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

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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

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.

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

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	Number of trials	Year of trial publication	Characteristics of funding statement assessed in the survey	Main findings
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'.
Montogomery 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 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 2012 [39]	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 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 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	89% included a funding statement, of which 96% reported being funded. 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 funders (26% as involved and 24% as not involved).

RCT: randomised controlled trial

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.

Table 2: Types 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 information, 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.

Table 3: General characteristics of the included randomised controlled trials (N=200)

	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 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 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.

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.

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 that is a health industry	14 (8%)
Private not-for-profit with evidence of support by private-for-profit that is not a health industry	15 (9%)
Private not-for-profit with no evidence of support by private-for-profit	25 (15%)
Statement included amount of funding received	2 (1%)
Paper reported to be sponsored by a source different than the source of funding/support	2 (1%)
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 (12%)
Not reported	110 (79%)

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

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%).

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

	Reported role as:		Did not report role
	Not involved N (%)	Involved 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 monitoring board	0 (0%)	1 (1%)	170 (99%)
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%)

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.

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.

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.

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 for-profit 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

Appendix 1: Search strategy

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.

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ETHICAL APPROVAL

Not required.

DATA SHARING

Data available upon request.

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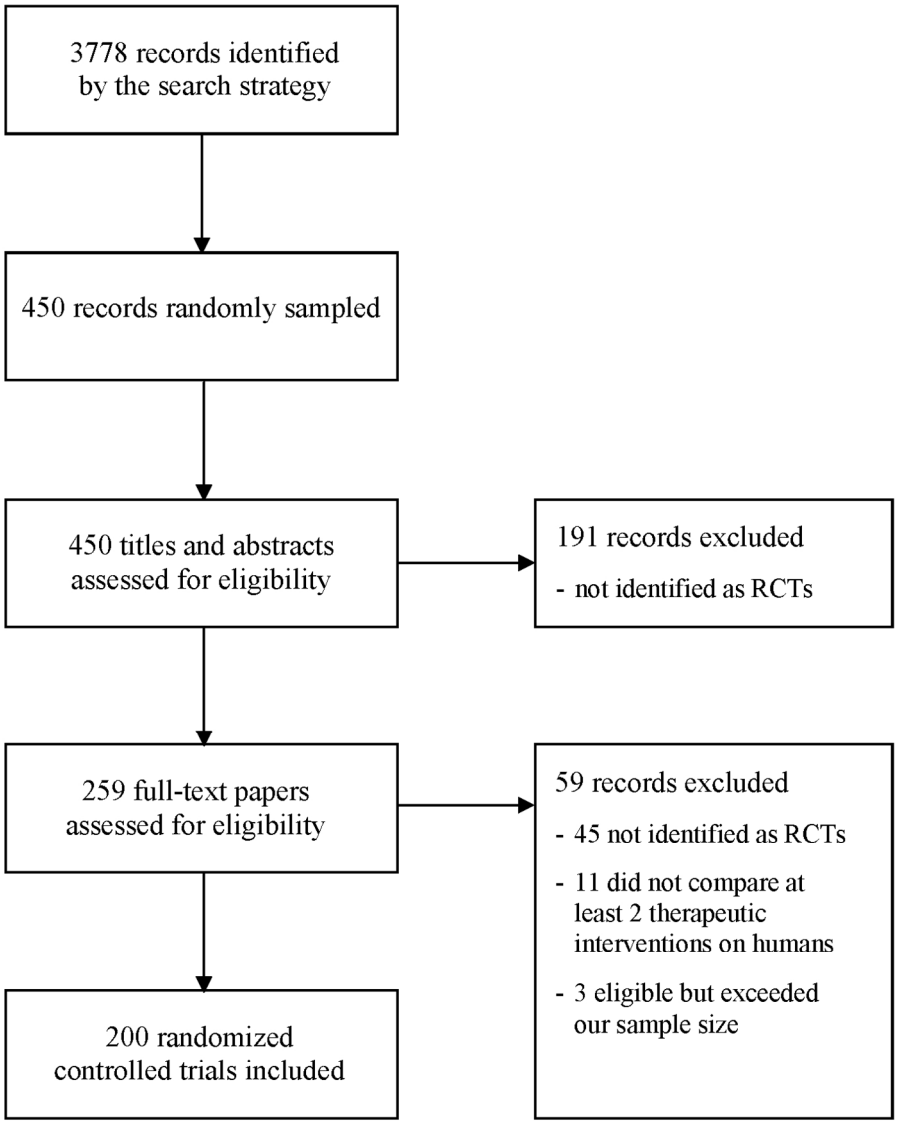

Study flow diagram

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)
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)

Results

	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

OR = odds ratio; CI = confidence interval
* p-values for statistically significant associations.

