sample of RCTs, as well as in a sample of systematic reviews.[46] Finally, we used Adobe[®] Acrobat XI[®] software to develop a fillable PDF document for use as an instrument for standardised reporting of funding information.

The process included both in-person and email discussions among the authors of this article and feedback from external experts. The individuals involved have the following profiles: author EAA is a clinical epidemiologist and was an associate journal editor for Health and Quality of Life Outcomes journal; author GG is a clinical epidemiologist and has been a member of editorial boards of 8 journals. The external experts we consulted include Dr. Elie Al-Chaer (health researcher with a law degree and editor-in-chief of International Journal of Women's Health and Dove Press), Dr. Joerg Meerpohl (associate editor of Health and Quality of Life Outcomes journal), and Dr. Peter Tugwell (co-editor of the Journal of Clinical Epidemiology).

RESULTS

Figure 1 presents the study flow diagram. Agreement proved substantial (kappa= 0.78) and near
perfect (kappa= 0.86) respectively for each of the two teams at the full-text screening stage.

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Characteristics of the randomised controlled trial

The first authors of most trials (90%) had affiliations in high-income countries and almost half (49%) assessed pharmacological interventions (table 1). About half the trials (54%) were multi-center, and had two as the median number of sites. Most trials (94%) reported on conflicts of interest and 54% disclosed presence of conflicts of interest. Almost all (178, 89%) included a

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- funding statement.

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| | Overall |
|---|------------|
| | n (%) \$ |
| Number of trial authors; median (IQR) | 9 (6 - 14) |
| Paper is the first full-text report of the trial findings | 171 (86% |
| Classification of the income level of the country in which the first author's institution is located: | |
| High-income | 179 (90% |
| Upper middle-income | 15 (8%) |
| Lower middle-income | 4 (2%) |
| Low-income | 2 (1%) |
| Type of intervention | |
| Pharmacological | 97 (49%) |
| Surgical/invasive procedure | 42 (21%) |
| Non-invasive procedure | 11 (6%) |
| Lifestyle intervention | 15 (8%) |
| Screening/diagnostic intervention | 9 (5%) |
| Psycho-therapeutic intervention | 4 (2%) |
| Rehabilitation | 6 (3%) |
| Other | 16 (8%) |
| Type of control | |
| Active control (as opposed to non-active) | 82 (41%) |

| Number of trial sites; median (IQR) | 2 (1 – 17) |
|--|---------------|
| Number of randomised participants; median (IQR) | 160 (60 - 485 |
| Level of risk of bias associated with allocation concealment | |
| High risk | 4 (2%) |
| Low risk | 59 (30%) |
| Unclear | 137 (69%) |
| Reporting of conflicts of interest | |
| Not reported | 12 (6%) |
| Reported with no conflicts of interest disclosed | 80 (40%) |
| Reported with conflicts of interest disclosed | 108 (54%) |
| Inclusion of a funding statement | |
| Included (as opposed to not included) | 178 (89%) |

2 \$ For continuous variables, numbers refer to median (IQR); indicated in the relevant row.

3 * The number of trial authors per trial ranged between 1 and 91.

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Characteristics of the reported funding

Table 2 presents the characteristics of the reported funding of the 178 trials with a funding statement, of which 171 (96%) reported being funded. The median number (IQR) of funding sources for each funded trial was 1 (1-3), with a range of 1 to 12 sources per trial. The top most frequent sources of funding were governmental (58%) and private-for-profit (40%). Of the 54 funding contribution statements in which the source was identified as being a not-for-profit organisation, we found evidence of support of those organisations from private-for-profit entity(ies) in 29 (54%), of which 26 (48%) did not disclose this support in the study report. Twenty-one trials (12%) reported funding from private-for-profit in addition to another source. Two trials reported the amount of funding received. Of the 139 RCTs assessing pharmacological or surgical interventions, 29 (21%) reported information on the supplier of the medication or

12 device.

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Table 2: Characteristics of the funding statements included in the randomised controlled trials

2 (N=178 trials)

| | Overall |
|--|-----------|
| | n (%) |
| Funding statement reported being: | |
| Funded (as opposed to not funded) | 171 (96%) |
| Source(s) of funding (when reported as funded; N=171) \$ | |
| Internally funded | 26 (15%) |
| Externally funded by: | |
| Government | 99 (58%) |
| Private-for-profit | 68 (40%) |
| Private not-for-profit with evidence of support by private-for-profit | 14 (8%) |
| that is a health industry | |
| Private not-for-profit with evidence of support by private-for-profit | 15 (9%) |
| that is not a health industry | |
| Private not-for-profit with no evidence of support by private-for- | 25 (15%) |
| profit | |
| Statement included amount of funding received | 2 (1%) |
| Paper reported to be sponsored by a source different than the source of | 2 (1%) |
| funding/support | |
| Paper reported information on supplies (i.e., drugs, devices, equipment, | |
| samples, or placebos) * | |

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| Yes, supplied by manufacturer same as funder | 12 (9%) |
|---|-----------|
| Yes, supplied by manufacturer different than funder | 17 (12%) |
| Not reported | 110 (79%) |

\$ More than one type could apply for trials reporting more than one source of funding.

