Journal of Clinical Epidemiology 104 (2018) 95−102

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Making protocols available with the article improved evaluation of selective outcome reporting

Louis CalméjaneMS, MSc[a,b,c], Agnès DechartresMD, PhD[a,b,c,d,e,*], Viet Thi TranMD, PhD[b,c], Philippe RavaudMD, PhD[a,b,c,d,f]

[a]*Faculté de Médecine, Université Paris Descartes, Sorbonne Paris Cité, Paris, France*
[b]*Centre d'Épidémiologie Clinique, Hôpital Hôtel Dieu, Assistance Publique−Hôpitaux de Paris (AP-HP), Paris, France*
[c]*INSERM, U1153, Paris, France*
[d]*Cochrane France, Paris, France*
[e]*Sorbonne Université, INSERM U1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, Département de Biostatistique, Santé Publique, Information Médicale, Hôpital Pitié Salpêtrière, AP-HP, Paris, France*
[f]*Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, USA*

Accepted 31 August 2018; Published online 6 September 2018

Abstract

Objective: To compare primary outcomes reported in publications, protocols and registries and to evaluate the contribution of available protocols to assess selective outcome reporting (SOR) as compared with registration alone.

Study Design and Setting: We included all randomized controlled trials (RCTs) published in 2015 and 2016 in the five leading general medical journals. For each RCT, we evaluated whether the protocol was available and searched for registration. We extracted all primary outcomes reported in publications, registries, and protocols. We evaluated whether SOR was suspected (i.e., at least one discrepancy in primary outcomes), unclear, or not suspected based on comparisons of publications and (1) trial registration alone or (2) protocols in addition to registration.

Results: Selective outcome reporting was suspected for 77/274 (28.1%), unclear for 30 (10.9%), and not suspected for 167 (60.9%) when comparing publications and trial registration alone. With protocols available, the classification changed for 38 RCTs (13.9%): 11 not suspected of SOR based on registration became suspected of SOR with protocols available, and 27 with unclear assessment based on registration became suspected of SOR ($n = 7$) and not suspected of SOR ($n = 20$) with protocols available.

Conclusions: Compared to registration alone, making protocols available allows for a more precise evaluation of SOR.

Keywords: Randomized controlled trial; Selective outcome reporting; Registries; Protocols; Publishing/standards; Outcome; Bias

1. Introduction

Although randomized controlled trials (RCTs) are considered to have one of the highest levels of evidence [1], about 30% of them may be affected by undisclosed discrepancies between the initially planned outcomes and those reported in the final publications [2,3]. These discrepancies can occur in various forms, including omission (non-reporting of outcomes), commission (changing definitions or measurements of outcomes), or over-reporting (reporting unplanned outcomes) [4,5]. Such practices referred as selective outcome reporting (SOR), tend to favor positive findings [6], which could distort the body of evidence available to clinicians and patients.

To help reduce SOR, the International Committee of Medical Journal Editors required in 2005 all trials to be registered before the recruitment of the first patient on selected open-access trial registries as a condition for publication [7]. Overall, the number of trials registered increased after this statement [8], but several issues remain. Depending on the medical area, only 45% to 70% of trials are registered [9−11] and many are registered retrospectively, including after study completion [9,12]. In addition, the quality of registration has been questioned, with a lack of precision in registry entries when reporting outcomes [5].

Conflict of interest: The authors declare that they have no competing interests in relation with this study.

* Corresponding author. Département Biostatistique, Santé Publique, Information Médicale − Hôpital Pitié Salpêtrière, 47/83 Boulevard de l'Hôpital, 75013 Paris, France. Tel.: +33 (0)1 42 16 05 99; fax: +33 (0) 1 42 16 03 32.

E-mail address: agnes.dechartres@aphp.fr (A. Dechartres).

https://doi.org/10.1016/j.jclinepi.2018.08.020
0895-4356/

What is new?

Key findings

- Almost six in 10 randomized controlled trials (RCTs) published in 2015 and 2016 in the leading general medical journals have a protocol available.
- Relying on only trial registration, selective outcome reporting (SOR) was suspected for 77/274 RCTs (28.1%) and was unclear for 30 (10.9%) because of insufficient description of the primary outcomes in the registry entry.
- With protocols available, there were only three RCTs (1.1%) for which the risk of SOR could not be assessed. In addition, we suspected additional cases of SOR that were not identified with trial registration alone.

What this adds to what was known?

- This study involves an original approach to evaluate the contribution of protocols to assessing SOR as compared to trial registration alone in a large sample of recently published RCTs.

What is the implication and what should change now?

- Making protocols available along with the article may improve evaluation of SOR.

For these reasons, there is an increasing pressure to make protocols available [13,14]. Since 2015, the Institute of Medicine [15] encourages authors to share clinical trial data, including initial, modified, and final protocols, to increase transparency. In addition, some general journals have recently started to require protocols of RCTs to be made available along with the article.

Due to these recent changes in journal policies, we aimed to (1) evaluate how many reports of RCTs published in the five leading general medical journals have their protocol available; (2) for these trials, compare primary outcomes reported in trial publications, registries, and protocols; and (3) evaluate the contribution of available protocols to assess SOR as compared with trial registration alone.

2. Material and methods

2.1. Search for any requirement to make RCT protocols available in the five leading general medical journals

In February 2017, we systematically examined the ''Instructions for authors'' on the websites of the five leading general medical journals to assess whether there was any requirement regarding availability of RCT protocols and when this was implemented.

2.2. Search and selection of trials

We searched MEDLINE via PubMed for all RCTs published in 2015 and 2016 in these five journals by using the Cochrane Highly Sensitive Search Strategy for RCTs [16]. We manually screened all citations retrieved by the search and selected phase III or IV RCTs. We excluded pilot studies, phase I/II trials as well as commentaries, nonrandomized studies, duplicate reports, follow-up studies, articles reporting results of several RCTs, factorial studies, and medicoeconomic studies. Reports were selected by a single reviewer (L.C.) with the help of a senior reviewer (A.D.) for any doubtful cases.

2.3. Evaluation of availability of protocols

For each RCT, we systematically evaluated whether a protocol was available along with the article or not. We considered that a protocol was available when it was provided as a Supplementary Appendix or via a functional Internet link in the publication. All trials without a protocol were further excluded.

2.4. Search for registration

For each RCT, we systematically searched for a registration number in the publication. At this step, we excluded trials registered after the primary completion date reported in the registry because SOR cannot be assessed in this case. When the terms ''currently recruiting'' or ''ongoing'' were found in the registry, we looked for the primary completion date and included RCTs for which the primary completion date was before the publication date [11]. This was done to distinguish the truly ongoing trials from those where the authors simply forgot to update the registry.

2.5. Extraction of outcomes and general characteristics

For each RCT, we collected data from publications, protocols and registries by using three separate data extraction forms. To independently collect data from each source, we first collected all relevant information from the publications including Appendices for all RCTs, then from the protocols and finally from registries.

2.5.1. Data collected from publications

We recorded all primary and secondary outcomes reported in the methods or results sections or the abstract of the reports. If no primary outcome was clearly reported, we collected the outcomes used in sample size calculation. When sample size calculation was absent, we considered any primary objectives or analyses reported in the publication. If no primary outcomes were found at the end of this process, we excluded the article. We also systematically