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.
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)
9. Funding from private-for-profit source(s) as opposed to all other sources of funding (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.

Appendix 3: Instrument for reporting of funding information

When filling this form, please report on all funding received to plan, conduct and/or report the research study under consideration, including the protocol, first and subsequent reports.

SECTION 1
STUDY INFORMATION

1. Name of corresponding author

   First name: Last name:

2. Manuscript title

SECTION 2
FUNDING RECEIVED

3. Did you receive any funding (monetary support, provision of supplies, assistance in manuscript writing, etc.) for the research study?

   Yes

   No

If yes, please answer the question below and complete the form. Definitions and examples are provided in section 7.

4. The funding received was used in the following steps of the research study (more than one option may apply):

   Planning

   Conduct

   Reporting

SECTION 3
FUNDING SOURCES

5. Please list the study's funding sources. For each source listed, please provide additional details and if applicable, report information on provision of supplies related to the research study.

Funding sources	Type of funder	Grant (if applicable)	Monetary support (indicate value)	Provision of supplies (if applicable)	
				e of supplies	Monetary value

SECTION 4
INVOLVEMENT OF FUNDING SOURCE

6. Please indicate the involvement of the funder(s) in the following roles by checking the respective cells.

Funding source	Study planning and conduct						Study reporting (manuscript)					Authorship
	Design	Participant recruitment	Data collection	Data management	Data analysis	Quality control	Medical writing assistance	Preparation	Review	Approval	Decision to submit	Are any of the authors employed by the funder?

7. If the funder was involved in any roles other than those listed above, please indicate them here:

SECTION 5
ADDITIONAL INFORMATION

8. Please use the space below to provide any additional information related to the study's funding sources.

SECTION 6
GUARANTOR CERTIFICATION

This person, , acts as the guarantor of the study, certifies that the information in this form is accurate and complete, and confirms the following:

The co-authors approved and verified the form for accuracy and completeness of the information.

The form was updated at the time of submission of the manuscript for consideration for publication.

The form was updated at the time of acceptance of the manuscript for final publication.

Date of last update (dd-mm-yyyy):

SECTION 7
DEFINITIONS AND EXAMPLES

TYPE OF FUNDER

- **Internal funder**: refers to a funder that is the author's own institution or employer. This term typically refers to an academic institution. Conceivably, it could refer to a non-academic institution (e.g., pharmaceutical company) when it funded a study conducted by its employees.
  Example statements: internal research account, support through being the "Chair of –", intramural fund, funding provided by the academic institution, university, or hospital.

- **External funder:** refers to a funder different than the author's own institution or employer. Types of external funders include:
  - **Government:** governmental bodies, organizations, or associations at the national, regional (e.g., provincial) or local (e.g., municipal) levels.
    Examples: National Institutes of Health (USA), the Danish Agency for Science Technology and Innovation.

  - **Inter-government:** two or more government agencies.
    Examples: European Union.

  - **Private-for-profit:** an organization whose primary goal is to make profit.
    Examples: drug or device industry, private company, insurance company, private laboratory.

  - **Not-for-profit supported by private-for-profit (a health industry):** a not-for-profit organization that is a partner of, or receives support (typically in the form of funding), from at least one private-for-profit organization known to manufacture drugs or surgical devices.
    Examples: "The Epilepsy Foundation's mission is funded through the generous gifts of individual donors and many partner organizations, including corporations and corporate foundations, member organizations, and both state and federal government agencies, including the Centers for Disease Control and Prevention.", "The Pfizer Foundation is a charitable organization established by Pfizer Inc."

  - **Not-for-profit supported by private-for-profit (not a health industry):** a not-for-profit organization that is a partner of, or receives support (typically in the form of funding), from at least one private-for-profit organization not known to manufacture drugs or surgical devices.

Examples: Bill and Melinda Gates Foundation, Ford Foundation.

- **Not-for-profit not supported by private-for-profit:** a not-for-profit organization (e.g., philanthropic foundation) that is not known to be a partner of or receive support from any private-for-profit organization.
Examples:an academic department or any philanthropic foundation not classified as any of the above.

INVOLVEMENT OF FUNDING SOURCE

Funders may play a role in one or more steps of the research study. It is important to indicate whether a funder is involved in each of the following steps:

- **Study planning and conduct**
  - Study design and drafting the protocol;
  - Study management;
  - Participant recruitment;
  - Data collection;
  - Data management (e.g., verifying accuracy, storing data);
  - Data analysis;
  - Quality control (e.g., oversight, auditing).