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 ber of t.

 * Calculated using the number of trials on pharmacological interventions and surgical/invasive

procedures (N=139).

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1 The reported roles of funders

Table 3 presents the reported roles of funders in the 171 trials that reported being funded. Eightyfive trials (50%) indicated the role of funders and provided descriptions of 22 different roles. The most frequent roles indicated in these 85 trials were participation in the design of the study (42%), data collection (27%), data analysis, interpretation, or management (41%), manuscript preparation (32%), decision to submit the manuscript (15%) and conduct of the study (15%).

decision

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1 Table 3: Reporting on the roles of funders in the randomised controlled trials that reported being

2 funded (N=171)

| | Reported role as: | | Did not report role |
|---|-------------------|----------|------------------------|
| | | | |
| | Not involved | Involved | |
| | n (%) | n (%) | n (%) |
| Any role of the below | 41 (24%) | 44 (26%) | 86 (50%) |
| Protocol/design of the study | 41 (24%) | 30 (18%) | 100 (58%) |
| Data collection | 31 (18%) | 16 (9%) | 124 (73%) |
| Verifying data accuracy/ fact checking | 0 (0%) | 3 (2%) | 168 (98%) |
| Outcome adjudication | 0 (0%) | 1 (1%) | 170 (99%) |
| Data analysis/ interpretation/ management | 40 (23%) | 31 (19%) | 100 (58%) |
| Funded a medical writer | 1 (1%) | 19 (11%) | 151 (88%) |
| Preparation of the manuscript | 34 (20%) | 20 (12%) | 117 (68%) |
| Review of the manuscript | 17 (10%) | 7 (4%) | 147 (86%) |
| Approval of the manuscript | 17 (10%) | 8 (5%) | 146 (85%) |
| Decision to submit the manuscript | 18 (10%) | 6 (4%) | 147 (86%) |
| Appointed an independent data and safety | 0 (0%) | 1 (1%) | 170 (99%) |
| monitoring board | | | |
| Auditing of study conduct | 0 (0%) | 3 (2%) | 168 (98%) |
| Management | 0 (0%) | 3 (2%) | 168 (98%) |
| Team assembly | 0 (0%) | 2 (1%) | 169 (99%) |
| Conduct of study | 13 (8%) | 12 (7%) | 146 (85%) |

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| 0 (0%) 0 (0%) 0 (0%) 0 (0%) | 1 (1%) 3 (2%) 1 (1%) | 170 (99%) 168 (98%) 170 (99%) |
|--------------------------------------|----------------------------|-------------------------------------|
| 0 (0%) | 1 (1%) | |
| | | 170 (99%) |
| 0 (0%) | | 1 |
| | 2 (1%) | 169 (99%) |
| 0 (0%) | 1 (1%) | 170 (99%) |
| 0 (0%) | 5 (3%) | 166 (97%) |
| | | |
| | | 0 (0%) 5 (3%) |

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Results of the regression analyses

Appendix 5 presents the details of the multivariable logistic regression analyses. Reporting being funded was positively associated with two variables (table 4), based on data from all included trials (n=200). Explicit reporting on the role of funder was positively associated with three variables (table 4), based on data from trials reporting being funded (n=171).

| Dependent variables | Independent variables | Adjusted OR | p-value |
|------------------------|---|----------------|---------|
| | | (95% CI) | |
| 'Reporting being | Journal impact factor | 1.44 | 0.011 |
| funded' model | | (1.09 – 1.90) | |
| (N=200) | Affiliation with an institution from a | 0.09 | 0.001 |
| | high-income country (reference | (0.02 – 0.37) | |
| | category being middle or low-income | | |
| | countries) | | |
| 'Explicit reporting on | Journal impact factor | 1.07 | < 0.000 |
| the role of funder' | | (1.04 - 1.10) | |
| model (N=171) | Journal requirement for reporting on | 3.76 | 0.002 |
| | the role of funder | (1.64 - 8.62) | |
| | Funding from private-for-profit | 5.7 | < 0.000 |
| | source(s) (reference category being all | (2.37 – 13.85) | |
| | other types of funding sources) | | |
| | C | | |
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Proposed guidance

The proposed guidance provides suggestions for both funding information and the reporting
process. Box 1 lists the funding information that relates to the phases of the research study for
which the funding was received, the funding sources and the involvement of the funders in the
process of the research study.

> **Box 1:** Suggestions for what funding information to report Funding sources (and Grant ID if applicable)

- All types of funding sources, including the following with specifications:
 - Internal funding (specifying institution)
 - Government(s) (specifying granting agency, level of government)
 - Inter-government (two or more government agencies such as the European Union)
 - Private-for-profit (listing companies/entities)
 - Private not-for-profit (listing organisations/philanthropies)
- Research phases for which funding was received: planning, conduct and/or reporting of the research study under consideration. When funding relates to provision of supplies, the appropriate answer is 'conduct'.
- Type of funding received including monetary support, provision of supplies, etc.
- Value of monetary support and value of other supports.
- Whether the funding provided by any of the funding sources is supported by an entity other than/external to the funding source.

Involvement (role) of funding sources

- Involvement (role) of each funder in the process of the research study, including:
 - Study planning and conduct: design and protocol drafting, study management, participant recruitment, data collection, data management, data analysis, quality control.
 - Study reporting (manuscript): preparation, review, approval, decision to submit.
 - Authorship: authors employed by the funder.

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| 2 3 4 | 1 | |
|----------------|----|--|
| 4 5 6 | 2 | As for the process of reporting funding information, we suggest that the corresponding author |
| 7 8 | 3 | plays the role of the guarantor of this information (given his/her primary responsibility of |
| 9 10 11 | 4 | communicating with both the journal and the readers) and take responsibility for: |
| 12 13 | 5 | • Collecting funding information and filling a standardised form, |
| 14 15 16 | 6 | • Sending the form to all co-authors for approval and verification of accuracy and |
| 17 18 | 7 | completeness of the information, |
| 19 20 21 | 8 | • Submitting the up-to-date form at the time of submission of the manuscript for |
| 21 22 23 | 9 | consideration for publication, |
| 24 25 | 10 | • Updating and re-submitting the form at the time of acceptance of the manuscript for final |
| 26 27 28 | 11 | publication. |
| 29 30 | 12 | |
| 31 32 33 | 13 | Appendix 6 provides a fillable PDF document for use as an instrument for standardised reporting |
| 34 35 | 14 | of funding information. |
| 36 37 38 | 15 | |
| 39 40 | 16 | DISCUSSION |
| 41 42 | 17 | Summary of findings |
| 43 44 45 | 18 | The objective of this study was to describe the characteristics of the funding statements in reports |
| 46 47 | 19 | of clinical trials. About nine in ten trial reports included a funding statement and 96% of those |
| 48 49 50 | 20 | statements indicated that funding existed. The latter statements specified the source, amount, and |
| 51 52 | 21 | role of funders in 100%, 1%, and 50% of cases respectively. The most commonly reported |
| 53 54 | 22 | sources of funding were government and private-for-profit sources. Of all funding contribution |
| 55 56 57 | 23 | statements in which the source was identified as being a not-for-profit organisation, about half |
| 58 59 60 | | 25 |

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related to not-for-profit organisations for which we found evidence of support by private-forprofit entity(ies). Only three of those statements disclosed the support by the private-for profitentities. For trials of pharmacological or surgical interventions, only a fifth reported information on the supplier of the medication or device. We identified descriptions of a total of 22 different roles for the funders. Trials most frequently reported on roles related to the design of the study, data collection, data analysis, and manuscript preparation. We also propose a guidance and instrument for standardised reporting of funding information.

9 Reporting of funding

10 The high percentage of trials that reported being funded may be explained by the fact that 11 conducting an RCT typically requires a large number of resources.[47-49] Also, we found a 12 positive association between reporting being funded and affiliation with an institution from a 13 high-income country. This may reflect better opportunities for, and higher ability of, institutions 14 from high-income countries to obtain funding.

Explicit reporting on the role of funder was associated with journal requirement for reporting on the role of funder. This might explain the relatively low percentage of trials that reported on the roles of funders given that only 31% of clinical journals require authors to state the role of funder (unpublished data from another cross-sectional survey [44]). Explicit reporting on the role of funder was positively associated with trial funding from private-for-profit sources. This may be due to the adherence of the industry to higher standards of reporting. Indeed, several studies found that industry-funded trials had higher quality scores as compared to trials funded by other sources.[24, 50-53]

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Both reporting being funded and explicit reporting on the role of funder were associated with higher journal impact factor. This is consistent with our previous findings that better reporting of authors' conflicts of interest is associated with higher journal impact factor for both systematic reviews and trials published in Core Clinical Journals.[46, 54]