- **Study reporting (manuscript)**
  - Medical writing assistance: refers to providing a medical writer or covering the writer's fees;
  - Preparation: relates to drafting the manuscript;
  - Review of the manuscript;
  - Approval of the final version of the manuscript;
  - Decision to submit the manuscript for publication.

- **Authorship**
  - This relates to at least one of the employees of the funder being an author on the manuscript.

- **Other roles**
  These include roles that are not captured by the steps listed above.

BMJ Open

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

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

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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.

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

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 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.

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 non-funded 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.

Eligibility criteria

We included reports of studies described as RCTs comparing at least two therapeutic 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 non-randomised trials, trials addressing basic sciences topics and non-clinical interventions, and research letters.

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 EndNote™ X7.5 software (Thomson Reuters, Philadelphia, PA, USA). 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 (EAA) as needed. A PRISMA study flow diagram [41] presents the results of the selection process (figure 1).

Data extraction process

We developed a standardised data extraction 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.[42] After completing calibration exercises, nine authors divided into teams of two extracted data in duplicate and independently (MBH was a reviewer on each of the eight teams). Each team compared results and resolved disagreements through discussion, or with the help of a third reviewer (EAA) as needed.

Data extracted

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 randomised participants;
- Level of risk of bias associated with allocation concealment (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 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.

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).

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]

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

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

of interest and 54% disclosed presence of conflicts of interest. Almost all (178, 89%) included a funding statement.

Table 1: General characteristics of the included randomised controlled trials (N=200)

	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 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%)

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

Table 2: 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(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 that is a health industry	14 (8%)
Private not-for-profit with evidence of support by private-for-profit that is not a health industry	15 (9%)
Private not-for-profit with no evidence of support by private-for-profit	25 (15%)
Statement included amount of funding received	2 (1%)
Paper reported to be sponsored by a source different than the source of funding/support	2 (1%)
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 (12%)
Not reported	110 (79%)

$ More than one type could apply for trials reporting more than one source of funding.
* Calculated using the number of trials on pharmacological interventions and surgical/invasive procedures (N=139).

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%).

Table 3: Reporting on the roles of funders in the randomised controlled trials that reported being funded (N=171)

	Reported role as:		Did not report role
	Not involved n (%)	Involved 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 monitoring board	0 (0%)	1 (1%)	170 (99%)
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%)

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 four variables (table 4), based on data from trials reporting being funded (n=171).

Table 4: Results of the multivariable regression analysis

Dependent variables	Independent variables	Adjusted OR (95% CI)	p-value
'Reporting being funded' model (N=200)	Journal impact factor	1.43 (1.11 – 1.86)	0.006
	Affiliation with an institution from a high-income country (reference category being middle or low-income countries)	16.25 (4.03 – 65.5)	<0.0001
'Explicit reporting on the role of funder' model (N=171)	Paper is the first reporting on the findings of the trial	3.47 (1.21 – 9.96)	0.021
	Journal impact factor	1.06 (1.03 – 1.10)	<0.0001
	Journal requirement for reporting on the role of funder	3.25 (1.43 – 7.38)	0.005
	Funding from private-for-profit source(s) (reference category being all other types of funding sources)	4.9 (2.11 – 11.83)	<0.0001

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.

As for the process of reporting funding information, we suggest that the corresponding author plays the role of the guarantor of this information (given his/her primary responsibility of communicating with both the journal and the readers) 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 6 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. The latter statements specified the source, amount, and role of funders in 100%, 1%, and 50% of cases respectively. The most commonly reported sources of funding were government and private-for-profit sources. 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 entity(ies). Only three of those statements disclosed the support by the private-for profit-entities. 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

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.[47-49] 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 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]

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.

Strengths and limitations

This is the first cross-sectional 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. 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.

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.

Only four out of the 22 studies assessed reporting on the roles of funders.[20, 22, 28, 36]. 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.[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.

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]

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.

Implications for future research

Future research should further explore the issue of funding of not-for profit organisations by for-profit 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.

FIGURES

Figure 1: Study flow diagram

SUPPLEMENTARY FILE

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

Appendix 2: Search strategy

Appendix 3: Types of funding sources

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

Appendix 5: Details of the multivariable logistic regression analyses

Appendix 6: Instrument for reporting of funding information

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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.

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ETHICAL APPROVAL

Not required.

DATA SHARING

Data available upon request.