We found that half of not-for-profit organisations included in funding contribution statements were supported by private-for-profit entity(ies). This is probably an underestimate due to lack of reporting of such support by authors. This also suggests that these types of relationships are prevalent. Indeed, one recent study found that 96 national health organisations accepted money from the Coca-Cola Company, PepsiCo, or both, [55] with a number of these organisations known to fund research (e.g., Juvenile Diabetes Research Foundation). This is very concerning given that the appearance of support by a not-for-profit may portray confidence in the study findings, in spite of the fact that the indirect for-profit support may have biased those findings. Indeed, while we explored whether private not-for-profit organizations were supported by private-for-profit entity(ies), this may also apply to other types of funding sources.

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18 Strengths and limitations

19 This is the first cross-sectional survey of a large and representative sample of clinical RCTs to 20 describe the characteristics of the funding statements in detail. Our proposed guidance and 21 instrument for standardised reporting of funding information may serve researchers from 22 different fields of health. Moreover, they may be used for other types of research studies and

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manuscripts and not only trials (e.g., systematic reviews). In addition, we used systematic and transparent methods for screening and data collection.

As our study focused on clinical trials, our findings may not apply similarly to other fields, for example, health policy and systems research. While we did not conduct a formal and extensive validation of the guidance (and instrument), we believe that it has both face and content validity given that we based it on a thorough review of the related literature, on the cross-sectional survey of trials, and we revised it based on feedback from journal editors and a lawyer.

10 Comparison to similar studies

We identified 22 studies on the reporting of funding information in clinical trials (see appendix 1) [5, 19-39]. While all 22 studies focused on trials published in specific clinical areas or journals, our study assessed a wide sample of clinical trials published in any of the Core Clinical Journals. None of the 22 studies looked at whether the amount of funding was reported. In fact, we found that two trials in our sample reported amount. Two out of the 22 studies assessed reporting of provision of supplies in trials published between 1987 and 1994.[34, 39] To our knowledge, our study is the first one to survey a recent sample of trials for reporting of amount of funding and information on supplies.

20 Only four out of the 22 studies assessed reporting on the roles of funders.[20, 22, 28, 36]. 21 Whereas these studies assessed this in industry-funded or partially industry-funded trials, we 22 assessed this across all types of funders. For example, we found that 44% of trials funded solely 23 by governmental sources reported on the role of funder. Example statements from those that

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reported involvement of the government as a funder include: "appointed an independent data and safety monitoring board", "had input into the study design and data interpretation" and "reviewed and approved the report".

Our previous study on clinical systematic reviews found that a third of systematic reviews did not report on funding or reported no funding in comparison to 15% of trials in this study.[46] When the included systematic reviews reported being funded, the most commonly reported sources of funding were internal funding and government (52% and 67% respectively). While only 2% of clinical systematic reviews reported funding from private-for-profit sources, we found that 40% of clinical trials reported such funding. Moreover, trials were twice more likely than systematic reviews to report on not-for-profit as their funding source (32% and 16% respectively). While half of funded trials reported on the role of the funder, a quarter of funded systematic reviews did so.

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In comparison to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)[56, 57] and the CONSORT checklist sections on funding,[10, 11] our guidance provides more detailed and specific recommendations for the reporting of funding information and includes detailed definitions and examples of types of funders. It also includes a clear classification of roles in which funders may be involved in the process of the trial. Whereas the International Committee of Medical Journal Editors (ICMJE) conflict of interest disclosure form includes a section for the reporting of "financial support", the questions and options that follow imply types of financial conflicts of interest for each individual author rather than the study's funding.[58]

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2 Implications for practice

Our proposed guidance may help with clearer and more detailed reporting of the characteristics of funding in trials. This may in turn help readers and systematic reviewers better assess the significance of the funding and how it might affect the credibility of findings.[8, 59] Specifically, we recommend that trial authors explicitly report more details on the funders, whether they are supported by for-profit organisations, the provision of drugs and equipment, [11] and on the role of funders. [20, 22, 28, 36] We suggest that authors do not to report funding information (i.e., grants received for the conduct of the study) in both the funding section and the conflict of interest section of the manuscript, but only in the former one. Also, our findings have implications for reporting statements (such as SPIRIT and CONSORT) for improving the reporting of funding information.

14 Implications for future research

Future research should further explore the issue of funding of not-for profit organisations by forprofit organisations and the role of the latter in the planning, conduct and reporting of research studies. Future research could also assess for the accuracy and completeness of reporting of trial funding and roles of funders. Moreover, it would be interesting to explore reporting of funding in primary studies of other research fields (e.g., health policy and systems), especially that roles of funders may vary from those described in clinical trials. Finally, our proposed guidance and instrument for the standardised reporting of funding information would benefit from formal and extensive validation.

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| 2 3 4 | 1 | |
| 5 6 | 2 | FIGURES |
| 7 8 9 | 3 | Figure 1: Study flow diagram |
| 10 11 | 4 | |
| 12 13 14 | 5 | SUPPLEMENTARY FILE |
| 15 16 | 6 | Appendix 1: Comparative chart including 23 related surveys of reporting of funding information |
| 17 18 10 | 7 | in trials |
| 19 20 21 | 8 | Appendix 2: Search strategy |
| 22 23 | 9 | Appendix 3: Types of funding sources |
| 24 25 26 | 10 | Appendix 4: Process followed to verify whether a private not-for-profit organisation was |
| 27 28 | 11 | supported by a private-for-profit entity |
| 29 30 | 12 | Appendix 5: Details of the multivariable logistic regression analyses |
| 31 32 33 | 13 | Appendix 6: Instrument for reporting of funding information |
| 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 4 55 56 57 58 59 | 14 | 81 |
| 60 | | 51 |

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funding information. We also thank the reviewers whose suggestions helped improve this
manuscript.

7 CONTRIBUTIONS

MBH, GG, and EAA conceived and designed the study. MBH coordinated the study throughout. EAA had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MBH, NJ, and MK screened papers for inclusion. MBH, NJ, EAA-J, DJH, EAA-J, LCL, MZH, MA-G, and SA extracted the data. MBH and EAA analysed and interpreted the data. MBH wrote the first draft of the manuscript with EAA. MBH and EAA developed the first draft of the fillable PDF document. All authors critically revised the manuscript and approved the final version. The lead author EAA affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

19 COMPETING INTERESTS

20 All authors have completed the ICMJE uniform disclosure form at
21 http://www.icmje.org/coi disclosure.pdf and declare no conflicts of interest.

23 FUNDING

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ETHICAL APPROVAL

DATA SHARING

Data available upon request.

Not required.

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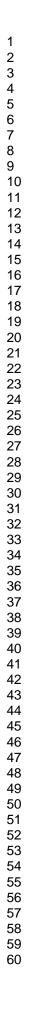
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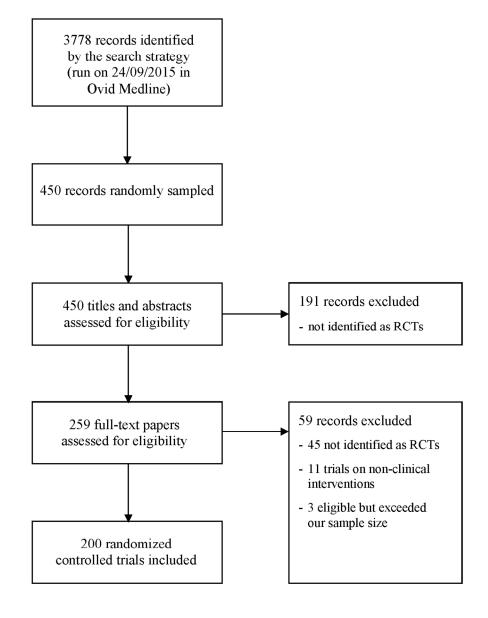
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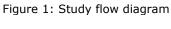
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| 8 9 10 11 | Survey | Eligibility criteria | Number of trials | Year of trial publication | Characteristics of funding statement assessed in the | for Main findings |
| 12 13 14 | | 0 | | | survey | 117. Dow nement ated to t |
| 15 16 17 18 | Als-Nielsen 2003 [19] | RCTs included in eligible meta-analyses in Cochrane reviews | 370 | 1971 - 2000 | - Source of funding | Fund to be a solution of the s |
| 19 20 21 22 | Etter 2007 [25] | RCTs on nicotine replacement therapy in Cochrane review | 90 | 1979 - 2003 | - Source of funding | 54% ved pharmaceutical company supper 46% showed no evidence of pharmaceutical company support. |
| 23 24 25 26 27 | Mugambi 2013 [5] | RCTs on infant formula supplementation of symbiotics, probiotics, or prebiotics | 67 | 1980 - 2012 | - Source of funding | 60% average funded by food industry. 24% bid not specify their source of funding. |
| 28 29 30 31 32 33 34 35 36 37 | Rochon 1994 [34] | Manufacturer-associated RCTs of NSAIDs listed in MEDLINE | 52 | 1987 - 1990 | Grant support Pharmaceutical authorship Provision of supplies Published in a pharmaceutical sponsored journal supplement | 19% geported grant support. 36.5% reported pharmaceutical authorship. 13.5% reported that manufacturer supplied drug. 31% vere published in a pharmaceutical sponsorel journal supplement. |
| 38 39 40 | Momeni 2008 [29] | Trials published in 4 major plastic surgery journals | 346 | 1990 - 2005 | - Source of funding | 20% reperted on financial support, of which 60% were supported by industrial sponsors |
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| Yaphe 2001 [39] | RCTs of drugs or food products published in 5 medical journals | 314 | 1992 - 1994 | Source of funding Pharmaceutical authorship Provision of supplies | 68% Feceived pharmaceutical industry suppert. 9 33% Feceived support as manpower (authorship or statistical help). 21% Feceived support as supply of drugs. |
| Peppercorn 2007 [31] | Breast cancer clinical trials published in 10 medical journals | 140 | 1993, 1998, 2003 | Source of funding Pharmaceutical authorship | 48% while categorised as pharmaceutical studies and studies and st |
| Bero 2007 [20] | Reports of RCTs comparing statin drugs | 192 | 1995 - 2005 | - Source of funding - Role of funder | 39% and a disclosure or no funding. 49% disclosed funding from industry, of whice disclosed the role of the spon |
| Djulbegovic 2000 [24] | RCTs for multiple myeloma | 130 | 1996 - 1998 | - Source of funding | 26% Performed funding solely or in part by commissions. |
| Clifford 2002 [23] | RCTs published in 5 high impact factor general medical journals | 100 | 1999 - 2000 | - Source of funding | 94% were funded, of which 66% were funded in whole or in part by industry. 6% ded not disclose their source of funding. |
| Bhandari 2004 [21] | RCTs published in 8 surgical and 5 medical journals | 332 | 1999 - 2001 | - Source of funding | 44% had no reported funding. 37% reported funding by industry. |
| Tuech 2005 [36] | Phase III cancer RCTs published in 12 journals | 655 | 1999 - 2003 | - Source of funding - Role of funder | 35% were industry-sponsored, of which 18% geperted the role of the study sponsor. : 21% gid got disclose funding and only 1 trial gescussed no financial support. |
| Shah 2005 [35] | Articles published in the Spine journal | 34 | 2000 - 2003 | - Source of funding | 23% were industry funded. |
| Tungaraza 2007 [37] | Original papers on psychiatric drug treatment published in two journals | 132 | 2000 - 2004 | Source of funding Pharmaceutical authorship | 85% wer industry-funded. 40% wer industry-authored studies. |