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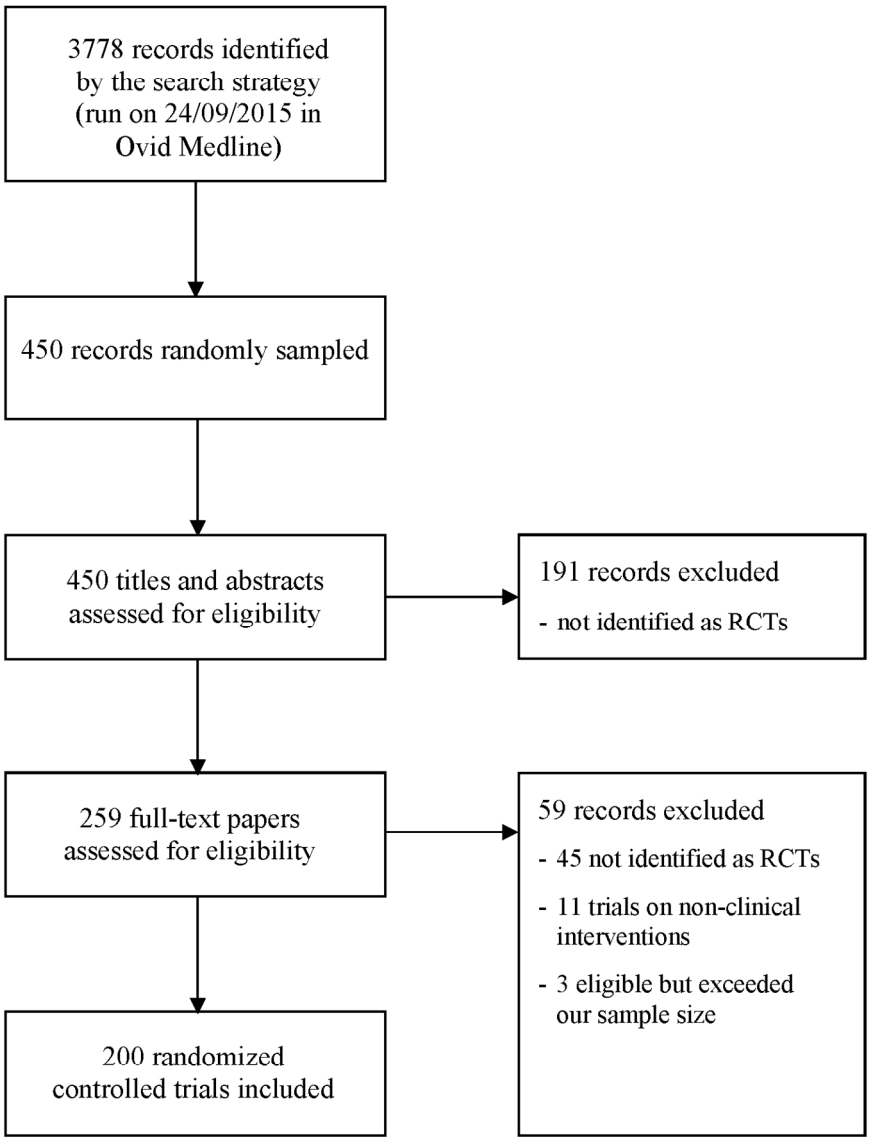

Figure 1: Study flow diagram

130x165mm (300 x 300 DPI)

APPENDICES

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

Survey	Eligibility criteria	Number of trials	Year of trial publication	Characteristics of funding statement assessed in the survey	Main findings
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 medical journals	314	1992 - 1994	- Source of funding - Pharmaceutical authorship - Provision of supplies	68% received pharmaceutical industry support. 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. 49% disclosed funding from industry, of which 7% 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 by 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.

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% omitted 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 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 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 (78%)
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	89% included a funding statement, of which 96% reported being funded. 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. - 58% reported on the roles of funders (26% as involved and 24% as not involved).

RCT: randomised controlled trial

References of studies included in Table 1
(in order of appearance in the manuscript)

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39. Yaphe, J., R. Edman, B. Knishkowy, et al., The association between funding by commercial interests and study outcome in randomized controlled drug trials. Fam Pract, 2001;18(6):565-8.

Appendix 2: 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.
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 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

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 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)

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

	Analysis 1		Analysis 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.

Appendix 6: Instrument for reporting of funding information

When filling this form, please report on all funding received to plan, conduct and/or report the research study under consideration, including the protocol, first and subsequent reports.