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| 1 2 | | | | | | pen-2017 copyrigt |
| 3 4 5 6 7 | Ridker 2006 [33] | Cardiovascular medicine RCTs published in 3 medical journals | 349 | 2000 - 2005 | - Source of funding | 31% were financed by not-for-profit organisations, 44% by for-profit manufactorizers, and 19% by both. 6% mated no source of funding. |
| 8 9 10 11 12 13 14 | Voineskos 2016 [38] | Surgical RCTs | 173 | 2000 - 2013 | - Source of funding | 58% did sot acknowledge a source of funding source of 14% resoluted funding from for-profit sources of 10% condiciently reported 'no funding received s |
| 15 16 17 18 19 | Montogom -ery 2004 [30] | RCTs on second generation antipsychotics for the management of schizophrenia | 86 | 2002 | - Source of funding | 84% version industry-funded. 16% avers non-industry-funded. au fring a |
| 20 21 22 23 24 25 26 | Perlis 2005 [32] | RCTs published in one of the four dermatology journals with the highest science citation impact factor scores and total citations | 179 | 2002 | - Source of funding | 57% Eggetted receiving at least some industry support. 26% Hadino information about funding. |
| 27 28 29 30 | Khan 2012 [27] | RCTs of drug therapy for rheumatoid arthritis | 103 | 2002 - 2003 2006 - 2007 | - Source of funding | 62% a d complete or partial industry fundigg. 19% a d an unspecified funding source. |
| 31 32 33 34 35 36 | Hodgson 2014 [26] | RCTs in chronic wound care | 167 | 2004 - 2011 | - Source of funding | 35% vers reported as having been commercially funded. 26% wither did not report the source of funding of the status of funding source was unclear. |
| 37 38 39 40 41 | Bridoux 2014 [22] | Surgical trials published in 10 surgery journals with impact factor >2 | 657 | 2005 - 2010 | Source of fundingRole of funder | 47% discoved funding. Of those 39% reported funding from industry or mixed funding, of which 35% reported the role of study sponsor. |
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| Lundh 2012 [28] | RCTs published in The Lancet and fully funded by a drug or device company | 69 | 2008 - 2009 | - Role of funder | Sponsor had a role in: Review and verification of information (71%) Entry of data into the study database (75%) Data study of data into the study database (75%) Coordination of results through co- authof study of database (75%) Data study of data into the study database (75%) Data study of data into the study database (75%) Coordination of results through co- authof study of database (75%) |
| Current survey | RCTs published in any of the 119 Core Clinical Journals, not restricted to a specific clinical domain | 200 | 2015 | Source of funding Amount Provision of supplies Role of funder | authols b) of approvalleview of the papel (3.4%) 89% ancluded a funding statement, of which 96% reported being funded. Of the funded trials (N=171): 160% specified the source; 48% ecceived funding from private-fog-profit sources; 18 reported the amount of funding; 21% of pharmacological/surgical trigles (N=139) reported information of supplies. 58% gported on the roles of funders (26% as involved and 24% as not involved). |