SECTION 1
STUDY INFORMATION

1. Name of corresponding author

   First name: Last name:

2. Manuscript title

SECTION 2
FUNDING RECEIVED

3. Did you receive any funding (monetary support, provision of supplies, assistance in manuscript writing, etc.) for the research study?

   Yes

   No

If yes, please answer the questions below and complete the form. Please see instructions provided in Section 7.

SECTION 3
FUNDING SOURCES

4. Please list the study's funding sources. For each source listed, please provide additional details and if applicable, report information on provision of supplies related to the research study.

Funding sources (include Grant ID if applicable)	Type of funder	Research phase(s) for which funding was received:			Monetary support (indicate value)	Provision of supplies (if applicable)	
		Planning	Conduct	Reporting		Type of supplies	Monetary value

5. Is the funding provided by any of the funding sources listed above supported by an entity other than/external to the listed source? (Please see examples provided in Section 7.)

Yes

No

Not known to the author

6. If Yes or No, please use the space below to provide additional details.

SECTION 4
INVOLVEMENT OF FUNDING SOURCES

7. Please indicate the involvement of the funder(s) in the following roles by checking the respective cells.

Funding source	Study planning and conduct						Study reporting (manuscript)				Authorship
	Design	Participant recruitment	Data collection	Data management	Data analysis	Quality control	Preparation	Review	Approval	Decision to submit	Are any of the authors employed by the funder?

8. If the funder was involved in any roles other than those listed above, please indicate them in the space below.

SECTION 5
ADDITIONAL INFORMATION

9. Please use the space below to provide any additional information related to the study's funding sources.

SECTION 6
GUARANTOR CERTIFICATION

This person, , acts as the guarantor of the study, certifies that the information in this form is accurate and complete, and confirms the following:

The co-authors approved and verified the form for accuracy and completeness of the information.

The form was updated at the time of submission of the manuscript for consideration for publication.

The form was updated at the time of acceptance of the manuscript for final publication.

Date of last update (dd-mm-yyyy):

SECTION 7
INSTRUCTIONS

Section 3

Question 4 addresses characteristics of the funding sources. Explanations on type of funder:

- **Internal funder**: refers to a funder that is the author's own institution or employer. This term typically refers to an academic institution. Conceivably, it could refer to a non-academic institution (e.g., pharmaceutical company) when it funded a study conducted by its employees.
  Example statements: internal research account, support through being the "Chair of –", intramural fund, funding provided by the academic institution, university, or hospital.

- **External funder:** refers to a funder different than the author's own institution or employer. Types of external funder include:
  - **Government:** refers to governmental bodies, agencies, organizations, or associations at the national, regional (e.g., provincial), or local (e.g., municipal) levels.
    Examples: National Institutes of Health (USA), the Danish Agency for Science Technology and Innovation.
  - **Inter-governmental:** refers to two or more government agencies.
    Examples: European Union.
  - **Private-for-profit:** refers to an entity that operates to make profit.
    Examples: drug or device industry, private company, insurance company, private laboratory.
  - **Private not-for-profit:** refers to an organization that is not conducted primarily to make profit.
    Examples: Doctors Without Borders, Bill and Melinda Gates Foundation.

Questions 5 and 6 address whether the funding provided by any of the funding sources listed in Section 3 is supported by an entity other than/external to the listed source.

- **Example:** a private not-for-profit organization that is a partner of, or receives support (typically in the form of funding), from at least one entity other than itself.
  - *"The Epilepsy Foundation's mission is funded through the generous gifts of individual donors and many partner organizations, including corporations and corporate foundations, member organizations, and both state and federal government agencies, including the Centers for Disease Control and Prevention."*
  - *"The Pfizer Foundation is a charitable organization established by Pfizer Inc."*

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 involved in each of the following steps:

- **Study planning and conduct**
  - Study design and drafting the protocol
  - Study management
  - Participant recruitment
  - Data collection
  - Data management (e.g., verifying accuracy, storing data)
  - Data analysis
  - Quality control (e.g., oversight, auditing)

- **Study reporting (manuscript)**
  - Preparation: relates to drafting the manuscript or medical writing assistance (providing a medical writer or covering the writer's fees)
  - Review of the manuscript
  - Approval of the final version of the manuscript
  - Decision to submit the manuscript for publication (e.g., to what journal)

- **Authorship**
  - This relates to at least one of the employees of the funder being an author on the manuscript.

- **Other roles**
  These include roles that are not captured by the steps listed above.

APPENDICES

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

Survey	Eligibility criteria	Number of trials	Year of trial publication	Characteristics of funding statement assessed in the survey	Main findings
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 medical journals	314	1992 - 1994	- Source of funding - Pharmaceutical authorship - Provision of supplies	68% received pharmaceutical industry support. 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 by 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.

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 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 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 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	89% included a funding statement, of which 96% reported being funded. 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 funders (26% as involved and 24% as not involved).

RCT: randomised controlled trial

References of studies included in Table 1
(in order of appearance in the manuscript)

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Appendix ~~1~~2: 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.
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 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

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 ~~2~~5: Details of the multi~~ple~~variable 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~~
~~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~~

~~OR = odds ratio; CI = confidence interval~~
~~* p-values for statistically significant associations.~~

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. 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)~~

~~19.~~9. Funding from private-for-profit source(s) as opposed to all other types of 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

	Analysis 1		Analysis 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.

Appendix 6: Instrument for reporting of funding information

Please see the PDF supplementary file (does not include tracked changes).

BMJ Open

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

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Keywords:	funding, role of funder, randomised controlled trial

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

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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.

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

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 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.

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 non-funded 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.

Eligibility criteria

We included reports of studies described as RCTs comparing at least two therapeutic 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 non-randomised trials, trials addressing basic sciences topics and non-clinical interventions, and research letters.

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 EndNote™ X7.5 software (Thomson Reuters, Philadelphia, PA, USA). 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 (EAA) as needed. A PRISMA study flow diagram [41] presents the results of the selection process (figure 1).

Data extraction process

We developed a standardised data extraction 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.[42] After completing calibration exercises, nine authors divided into teams of two extracted data in duplicate and independently (MBH was a reviewer on each of the eight teams). Each team compared results and resolved disagreements through discussion, or with the help of a third reviewer (EAA) as needed.

Data extracted

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,
- Number of randomised participants,

- 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

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.

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).

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]

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 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). 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 funding statement.

Table 1: General characteristics of the included randomised controlled trials (N=200)

	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%)

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

Table 2: 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(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 that is a health industry	14 (8%)
Private not-for-profit with evidence of support by private-for-profit that is not a health industry	15 (9%)
Private not-for-profit with no evidence of support by private-for-profit	25 (15%)
Statement included amount of funding received	2 (1%)
Paper reported to be sponsored by a source different than the source of funding/support	2 (1%)
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 (12%)
Not reported	110 (79%)

$ More than one type could apply for trials reporting more than one source of funding.
* Calculated using the number of trials on pharmacological interventions and surgical/invasive procedures (N=139).

The reported roles of funders

Table 3 presents the reported roles of funders in the 171 trials that reported being funded. Eighty-five 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%).

Table 3: Reporting on the roles of funders in the randomised controlled trials that reported being funded (N=171)

	Reported role as:		Did not report role
	Not involved n (%)	Involved 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 monitoring board	0 (0%)	1 (1%)	170 (99%)
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%)

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).

Table 4: Results of the multivariable regression analysis

Dependent variables	Independent variables	Adjusted OR (95% CI)	p-value
'Reporting being funded' model (N=200)	Journal impact factor	1.44 (1.09 – 1.90)	0.011
	Affiliation with an institution from a high-income country (reference category being middle or low-income countries)	0.09 (0.02 – 0.37)	0.001
'Explicit reporting on the role of funder' model (N=171)	Journal impact factor	1.07 (1.04 – 1.10)	<0.0001
	Journal requirement for reporting on the role of funder	3.76 (1.64 – 8.62)	0.002
	Funding from private-for-profit source(s) (reference category being all other types of funding sources)	5.7 (2.37 – 13.85)	<0.0001

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.

As for the process of reporting funding information, we suggest that the corresponding author plays the role of the guarantor of this information (given his/her primary responsibility of communicating with both the journal and the readers) 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 6 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. The latter statements specified the source, amount, and role of funders in 100%, 1%, and 50% of cases respectively. The most commonly reported sources of funding were government and private-for-profit sources. 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 entity(ies). Only three of those statements disclosed the support by the private-for profit-entities. 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

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.[47-49] 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 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]

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.

Strengths and limitations

This is the first cross-sectional 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. 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.

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.

Only four out of the 22 studies assessed reporting on the roles of funders.[20, 22, 28, 36]. 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.[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.

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]

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.

Implications for future research

Future research should further explore the issue of funding of not-for profit organisations by for-profit 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.

FIGURES

Figure 1: Study flow diagram

SUPPLEMENTARY FILE

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

Appendix 2: Search strategy

Appendix 3: Types of funding sources

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

Appendix 5: Details of the multivariable logistic regression analyses

Appendix 6: Instrument for reporting of funding information

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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.