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We searched Ovid Medline (In-Process & Other Non-Indexed Citations and Ovid MEDLINE) in September 2015 using the MEDLINE (Ovid interface) search strategy for randomized controlled trials (Filter obtained from the Cochrane Handbook, under the Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision):

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| External funding: | |
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| 2. Private-for-profit | drug/device industry or private company |
| 3. Private not-for-profit with evidence of support by private-for-profit that is a health industry | foundation or organisation that receives funding from a drug industry, as stated in information provided online |
| 4. Private not-for-profit with evidence of support by private-for-profit that is not a health industry | foundation or philanthropy that was founded by billionaires or that receives funding from a private industry that is not known to produce drugs/devices, as stated in information provided online |
| 5. Private not-for-profit with no evidence of support by private-for- profit | foundation or organisation that is not known to receive funding from any governmental or private company, as stated in information provided online |
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Appendix 4: Process followed to verify whether a private not-for-profit organisation was supported by a private-for-profit entity

- 1- We searched for the official website of the funding source reported in the trial using an online search engine (e.g., Google).
- 2- We searched for relevant information in the following sections: About Us, Who we are, Supporters, Donors, Partners, Partnerships, Sponsors, Financial support, Financial statements, Finances, Financials.
- 3- If no relevant information was obtained from the official website, we searched the organisation on Wikipedia, LinkedIn profiles and Facebook.
- PS: We did not contact funding sources to obtain any additional information.

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Appendix 5: Details of the multivariable logistic regression analyses

Analysis 1

Dependent variable (categorical)

• Reporting being funded (funded vs. not funded/not reported); all trials (N=200)

Independent variables

- 1. Type of intervention (categorical, pharmacologic vs. non-pharmacologic)
- 2. Paper is the first one reporting on the findings of the trial (categorical, yes vs. no)
- 3. Conflict of interest disclosure (COI present vs. COI absent/not reported) We did not include this variable in the final model since we found it to be highly correlated with the dependent variable.
- 4. Level of risk of bias associated with allocation concealment (categorical, low risk vs. high risk/unclear)
- 5. Journal impact factor (continuous)
- 6. Number of trial sites (continuous)
- 7. Classification of the country of the institution to which the first author is affiliated (categorical, high-income vs. middle or low-income)
- 8. Journal requirement for reporting on the role of funder (categorical, yes vs. no)

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Analysis 2

Dependent variable (categorical)

• Explicit reporting of the role of funder (reported vs. not reported); trials that reported being funded (N=171)

Independent variables

In addition to the eight independent variables listed in analysis 1, we also included the following variable:

9. Funding from private-for-profit source(s) as opposed to all other types of funding sources (categorical, yes vs. no)

Results

| | Anal | ysis 1 | Analysis 2 | | |
|---|-------------------------|---------|-------------------------|------------|--|
| | Adjusted OR (95% CI) | p-value | Adjusted OR (95% CI) | p-value | |
| Type of intervention (pharmacologic as opposed to non-pharmacologic) | 0.84 (0.29 – 2.54) | 0.758 | 1.60 (0.71 – 3.63) | 0.260 | |
| Paper is the first one reporting on the findings of the trial | 1.24 (0.21 – 7.30) | 0.815 | 2.67 (0.94 - 7.58) | 0.065 | |
| Level of risk of bias associated with allocation concealment (low risk as opposed to high risk/unclear) | 0.62 (0.16 – 2.40) | 0.489 | 0.47 (0.19 – 1.16) | 0.100 | |
| Journal impact factor | 1.44 (1.09 – 1.90) | 0.011 * | 1.07 (1.04 - 1.10) | < 0.0001 * | |
| Number of trial sites | 1.25 (0.97 – 1.62) | 0.082 | 0.99 (0.99 – 1.00) | 0.299 | |
| Classification of the country of the institution to which the first author is affiliated (high-income as opposed to middle or low-income) | 0.09 (0.02 – 0.37) | 0.001 * | 2.85 (0.44 – 18.23) | 0.270 | |
| Journal requirement for reporting on the role of funder | 1.04 (0.36 – 3.03) | 0.947 | 3.76 (1.64 – 8.62) | 0.002 * | |
| Funding from private-for-profit source(s) (as opposed to all other types of funding sources) | N/A | N/A | 5.7 (2.37 – 13.85) | <0.0001 * | |

OR = odds ratio; CI = confidence interval

* p-values for statistically significant associations.

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Appendix 6: Instrument for reporting of funding information

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| 9. Please us | se the spa | ce below to p | provide any | additional info | ormation r | elated to th | e study's fun | ding sour | ces. | Downloaded from http://bm/open.bmj.com/ on June 13, 2025 a ent Superieur (ABES) . I to text and data mining, AI training, and similar technologies | |
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| Section 3 | |
| Question 4 addresses characterist | tics of the funding sources. Explanations on type of funder: 통명형 |
| | s sei |
| Internal funder: refers to a | a funder that is the author's own institution or employer. This term typically refers to an addemic institution. |
| Conceivably it could refer t | to a non-academic institution (e.g., pharmaceutical company) when it funded a study got d icted by its employees. |
| Example statements: interna | al research account, support through being the "Chair of $-$ ", intramural fund, funding be wided by |
| the academic institution, un | |
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| • External funder: refers to a | a funder different than the author's own institution or employer. Types of external fugters include: |
| - Government: refer | s to governmental bodies, agencies, organizations, or associations at the national, reginged (e.g., provincial), or |
| local (e.g., municipa | |
| Examples: National | Institutes of Health (USA), the Danish Agency for Science Technology and Innovation |
| • | al) levels. <i>Institutes of Health (USA), the Danish Agency for Science Technology and Innovation, Altraining I: refers to two or more government agencies.</i> <i>In Union.</i> |
| - | l: refers to two or more government agencies. |
| Examples: European | I: refers to two or more government agencies. If the provide state is a second state is a secon |
| - Private-for-profit | |
| | device industry, private company, insurance company, private laboratory. |
| | refers to an entity that operates to make profit. device industry, private company, insurance company, private laboratory. fit: refers to an organization that is not conducted primarily to make profit. Without Borders, Bill and Melinda Gates Foundation. |
| - Private not-for-prot | fit: refers to an organization that is not conducted primarily to make profit. |
| Examples: Doctors V | Without Borders, Bill and Melinda Gates Foundation. |
| | hn e t |
| Questions 5 and 6 address whether | the funding provided by any of the funding sources listed in Section 3 is suppored by an entity other |
| han/external to the listed source. | gies gies |
| • Example: a private not for | r-profit organization that is a partner of, or receives support (typically in the form of funding), from at least one entity |
| other than itself. | -profit organization that is a partner of, or receives support (typicany in the form of fundarity), from at least one entry |
| | idation's mission is funded through the generous gifts of individual donors and many par \vec{k} er organizations, including |
| | prporate foundations, member organizations, and both state and federal government ager disc, including the Centers |
| for Disease Control | and Provention " |
| - "The Pfizer Founda | ition is a charitable organization established by Pfizer Inc." |
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| Questions 7 and 8 address the involvement of funding sources. | | ling | |
| Funders may play a role in one or more steps of the research study. following steps: | . It is important to indicate whet | ther a funder is involved in each of | the |
| • Study planning and conduct | | eigner relate | |
| - Study design and drafting the protocol | | 6 J · | |
| - Study management | | Dow to to | |
| - Participant recruitment | | lext sul | |
| - Data collection | | and | |
| Data management (e.g., verifying accuracy, storing of Data analysis | data) | d da | |
| Data analysisQuality control (e.g., oversight, auditing) | | (AE | |
| - Quanty control (c.g., oversight, additing) | | nini BES | |
| Study reporting (manuscript) | | ing, | |
| - Preparation: relates to drafting the manuscript or med | dical writing assistance (providi | ing a medical writer Ar 💩 vering the | e writer's fees) |
| - Review of the manuscript | | lraii | |
| - Approval of the final version of the manuscript | | ijopen.b | |
| - Decision to submit the manuscript for publication (e. | e.g., to what journal) | bmj.com/ g, and si | |
| Authorship | | | |
| - This relates to at least one of the employees of the fu | under being an author on the ma | | |
| | C C | | |
| • Other roles | | June [,] | |
| These include roles that are not captured by the steps listed | above. | 13, : | |
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