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ETHICAL APPROVAL

Not required.

DATA SHARING

Data available upon request.

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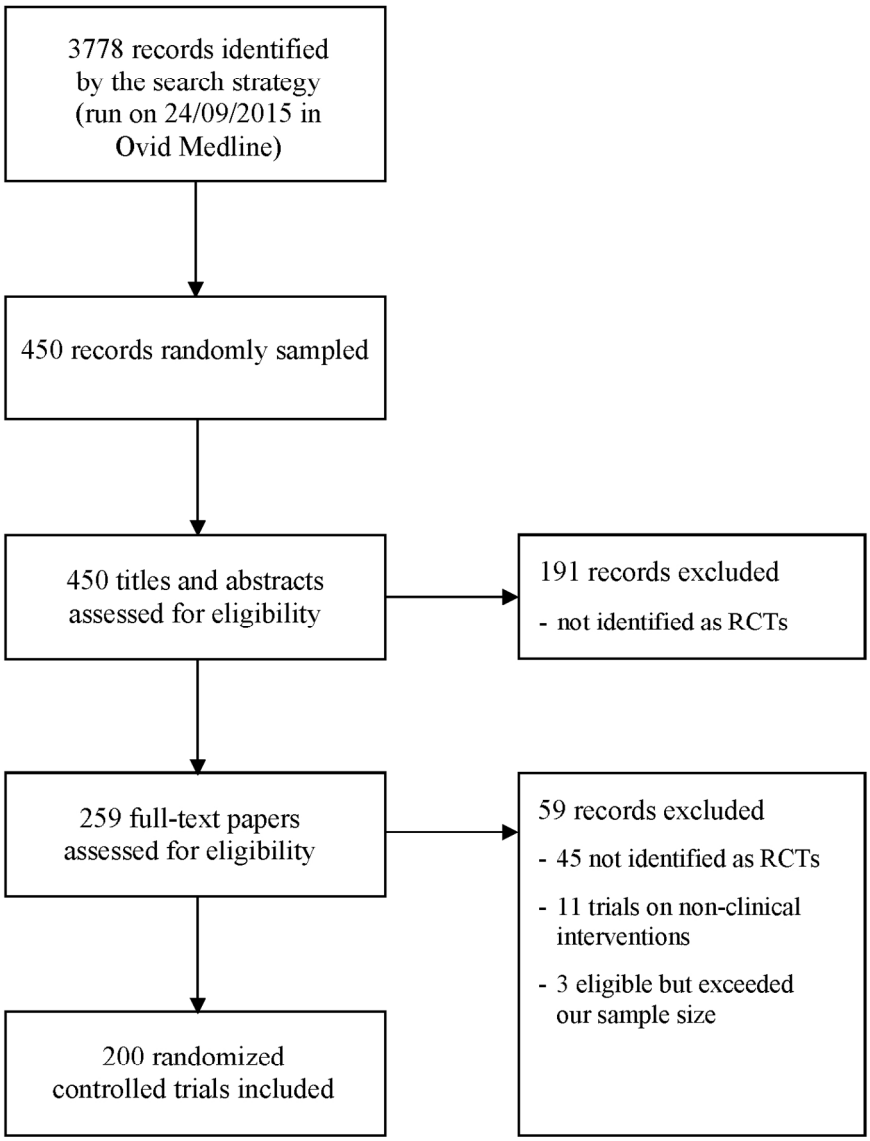

Figure 1: Study flow diagram

130x165mm (300 x 300 DPI)

APPENDICES

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

Survey	Eligibility criteria	Number of trials	Year of trial publication	Characteristics of funding statement assessed in the survey	Main findings
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.

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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. 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. 49% disclosed funding from industry, of which 7% 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 by 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.

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% mentioned 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 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 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 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	89% included a funding statement, of which 96% reported being funded. 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 funders (26% as involved and 24% as not involved).

RCT: randomised controlled trial

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(in order of appearance in the manuscript)

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39. Yaphe, J., R. Edman, B. Knishkowy, et al., The association between funding by commercial interests and study outcome in randomized controlled drug trials. Fam Pract, 2001;18(6):565-8.

Appendix 2: 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.
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 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

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 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)

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

	Analysis 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.

Appendix 6: Instrument for reporting of funding information

Please see the PDF supplementary file (does not include tracked changes).

Appendix 6: Instrument for reporting of funding information

When filling this form, please report on all funding received to plan, conduct and/or report the research study under consideration, including the protocol, first and subsequent reports.

SECTION 1
STUDY INFORMATION

1. Name of corresponding author

   First name: Last name:

2. Manuscript title

SECTION 2
FUNDING RECEIVED

3. Did you receive any funding (monetary support, provision of supplies, assistance in manuscript writing, etc.) for the research study?

   Yes

   No

If yes, please answer the questions below and complete the form. Please see instructions provided in Section 7.

SECTION 3
FUNDING SOURCES

4. Please list the study's funding sources. For each source listed, please provide additional details and if applicable, report information on provision of supplies related to the research study.

Funding sources (include Grant ID if applicable)	Type of funder	Research phase(s) for which funding was received:			Monetary support (indicate value)	Provision of supplies (if applicable)	
		Planning	Conduct	Reporting		Type of supplies	Monetary value

5. Is the funding provided by any of the funding sources listed above supported by an entity other than/external to the listed source? (Please see examples provided in Section 7.)

Yes

No

Not known to the author

6. If Yes or No, please use the space below to provide additional details.

SECTION 4
INVOLVEMENT OF FUNDING SOURCES

7. Please indicate the involvement of the funder(s) in the following roles by checking the respective cells.

Funding source	Study planning and conduct						Study reporting (manuscript)				Authorship
	Design	Participant recruitment	Data collection	Data management	Data analysis	Quality control	Preparation	Review	Approval	Decision to submit	Are any of the authors employed by the funder?

8. If the funder was involved in any roles other than those listed above, please indicate them in the space below.

SECTION 5
ADDITIONAL INFORMATION

9. Please use the space below to provide any additional information related to the study's funding sources.

SECTION 6
GUARANTOR CERTIFICATION

This person, , acts as the guarantor of the study, certifies that the information in this form is accurate and complete, and confirms the following:

The co-authors approved and verified the form for accuracy and completeness of the information.

The form was updated at the time of submission of the manuscript for consideration for publication.

The form was updated at the time of acceptance of the manuscript for final publication.

Date of last update (dd-mm-yyyy):

SECTION 7
INSTRUCTIONS

Section 3

Question 4 addresses characteristics of the funding sources. Explanations on type of funder:

- **Internal funder**: refers to a funder that is the author's own institution or employer. This term typically refers to an academic institution. Conceivably, it could refer to a non-academic institution (e.g., pharmaceutical company) when it funded a study conducted by its employees.
  Example statements: internal research account, support through being the "Chair of –", intramural fund, funding provided by the academic institution, university, or hospital.

- **External funder:** refers to a funder different than the author's own institution or employer. Types of external funder include:
  - **Government:** refers to governmental bodies, agencies, organizations, or associations at the national, regional (e.g., provincial), or local (e.g., municipal) levels.
    Examples: National Institutes of Health (USA), the Danish Agency for Science Technology and Innovation.
  - **Inter-governmental:** refers to two or more government agencies.
    Examples: European Union.
  - **Private-for-profit:** refers to an entity that operates to make profit.
    Examples: drug or device industry, private company, insurance company, private laboratory.
  - **Private not-for-profit:** refers to an organization that is not conducted primarily to make profit.
    Examples: Doctors Without Borders, Bill and Melinda Gates Foundation.

Questions 5 and 6 address whether the funding provided by any of the funding sources listed in Section 3 is supported by an entity other than/external to the listed source.

- **Example:** a private not-for-profit organization that is a partner of, or receives support (typically in the form of funding), from at least one entity other than itself.
  - *"The Epilepsy Foundation's mission is funded through the generous gifts of individual donors and many partner organizations, including corporations and corporate foundations, member organizations, and both state and federal government agencies, including the Centers for Disease Control and Prevention."*
  - *"The Pfizer Foundation is a charitable organization established by Pfizer Inc."*

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 involved in each of the following steps:

- **Study planning and conduct**
  - Study design and drafting the protocol
  - Study management
  - Participant recruitment
  - Data collection
  - Data management (e.g., verifying accuracy, storing data)
  - Data analysis
  - Quality control (e.g., oversight, auditing)

- **Study reporting (manuscript)**
  - Preparation: relates to drafting the manuscript or medical writing assistance (providing a medical writer or covering the writer's fees)
  - Review of the manuscript
  - Approval of the final version of the manuscript
  - Decision to submit the manuscript for publication (e.g., to what journal)

- **Authorship**
  - This relates to at least one of the employees of the funder being an author on the manuscript.

- **Other roles**
  These include roles that are not captured by the steps listed above.